Other clusters had a mixture of members from one social network and individuals who were unknown to each other directly. Among those who knew another decedent, the degree of acquaintance varied--from closest friends to those in the same school or church who knew of each other but had little direct personal contact.

Methods may be similar for most deaths within a cluster, indicating a possible underlying imitative mechanism. The clearest imitation of method is seen in a cluster of suicides by jumping from an expressway overpass in Seattle. Jumping from overpasses had previously been extremely rare in that community. Identical methods, however, may not always reflect direct imitation of another decedent in the cluster. Although all of the Wind River suicides were by hanging, cultural factors may have predominated in that choice of method. Hanging has been the method favored by most native American suicides in that community.

Time-space cluster analysis is another type of ongoing study in which epidemiological techniques are used to detect and statistically assess temporal and geographic clustering of suicides (Gould MS, Shaffer D: A study of time-space clustering of suicide. RFP #200-85-0834 (P), Centers for Disease Control, 10-85-4/87). Several epidemiologic techniques had been developed to examine the occurrence and significance of time-space clusters of diseases (28-30). These methods are being adapted to establish clustering. They can demonstrate an excess frequency of suicide in certain times and places or show a significant relationship between the time and space distances between pairs of suicides. These techniques are being applied to U.S. mortality data on suicides occurring during the two 5-year periods 1978 to 1982 and 1955 to 1959, and also to data from a consecutive series of adolescent suicides in the Greater New York Metropolitan area in 1984. The principal aims of the study are to determine whether outbreaks of suicide are real; that is, (1) whether clusters are occurring more frequently than by chance alone; (2) what proportion of suicides occur in clusters; (3) whether clustering of suicides is predominantly a phenomenon of youth; and (4) whether the proportion of cluster outbreaks is increasing. The analyses will also provide guidelines on the time and space parameters that should define a suicide cluster.

A limitation of statistical time-space cluster analyses is that they cannot indicate whether clusters are due to the influence of a model suicide, or whether the model merely happened to be the first individual who committed suicide in response to conditions that then led others to die. Field studies are better suited to identifying the mechanisms of the clusters. A goal of the time-space cluster analytic study is to identify a representative sample of clusters for future complementary field investigations.

Media Influence

Most of the research on imitative suicide has focused on the impact of suicide reporting in the mass media. This research strategy examines the possibility of contagion being transmitted indirectly through the media, in contrast to direct, person-to-person propagation. Phelps conducted a prototypic ecological study of media influences on suicide in 1911 and concluded:

> The practically universal increase in the mortality of suicides of late years, however, can be demonstrated by official figures of at least comparative accuracy; and as this increase historically parallels that in the number and percentage of sensational, crime-inciting books and newspapers, at least a semblance of positive evidence of the relations of the two is thereby afforded--though not for a moment, of course, can the open-minded student of the painfully complex problem of the increase in suicide forget the fact that the suggestion of printers' ink is but one of the many factors involved (32).

More current studies of the impact of nonfictional suicide reporting will be reviewed

(Table 3A) as well as the impact of fictional suicide stories (Table 3B).

Nonfictional Suicide Stories

Phillips and his colleagues have provided increasing evidence suggesting that imitative behavior follows media coverage of nonfictional suicides (33-37). They reported that prominent newspaper coverage of a suicide has the effect of increasing suicidal behavior within the readership area of the newspaper. The magnitude of the increase is related to the "attractiveness" of the individual whose death is being reported and the amount of publicity given to the story. This finding has been replicated with data from the United States (38) and from The Netherlands (39). In addition, Wasserman found that a significant rise in the national suicide rate occurred only after celebrity suicides were covered on the front page of the New York Times (40).

Sex- and age-specific imitative effects have been noted by Barraclough, Shepherd, and Jennings (41), who found an association between reports of suicide inquests in a local paper and the subsequent suicide of men under 45 years of age. Further support for a sex- and age-specific effect was reported by Motto (42), who found a reduction in suicides among women younger than 35 years of age during a newspaper strike in Detroit. This specific reduction was replicated in another city (43).

Although these investigations support the role of imitative behavior in suicides following nonfictional suicide stories, results of a number of studies have demonstrated no effect (44-47). Baron and Reiss reported that the findings of Bollen and Phillips indicating a significant imitative effect of nonfictional television news stories, were due to statistical artifact and the timing of media events (44). Upon reanalyzing Phillips' data, they reported that the media events had their effects only during periods when suicides were already high; the variables measuring the purported effects of the media events were actually capturing regularities in the distribution of suicides. Bollen and Phillips did report, however, an excess in suicides that could not be predicted by any day-of-the-week, month, year, or holiday effect and confirmed the excess with two analytic strategies (38).

Stack found no relationship between the monthly national suicide rate and the amount of television coverage per month on suicide stories (46). This lack of a relationship, however, may have been an artifact of the methodology used in the study. Monthly rates of suicide may not be sensitive enough to detect imitative influences, since a contagion effect of the media has been reported not to extend beyond 10 days (35,38). Methodological artifacts may also account for Littmann's not finding a relationship between suicide-related newspaper reports and the occurrence of subway suicides in Toronto. Littman reported that there was no significant excess of newspaper reports before subway suicides in both epidemic and non-epidemic years (47). There were overlaps, however, in the "before" time periods for one suicide with the "after" time periods for another suicide, making independent examination of the "before" period impossible. The examination was limited to subway suicides. An examination of all suicides might have yielded a different result.

The core independent variable in Stack's study was the number of seconds of television coverage of suicide stories included in the 6 o'clock news. There is evidence that it is not only the amount of coverage, but also the type of story that has an impact on subsequent suicides (37,40,45). Articles, reports, features, and editorials are likely to have differential effects. In another study, Stack commented on the tenor of news reporting that may offset imitative effects (45). He found no increase in U.S. suicide rates after widespread coverage of the Jonestown mass suicides. He attributed the lack of imitation to the labeling of decedents as cultists, the presentation of many deaths there as involuntary, and the horror conveyed by postmortem photos.

Differential susceptibility to the imitative effects of the media may also reflect selective coverage in even routine reports. Shepherd and Barraclough analyzed reports of suicides appearing in the Portsmouth News between 1970 and 1972. They found that longer reports were written on violent suicides than on less violent suicides and that violent suicides were more likely to stimulate multiple reports ($p<.001$). Suicides of the very young or very old were more often reported than suicides of other-aged persons. They regarded this distortion of the news as a publishing commitment to entertainment and to the belief that violence is intrinsically newsworthy (48).

Fictional Suicide Stories

Very little research has been carried out on the impact of fictional representations of suicide. In the context of an epidemiological study of childhood suicide, Shaffer implicated this mechanism as a precipitant in one of the 30 consecutive suicidal deaths he studied (49). A teenage victim was found dead with copy of Graham Greene's novel *Brighton Rock*, in which the young, central character commits suicide. There have been anecdotal reports of suicide rates increasing in response to the publication and popularity of other novels and poems. Publication of Goethe's *The Sorrows of Young Werther* in 1774 launched a fad among young men of wearing blue tailcoats and yellow waistcoats like Werther and, in many cases, imitating his suicide (50,51).

Results of recent studies that focus on the effects of media coverage of fictional suicide stories are controversial. Kessler and Stripp (52) failed to replicate Phillips' (37) finding that fictional television suicide stories on daytime television serials--or "soap operas"--triggered imitative deaths. They attributed the discrepancy to Phillips' misspecification of the dates of 8 of the 13 television suicide stories, invalidating Phillips' one attempt to examine the impact of fictional suicide stories.

Holding (53,54) examined the impact of an 11-episode weekly series that was presented by the BBC in Edinburgh to dramatize the suicide prevention work of the Samaritans. The series resulted in a significant increase in new client referrals to the Samaritans in the 4 weeks following the programs. If the series had produced a preventive effect, the rise in referrals should have been associated with a fall in completed suicides. To the contrary, suicides did not decrease during the 10-week period following the series. Moreover, this period did not show the decline that was evidenced in corresponding weeks in comparison years. These results suggest a deleterious effect of fictional suicide stories in the media.

Gould and Shaffer (55) examined the variation in youth suicide and attempted suicide before and after four fictional television films that were broadcast in the fall and winter of 1984/1985. They reported that the observed number of attempted suicides after the broadcasts was significantly greater than expected and that there was significant excess of completed suicides after three broadcasts. Their findings are consistent with an imitation mechanism.

Critique of Methods

The major limitation of the studies in which investigators examined the impact of media coverage of suicides is that all have employed aggregate data (see Tables 3A and 3B). A major constraint of such a design is that it cannot demonstrate whether the suicide victims were actually exposed to the media events. There is always the danger of an ecological fallacy, therefore, which involves making spurious individual-level inferences from aggregate relationships.

As early as 1911, Hemenway outlined a study to determine the effects of newspapers on suicides. He proposed using coroners to collect data in such a way as to avoid making conclusions from aggregate relationships. Coroners would obtain the following information:

1) Dates of prominent publication of

details of suicides, with the method selected by the unfortunates. 2) Dates of subsequent suicides with special references to the grouping of cases according to methods. 3) Direct evidence, by asking at inquests for information as to the possible relationship of the suicide being investigated as to previous cases either read about or known of (56).

As Table 3 indicates, Hemenway's proposals have not been acted upon.

Despite the limitation imposed by the use of aggregate data, the investigators in the studies taken as a whole, have employed rigorous statistics, comparison periods, and control variables. Their findings meet a number of criteria that assist judgments about the causal significance of associations. Five criteria for judging causal relationships are time sequence of variables, consistency of associations on replication, strength of association, specificity of association, and coherent explanation (57).

Results of several studies (33,34,36,39,40) established the time sequence of the variables, for instance, that the increase in mortality occurred only after the media events. The suicide stories, it was shown, did not occur during a "suicide wave," but before it.

Consistent findings in support of an imitation hypothesis were reported by the most investigators, despite their differences in method, location, and types of variables. A number of investigators examined an excess of deaths following the appearance of suicide stories (33,34,36,38,40,41,55). Others examined the decrease in deaths during the cessation of newspaper stories (42,43). Different types of control periods were employed, varying from control periods immediately before the suicide story (36), to control periods in different years (34,42), and indirect control periods used in time-series analyses (40). Both quasi-experimental designs (33) and regression analytic strategies (36) were employed. Despite the consistency in the findings, however, the possibility of confounding variables cannot be entirely ruled out.

The strength of the association is indicated by the reports that suicide stories had larger effects on suicide rates than did day of the week, month, or holidays, which are variables known to affect the suicide rate (38). Furthermore, reports of suicides by celebrities resulted in a large increase in suicides (40).

The final criterion suggested for judging a causal association is whether it is coherent or consistent with existing knowledge. Media coverage of suicides is associated with an increase in subsequent suicides. This increase in suicides relates to the amount of publicity and is restricted to the area in which the stories are publicized. This is consistent with the consensus of laboratory findings that mass media violence can elicit aggression (58). The association is also consistent with a number of mechanisms of contagion, such as imitation and familiarity with the idea of suicide. These mechanisms will be discussed in a subsequent section.

In summary, growing evidence forcefully supports the contention that imitative suicides follow media coverage of nonfictional suicides. The effect extends to both newspaper and television coverage. Some of the inconsistencies that exist among studies could have arisen as a result of significant methodological differences among them. Although there is some evidence that fictional suicide stories have an impact, little information is available and the results of available studies are contradictory.

Mechanisms of Suicide Contagion

Mechanisms underlying the phenomenon of contagion have not been studied in the context of cluster suicides. In social-learning theory, however, behavioral scientists have constructed a foundation on which many aspects of suicide contagion may build. According to this theory, most human behavior is learned through observation and modeling (59). People learn from example. Imitative learning is influenced by a number of factors, including the characteristics of the model and

the consequences or rewards associated with the observed behavior (59). Models who possess engaging qualities or who have high status are more likely to be imitated. Behaviors depicted as resulting in gains, including notoriety, are more effective in prompting imitation.

Consistent with these principles, Phillips and his colleagues have reported that the magnitude of the increase in suicide behavior after prominent newspaper coverage is related to two factors: (1) the "attractiveness" of the individual whose death is being reported, and (2) the amount of publicity given to the story. Likewise, Wasserman found that the national suicide rate rose significantly after suicides of celebrities were reported on the front page of the New York *Times* but not after less prominent suicides (40).

People cannot learn much by observation unless they attend to the modeled behavior (59). A number of factors, some involving the observers' characteristics, regulate the amount of attention to witnessed or reported behavior. Research thus far has only roughly sketched the host characteristics that may yield a greater susceptibility to imitating suicide. Sacks and Eth proposed as one such characteristic a history of similar past experiences that lead to "pathological identification" with the victim (19).

In addition to imitative effects, the occurrence of suicides in the community or in the media may produce a familiarity with, and acceptance of, the idea of suicide. Rubinstein postulated this mechanism in his study of a suicide epidemic among Micronesian adolescents. Familiarity with suicide may eliminate the "taboo" of suicide. It may also lower the threshold point at which the behavior is manifested and may introduce suicide as an acceptable alternative response or option to life stresses (20).

CONCLUSIONS

A review of (1) reports of suicide epidemics, of ongoing studies of suicide clusters, and of investigations of the news media and their relationship to suicide and (2) work in the behavioral sciences indicates four conclusions:

- Time-space clusters of suicide occur, have been reported among various age groups, and are not a new phenomenon.
- Nonfictional media coverage of suicides is associated with an increase in the observed number of suicides over the number expected. The increase may not be uniform for all age-sex groups.
- Susceptible individuals may be affected by direct or indirect exposures to suicide.
- Imitative learning is fostered if the model is held in high regard and if rewards are expected for the behavior.

Remaining questions are legion. Only substantial research will resolve them. Some of the questions for future research follow:

- What proportion of suicides occur in clusters? Are clusters more common in certain age groups, geographic locations, or times? Is the proportion of cluster outbreaks increasing?
- In comparison with other age groups, in what ways are young people exposed to and susceptible to suicide contagion?
- Which characteristics of model suicides are most likely to cause an increase in suicides?
- Which combination of host susceptibility and contagion factors are most lethal?
- What sorts of prevention and intervention efforts could most effectively avert cluster suicides?
- Does media coverage create new suicides or accelerate suicides that would have occurred anyway?

Youth suicide clusters are a particularly grievous loss of life and are potentially more preventable than single suicides. Interim recommendations are needed even though our knowledge base has sobering gaps. Five basic recommendations follow:

- News media representatives should be encouraged to avoid romanticizing suicide, emphasizing violent aspects, and making celebrities of persons who die by suicide.
- News media representatives should be invited to collaborate in studies to identify the destructive and constructive components of fictional accounts of suicide. Before a decision is made to broadcast such a story, these components should be identified and assessed, and a warning that the program might adversely affect some persons should precede any such broadcast.
- In research studies, variables should be operationally defined, comparison groups used, and individual rather than aggregate- only exposures assessed.
- Surveillance for potential suicide clusters should be established so that potential clusters could be averted and existing clusters kept from spreading. Surveillance would alert researchers to suicide clusters which might be more thoroughly investigated.
- Intervention efforts should be directed toward those who are most exposed (either directly or indirectly) to the "model" suicide and toward those who are most susceptible, for example, those whose emotional health is poor and those who strongly identify with the person who has taken his or her life.

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Descriptive Studies of Epidemic or Cluster Suicide

Reference	Data Source	Population Studied	Description/Findings	Proposed Mechanism
Anonymous, 1977 (25)	Case histories	Psychiatric inpatient suicides	—3 suicides on 1 ward occurred within 6 months and no others in 10 years in that psychiatric hospital.	—"fragmented leadership, faulty supervision, and staff demoralization and anomie may contribute to poor psychiatric care and to epidemics of suicide in psychiatric hospitals."
Ashton and Donnan, 1981 (9)	Coroner's reports and death certificates	82 suicides by self-immolation, 1978-79 in England and Wales	—Between 10/78 and 9/79, there were 82 suicides by burning compared with a yearly average of 23 between 1963 and 1978. —Most of the suicides were known to be psychiatrically ill and were predominately young men or older married women.	—Imitation, 'mediated by news coverage.'
Crawford and Willis, 1968 (10)	Psychiatric hospital records	24 inpatient suicides at Stone House Hospital, England, between 1878 and 1965 from which "similar" suicides occurring within 12 months were identified	—3 pairs of similar suicides were identified plus 1 suicide that imitated that of a patient from another psychiatric hospital whose body was found on the hospital grounds. —Each of the 4 pairs used the same method: cut throat, hanging (2 pairs), jumping. —1 pair were close friends. —2 pairs used identical locations.	—The second patients were "infected" by the success of the first. —Suicide as an effort to join a deceased friend. —Imitation.
Hankoff, 1961 (8)	Case histories	12,000 U.S. Marine Corps troops stationed in a remote, isolated place	—16 suicide attempts and 1 suicide occurred in 12 months. —7 of the attempts occurred in July and August and were knife wounds. The suicide occurred during this span.	—The suicide attempts represented infectious acting-out, the epidemic being 'an emergent event of a shared group process...' —Choice of method seemed 'more a matter of suggestion or conformity than of specific motivational significance.' —July-August attempts were 'inaugurated by an attempt which attained 'maximum' secondary gains (no hospitalization).'
Kahne, 1968 (24)	Questionnaires and interviews	Psychiatric inpatients	—An 'epidemic' of 8 suicides occurred.	—"all eight suicide cases occurred ruing a period of marked social disorganization within the hospital, a period which is most appropriately described as anomic."
Kobler and Stotland, 1964 (26)	Hospital records, interviews	Psychiatric inpatients, average census = 26	—1 patient attempted suicide 12/23/59 and 3 others committed suicide between 1/1 and 1/19/60. Another suicide occurred 6/60.	—Social expectations among hospital staff of helplessness and hopelessness were communicated to patients as an implicit or explicit expectation of suicide.
Nalin, 1973 (12)	Hospital records, and case reports	Suicides and suicide attempts by malathion poisoning in Guyana	—Malathion was introduced to Guyana between 1960-62, and malathion poisoning cases increased from 16 in 1962 to 100 in 1964. —From hospital records the malathion suicide attempt rate was 31 per 100,000 and increasing.	—"Retroflexed rage, impulsively expressed and without obvious depression" —Uncontrolled availability of malathion. —"Widespread press publicity exploiting the dramatic aspects of cases in which rejected love is the motivation for poisoning has helped to give malathion an aura of lethality." —Attempters may expect newspaper publicity of their act to affect their families.
Niemi, 1978 (15)	Questionnaires sent to police districts	Suicides in jail in Finland, 1963-1967. N = 28	—"the number of suicides committed in the lock-up within 24 and 48 hours counted from the previous suicide in the lock-up was significantly greater than expected"	—Identification and a "mental state of readiness"

Table 1.

Descriptive Studies of Epidemic or Cluster Suicide

Reference	Data Source	Population Studied	Description/Findings	Proposed Mechanism
Robbins and Conroy, 1983 (16)	Case reports of patients seen at a psychiatric hospital	Chappaqua high-school students, New York, who presented with suicide attempt or ideation	—After 2 suicides in a high school population, 5 students attempted and 1 was admitted with severe suicidal ideation within 7 weeks. The first attempter was visited ruing his hospitalization by the other 5. They comprised a peer group at school.	—"suicide attempts may cluster among groups of young people with risk factors for self-destructive behavior."
Rovinski, 1898 (11)	Interviews	"Epidemic" suicides near Odessa, Russia	—Members of a religious sect committed suicide by being buried alive. —Deaths occurred in groups on 4 occasions during a 3-month period. —N=9, 5, unknown, 5.	—The sect leader convinced followers that death from the Anti-Christians was imminent and unavoidable and that it was preferable to "die for Christ" volitionally by suicide. —Influence of the charismatic leader on "psychopathic tendencies" of the members–"the spark applied to the inflammable material."
Rubinstein, 1983 (20)	Hospital and medical records, all death certificates, police records, church records; and 250 semi-structured interviews with suicide attempters and friends and relatives of suicide victims	Micronesia (the U.S. Trust Territory of the Pacific Islands)	—Over 12 years, 25 suicides occurred in clusters of 3 or 4 in several months, then none for a year or so. —8-fold increase in suicide rates since 1960 among 15- to 24- year-old males.	—"as suicide grows more frequent in these communities, the idea itself acquires a certain familiarity if not fascination to young men, and the lethality of the act seems to be trivialized." —Prominence of role model a factor. —"suicides have acquired subcultural significance among male youth, giving use to fad-like and imitative acts." —"the significance of the act acquires an aspect of collective identification and familiarity, making it less aversive to troubled youth."
Sacks and Eth, 1981 (19)	Case histories	Psychiatric inpatients	—1 patient's suicide precipitated another's suicide attempt and suicidal preoccupation in another. —The suicide attempter used the same method as the suicide (jumping). Patient with suicidal preoccupation had made a previous attempt by this method and had visited the attempter in ICU after his fall.	—Risk is high in "those who have formed pathological identifications with the victim as the result of a history of similar past experience, especially that of a suicidal or abandoning parent." —The schizophrenic's impaired object relations and reality testing may increase "vulnerability to the partial and bizarre identifications that might have contributed to their suicidal preoccupation and behavior."
Seidan, 1967 (7)	Hospital records, police reports, coroner's reports, newspapers, interviews	Suicides on a college campus	—5 male suicides by jumping occurred on the University of California, Berkeley campus during 1 month in 1967. —Subjects had histories of chronic and severe mental disorders.	—Hypothesis of symbolic location rather than behavioral contagion. —"particular locations maybe highly valued and perhaps even necessary for the commission of suicide."
Walton, 1978 (6)	Case reports	Accidental poisonings, suicides and suicide attempts by antifreeze in England	—After a widely publicized unintentional death from antifreeze, 5 suicides and 6 attempts occurred by that method. —All of the suicides had preexisting psychiatric illness.	—"There is little doubt that the publicity attached to the first unfortunate accident resulted in five imitative suicidal deaths."
Ward and Fox, 1977 (14)	Interviews with family, neighbors, police & coroner's reports, hospital records	Native Americans in Ontario	—Eight suicides occurred within 12 months in a small rural community of 3,000.	—"The stimulus of one suicide could suggest to others a similar mode of escaping an intolerable life situation." —Contagion among vulnerable persons.

Table 1 concluded.

CHARACTERISTICS OF RECENT SUICIDE CLUSTERS

Location	Number of Suicides	Sex	Age Range	First Date of Death	Last Date of Death	Methods	Social Relation to Another in Cluster
Plano, Texas	8	7M 1F	14-18	2/23/83	5/8/84	4 Gunshot 4 Carbon monoxide	Some
Westchester and Putnam Counties, New York	5*	5M	13-19	2/4/84	3/13/84	3 Hanging 1 Gunshot 1 Carbon monoxide	None
Clear Lake, Texas	6	5M 1F	14-19	8/9/84	10/11/84	3 Gunshot 2 Hanging 1 Carbon monoxide	Some
Seattle, Washington	3	3M	20's-42	7/9/85	7/14/85	3 Jumping from expressway overpass	Unknown
Wind River, Wyoming	9†	9M	14-25	8/10/85	10/1/85	9 Hanging	Some
Omaha, Nebraska	3	2M 1F	15-18	2/3/86	2/7/86	1 Gunshot 2 Overdose	Some

* An unintentional hanging also occurred

† 4 other suicides of tribal members ages 17-34 occurred between 1/2/85 and 10/18/85. All were by hanging.

Table 2.

STUDIES EXAMINING MEDIA INFLUENCES ON SUBSEQUENT IMITATIVE SUICIDES*

A. Nonfictional Suicide Stories

Citation	Period and Population Studied	Methodology	Comparison Group/Period	Findings	Statistics	Support of Imitation
Baron, and Reiss, 1984 (44)	Daily U.S. suicides for 1972-1976 (also examined homicides for 1973-1976--only the portion pertaining to the suicides is presented here).	Employed a list of publicized suicide stories carried on network news programs, a list originally used by Bollen & Phillips (1982). A different set of publicized stories was used also (details of added stories not given). The study was designed to extend the earlier study by Bollen & Phillips. Regression analytic design. Ecological design.	Indirect control periods through the use of regression analysis.	Suicide stories only had their effects during periods when suicides were already high. Explained the discrepancy between this finding and Bollen & Phillips' earlier finding by the fact that the earlier regression model did not include a term to represent an interaction between the day of the week and holidays and suicide story. However, Bollen & Phillips did control for main effects of day, week and holidays in their regression model.	Time series regression analysis. Most coefficients of story by day variable were not significant.	No
Barraclough, Shepherd, and Jennings, 1977 (41)	Suicides and undetermined deaths in Portsmouth, England, between 3-year period--1/1/70 to 12/31/72. There were 76 deaths (54 suicides and 22 undetermined).	Newspaper reports about suicide inquests were identified in the local daily newspaper in the area (128 reports were identified). They determined the number of days that had been preceded within 2, 4, and 7 days by one or more reports to derive an "expected" distribution. They compared this to the "observed" distribution of the number of days on which a suicide occurred that had been preceded by a report. Four age/sex groups (aged 44 and younger; 45 and older) were independently tested. Ecological study--cannot determine whether suicides need the newspaper.	Observed-to-expected distribution of days preceded by a newspaper report.	Association between newspaper reports of suicide inquests and men under 45, but not for other age and sex groups. Characteristics of the suicides did not correspond to the reports.	Chi-square goodness of fit test (or binomial test, if the expected frequency was <5). 2 days before: binomial $p<.03$. 4 days before: $X^2=7.30$ $p<.01$. 7 days before: $x^2 = 5.03$ $p<.05$.	Yes. Sex- and age-specific
Blumenthal and Beroner, 1973 (43)	Period of major newspaper strike in NYC: 4/26/66 to 9/1/66 (140 days) 3/6 newspapers on strike.	The age, sex and method of each suicide during the strike period was determined and suicide rates per 100,000 were calculated. The same data were obtained for each of the preceding 3 years. Designed as replication of Motto (1970) study. Ecological study.	Period of strike was compared with identical periods in preceding 3 years. 2 later years also examined.	The overall rate during the period was significantly lower than the mean rate for the preceding 3 years. However, for women aged 15-24 and 25-34 the suicide rates during the blackout were the lowest in the 6 years studied.	Wilcoxon matched pairs signed rank test. Male and females considered separately and each age group was used to form matching pairs (3-year mean rate vs. rate during strike). Actual statistics not given.	Yes. Age- and sex-specific

Table 3.

STUDIES EXAMINING MEDIA INFLUENCES ON SUBSEQUENT IMITATIVE SUICIDES*

A. Nonfictional Suicide Stories

Citation	Period and Population Studied	Methodology	Comparison Group/Period	Findings	Statistics	Support of Imitation
Bollen and Phillips, 1981 (36)	Daily Detroit mortality statistics for 1973-1976 Motor vehicle fatalities considered covert suicides.	Compiled a list of all suicide stories appearing on the front pages of the 2 largest daily newspapers in Detroit (9 suicide stories identified). Examined relationship between publicized suicides and motor vehicle fatalities (MVF). Designed as replication of Phillips (1979) study. Quasi-experimental analysis similar to Phillips' study and regression analysis. Ecological study.	In quasi-experimental analysis the experimental period was the third day after the publicized suicide. The control period was 1 week before.	Motor vehicle fatalities increased significantly on the third day after a suicide was publicized in the newspaper. Third day corresponds to peak found in Phillips' (1979) study.	T-test for matched pairs: $t=2.77$, 8df, $p=.012$. In regression analysis, variables representing the day of week, month, year, and national holidays were included as explanatory variables. Lagged variables form 0 to 6 days were included to estimate duration of the effect. Controlling for daily, monthly, and yearly effects, increase of 1.83 (regression coefficient, $t=2.26$) in MVF 3 days after story.	Yes
Bollen and Phillips, 1983 (38)	U.S. daily mortality statistics (suicides), 1972-1976.	The Vanderbilt Television News Index was searched for all stories about specific individual suicides carried on 2 or more network news programs (presented by ABC, CBS, and NBC). Several publicized suicides identified. Examined the relationship between publicized TV suicides and subsequent suicides. Quasi-experimental design as well as regression analysis. Ecological study.	In quasi-experimental analysis the experimental period was the entire week after the publicized suicide. The control period was the week before the experimental period.	Suicides generally increased in the week after publicized suicide story. The effect did not extend beyond 10 days.	T-test for matched pairs: $t=1.725$, 6df, tailed, $p=.068$' In regression analysis controlled for day of week, month, year, holidays. Regression coefficients representing effect on the same day and 1, 6, and 7 days after were statistically significant. The suicide stories had larger effects than the other variables considered. There was no statistically significantly increment in explained variance beyond a lag of 10 days. To test for spuriousness of results, examined effects before story--no significant increase before story.	Yes

Table 3 continued.

STUDIES EXAMINING MEDIA INFLUENCES ON SUBSEQUENT IMITATIVE SUICIDES

A. Nonfictional Suicide Stories

Citation	Period and Population Studied	Methodology	Comparison Group/Period	Findings	Statistics	Support of Imitation
Littmann, 1985 (47)	Toronto subway suicides, 1968-1977. Epidemic of subway suicides in 1971 (N=96 subway suicides).	Examined the temporal relationship between subway suicides and all suicide-related reports (reports, articles, features and editorials) in Toronto Star newspaper. Ecological study.	Before and after periods (ranging from 1 to 21 days) for each subway suicide. An annual before and after average was calculated for each interval.	No significant difference between the number of suicide-related newspaper reports before and after subway suicides. However, as author reports, there were overlaps of before periods of some suicides with the after periods of other suicides.	No specifics given	No
Motto, 1967 (58)	Suicide rates in 7 cities that had complete cessation of newspaper publication during strikes (Baltimore: 48 days in 1965; New York: 109 days in 1963; Detroit: 135 days in 1963; Portland: 25 days in 1949: Seattle: 56 days in 1945; Honolulu: 63 days in 1963). Ecological study.	Compared incidence of suicide during newspaper blackout to incidence during the same months of the 5 years before the newspaper blackout. An imitation hypothesis would predict the reduction of suicides during a newspaper blackout.	Blackout period compared with same months in 5 prior years (Use of prior 5 years as comparison period introduces possible confounding of secular trends.)	No significant difference between the incidence during the blackout and the mean of the prior 5 years. However, there was a trend for the incidence to be lower during the blackout in 5 cities. In Detroit, the previous rising trend of suicide attempts appeared to be interrupted by the blackout. Attempts were examined only in this city.	Wilcoxon matched pairs signed ranks test not significant.	No (although trends in data give some support)
Motto, 1970 (42)	Period of newspaper blackout in Detroit, 11/17/67 through 8/10/68 (268 days).	The age, sex, and method of suicides during the newspaper blackout were determined and the suicide rates of age and sex specific groups were calculated. The same data were obtained for the same period of the preceding 4 years, and the year after the blackout year. Ecological study.	Blackout period compared with same period in 4 prior years and 1 subsequent year.	60% drop in incidence during blackout from women's prior mean. Specific age groups showed consistent decline in incidence during blackout with exception of 55 to 64 year group. Women aged 15 to 24 and 25 to 35 showed the most marked decline.	Wilcoxon matched pairs signed ranks test performed separately for men and women (4-yr. mean compared with blackout mean)–significant difference for women at .01 level.	Yes age- and sex-specific
Phillips, 1974 (33)	Monthly U.S. suicide statistics for 1947 to 1967.	Compiled a list of suicide stories appearing on the front page of the New York Times. The New York Daily News, Chicago Tribune, and London Daily Mirror were used to examine the effect of the amount of publicity. 35 front page suicide stories were identified; 3 pairs shared same dates. Quasi-experimental design. Ecological study.	In quasi-experimental analysis the experimental period was the month of the suicide story. The control period was the average of the same months in the prior and subsequent years. For suicide stories late in a month (after the 23rd), the experimental period was the month after the story. The 23rd was an arbitrary cutoff; however, results were consistent when other cutoffs were used.	Suicides increased after 25 front-page stories. Excess suicides occurred only after stories, not before stories. The more publicity, the large the rise in subsequent suicides. The rise is restricted to the area of publication. Bereavement, effect of prior conditions, and misclassification were ruled out as explanations.	Probability of increase after 26 of 33 front page stories is .00088 (binomial test, p=.5, n=33); rank order or suicide stories according to amount of publicity (0 to 4 days) in precise predicted order (p=.0083 [1/120]); Wilcoxon matched pairs signed rank test on rise in publicized area vs. other area significant (.005).	Yes

Table 3 continued.

STUDIES EXAMINING MEDIA INFLUENCES ON SUBSEQUENT IMITATIVE SUICIDES*

A. Nonfictional Suicide Stories

Citation	Period and Population Studied	Methodology	Comparison Group/Period	Findings	Statistics	Support of Imitation
Phillips, 1979 (34)	Daily motor vehicle fatalities in California 1966-73.	Compiled list of front-page suicide stories from the Los Angeles Times and San Francisco Chronicle. 23 front page suicides identified; 2 and 2 suicides occurred within 1 week of each other and therefore each group treated as 1 story. To examine the effect of publicity, the 5 largest papers in California were examined. Ecological study.	The experimental period was the week after the story. The control period was the same period in remaining (prior and subsequent) years of study. A regression line was fitted to the number of MVF in the control periods to estimate the expected number of deaths in the period. For the analysis of the duration of the effect, the periods varied from 2 days before to 11 days after the story.	The number of MVF increased an average of 9% in the week after each suicide story. The greatest increase occurred 3 days after story (31%). The more publicity, the greater increase in MVF. The age of the drivers was correlated to the age of the person described in the story. Single car accidents increased more than other types. Fatalities more frequent in area where story was publicized. Last, crashes after suicide stories were more lethal than crashes at other times, as indicated by time between crash and death.	Walsh test, $p = .010$ 1 tailed (used for examination of increase). Pearson correlation between amount of publicity and change in MVF = .59, $p < .005$. Ratio of death from single vehicle accidents to other types of death is .88 for experimental period and .43 for control period. The difference between the 2 ratios is significant at .0213 (hypergeometric, 1 tail). Correlation between age of publicized suicide and age of drives is .46 ($p = .02$, t-test, 1 tailed, 16df).	Yes
Stack, 1983 (45)	Monthly U.S. suicide rates for Jan. 1977-June 1980 and unemployment rates.	Two months of media coverage were set at a score of 1 to be a dummy variable.	Pre- and post-exposure time periods were compared.	There was no relationship between reporting of the Jonestown suicides and U.S. suicide rates. The greater the unemployment rate, though, the greater the suicide rate.	Cochrane-Orcutt time series techniques: beta = −.179, $F = 1.45$, $p > .05$ for Jonestown event, and beta = .327, $F = 4.83$, $p < .05$ for unemployment rate.	No
Stack, 1984 (46)	Monthly U.S. suicide statistics for 1972 through 1980.	Two indices of television of suicide events were developed. The first index represented the number of events per month on the evening news (ABC, NEC, CBS). The second index was the seconds of coverage per month. The data were taken from the Vanderbilt Television News Archives. Time series analysis to examine the relationship between TV coverage and monthly suicide rate. Additional variables in multi-variate model were monthly divorce rate, unemployment rate, and duration of employment. Ecological study.	Indirect control periods through the use of regression analysis.	Amount of television coverage was unrelated to monthly suicide rate. Duration of unemployment and springtime were related to increase in suicide rate.	Cochrane-Orcutt procedure, a form of generalized least-squares estimation (multivariate time series analysis). Standardized coefficient for index representing number of seconds of TV news coverage was −.01.	No.

Table 3 continued.

STUDIES EXAMINING MEDIA INFLUENCES ON SUBSEQUENT IMITATIVE SUICIDES*

A. Nonfictional Suicide Stories

Citation	Period and Population Studied	Methodology	Comparison Group/Period	Findings	Statistics	Support of Imitation
Wasserman, 1984 (40)	Monthly U.S. suicide rates for 1947 through 1977.	Extended Phillips' (1974) list of front page suicides in the New York Times (N=46 cases). Also indicated whether the suicides were rational celebrities. Quasi-experimental design as well as multivariate time series analysis. Used months as the unit of analysis. Included duration of unemployment as another explanatory variable, controlling for seasonal effects and wars. Ecological study.	For quasi-experimental analysis the experimental period was the month after the suicide story; the control period was the same month in prior and subsequent years. Indirect control periods time-series analysis.	There was a rise in suicides after 34 of the 46 cases. The increase was due to the celebrity suicides. There was a mean rise of 133.8 suicides after the suicides of entertainment celebrities, a rise of 98 for rational political celebrities, and a rise of 35.8 after the suicide of an international celebrity.	Probability of increase after 34 of 46 cases is .00027 (binomial test). In time series analysis, the slope coefficient representing the celebrity story was .47 ($t=3.68$, $p<.01$).	Yes

*A few studies on 'covert suicides' are included (Bollen & Phillips, 1981; Phillips, 1979). A study that examined the impact of murder-suicide stories on subsequent airplane crashes (Phillips, 1980) was not included. The findings from the 1980 study do support a theory of imitation and suggestion.

Table 3 continued.

STUDIES EXAMINING MEDIA INFLUENCES ON SUBSEQUENT IMITATIVE SUICIDES
B. Fictional Suicide Stories

Citation	Period and Population Studied	Methodology	Comparison Group/Period	Findings	Statistics	Support of Imitation
Gould and Shaffer, 1986 (53)	Adolescent suicides and attempted suicides aged 19 years and younger during the period 9/16/84 through 3/9/85 in the Greater New York Metropolitan Area.	The variation in suicide and attempted suicide before and after 4 made-for-television movies broadcast in the fall of 1984 and winter of 1985 was examined. Ecological study.	2-week periods before and after each movie were compared. In addition, observed numbers of suicides and attempts during the "after" periods were compared with expected numbers derived from the average of all weeks.	The observed number of attempted suicides following the television movies was significantly greater than expected, and a significant excess of completed suicides was found after 3 broadcasts. Referral bias, sensitization of medical examiners, or hospital personnel were unlikely to account for the increase in attempted and completed suicides.	The mean number of attempts after the broadcasts (22, sd=4.2) was significantly greater than the mean before the broadcasts (14, sd=3.6) (t=2.61, df=5, p.05). The observed proportion of attempted suicides to occur during the 4 2-week periods after the movies, 40% (n=88) was significantly greater than expected (32%, n=70) (p=.007, based on the binomial distribution). The mean number of completed suicides after 3 broadcasts (4.33, sd=.58) was significantly greater than the mean before the 3 broadcasts (1, sd=1) (t=4.99, df=4, p.01). The observed number of completed suicides (13) after the 3 broadcasts was significantly greater than the expected number (7.44) (p=.02, based on the binomial distribution).	Yes
Holding, 1974, 1975 (59,60)	Completed suicides and undetermined deaths in Edinburgh during the same 30-week period in 1968-1973.	The variation in deaths before, during, and after "The Befrienders," an 11-episode weekly series on BBC in 1972 was examined. As described in Holding (1974), the series dramatized the suicide prevention work of the Samaritans. Corresponding weeks in comparison years (1969-1971, and 1973) were examined. Ecological study.	The 4 weeks before the series broadcast date each year were used as the baselines. Numbers of referrals and suicide attempts during and after the series dates were compared with baseline numbers for each year.	Average weekly suicide attempt admissions increased by 13% during the "Befrienders" series and by 22% during the following 4 weeks. Samaritan new client referrals increased by 112% during the series and 140% in the next 4 weeks.	None	Yes

Table 3 continued.

STUDIES EXAMINING MEDIA INFLUENCES ON SUBSEQUENT IMITATIVE SUICIDES
B. Fictional Suicide Stories

Citation	Period and Population Studied	Methodology	Comparison Group/Period	Findings	Statistics	Support of Imitation
Kessler and Stripp, 1984 (52)	Same as Phillips (1982).	Designed as a replication and extension of Phillips' (1982) work. Used additional sources of soap opera summaries and found 3 additional suicide stories overlooked by Phillips. A story used in Phillips's work was deleted here because it involved only a discussion of a past suicide attempt. Most noteworthy was the use of the exact date of the story. Phillips' earlier study, by employing weekly summaries, inadvertently misspecified the dates of 8 of the 13 stories. In the present study, the corrected data were reanalyzed with a quasi-experimental analysis and a time-series regression analysis.	In quasi-experimental design, the experimental period was the 4 days including and after the story. The control period was the closest time interval preceding the story that contained the same days of the week as the experimental period and did not contain any holidays, real-life celebrity suicides, or soap-opera suicide stories. In the regression analysis, the control variables were days of the week, months of the year, and 2 celebrity deaths.	Soap-opera suicides had no significant effect on real suicides.	The mean difference (3.55) between the experimental and control periods was not significant ($t = .4$, 10df). None of the story coefficients in the time-series equations were significant. Separate time-series equations estimated for subgroups defined by sex and urban-rural location yielded no significant story effects.	No

Table 3 continued.

STUDIES EXAMINING MEDIA INFLUENCES ON SUBSEQUENT IMITATIVE SUICIDES
B. Fictional Suicide Stories

Citation	Period and Population Studied	Methodology	Comparison Group/Period	Findings	Statistics	Support of Imitation
Phillips, 1982 (37)	U.S. suicides and motor-vehicle deaths for 1977. Restricted to persons described as 'white' on their death certificates.	Compiled a list of television soap-opera episodes in which a suicide or suicide attempt occurred. The list was derived from a newspaper column, 'The Soaps,' published in the Los Angeles Times. The plot summaries identified the week in which a soap-opera suicide occurred, but not the specific day. Examined whether suicide and motor vehicle deaths increased after these episodes. 13 soap opera suicide stories were identified. Quasi-experimental design. Ecological study.	A 1-week experimental period was used; this was defined as the week, Monday-Sunday, in which the TV soap opera suicide episode occurred. The control period was 1 week before the experimental period. If an experimental period of a particular episode overlapped with a major holiday, it was deleted from the sample. If the control period overlapped with a major holiday, it was replaced by the nearest available control period that occurred before the holiday. To compensate for a possible linear trend in deaths, the control periods, which by design always preceded the experimental periods, were given an adjustment to reflect the slope of the regression line . . . fit the . . .	White suicides increased significantly on and just after the dates of soap-opera suicide stories. Single-vehicle crash deaths also increased after the suicide stories, whereas multiple-vehicle deaths did not increase. This provides additional support for the belief that single-vehicle crash deaths may be 'covert' suicides.	T-test for matched pairs = 2.449, 8df, 1 tailed test, $p < .02$. Same results for analysis that did not correct for linear trends.	Inconclusive because an inaccurate and nonexhaustive index of TV suicide stories was used. See Kessler and Stripp (1984).

Table 3 concluded.

STRESS AND LIFE EVENTS

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RECENT LIFE EVENTS AND SUICIDAL BEHAVIOR

Methodology

This paper reviews studies of suicidal behavior in youth in relation to recent and early stressful life events. By a "recent life event" we mean a change in the external social environment that can be dated approximately. A life event represents a change, in contrast to a chronic difficulty or problem, such as a bad marriage or chronic poverty. The change is external and not just one of perception: increased worry over work is not a life event unless it reflects some actual change in circumstances. One "internal event" is physical illness, which is externally verifiable and carries major implications for change of life pattern.

Adequate study of recent life events has entailed solving a number of methodological problems (1), the most prominent of which is retrospective reporting of events. The ordinary inaccuracies of recall may be magnified in suicidal patients by the effort to give meaning, in terms of life experience, to such a major occurrence as suicide, and by pessimism, quilt, and other misperceptions due to psychiatric disorder.

The technique for data collection is probably crucial. The complexities involved in eliciting information, accurately dating occurrences to the relevant period, and deciding whether the threshold and definition for a specific life event have been met, are of such magnitude as to require a systematic and probing interview, rather than a self-report checklist. Review of reliability studies (1) shows that self-report methods such as the questionnaire used by Holmes and Rahe (2) tend to give low reliabilities; interview methods, usually employing semi-structured format with considerable probing, give moderately high reliabilities. Interview methods also produce better patient-informant concordances of the order of 0.8, and relatively little retrospective fall-off of event recall as time periods extend back.

Psychiatric disorders may produce new events, such as loss of job, which are consequences rather than causes of illness. To eliminate these from study, two approaches have been adopted. One is to confine attention to time periods preceding symptomatic onset. The second is to concentrate on "independent" events (3)--those which, evaluated in terms of their specific circumstances, appear highly unlikely to have been brought about by the patient.

Alternative methods of quantifying the stress in events have included consensus scaling and a summation to total-stress scores (2), individual judgments of contextual threat (3), and categorization of events into groups depending on their qualities (1). The different methods, in practice, produce rather similar findings.

The methodology of chronic stress is less well worked out. Brown and Harris (3) have studies "difficulties"--long-standing rather than recent stresses--and have successfully used methodology parallel to that of life events. There are, however, fewer studies of reliability and validity in this area, or in the closely related area of social support as a protective factor (4). It can be particularly difficult here to be sure that the stress is external: to separate perception and reality. It can also be difficult to make sure that the stress is truly independent of the person. Personal resources influence the creation of social networks and close relationships and the finding of solutions to long term problems, so that social isolating and chronic problems may reflect personal qualities as well as external circumstances.

Additional Problems in Relation to Youth Suicidal Behavior

Some additional problems arise in studies of suicidal behavior in youth. First, the methodology of life events in children has not been as well worked out. Adult life event lists are not appropriate. Some adaptations of scaling to children's life event lists have been described (5,6,7) although they have received only limited application in studies of suicidal behavior (8,9).

Second, the retrospective detailed interviewing method that is usually employed and validated in life stress studies can only be applied to suicide attempts. For completed suicide, the principal witness is no longer available. Other sources of information may be used--interview with relatives or access to various kinds of records--but these are likely only to be reliable in relation to the most major events, namely, bereavement.

Studies are therefore predominately of attempted rather than completed suicide. The differences between these two groups are well known and it cannot be assumed that findings valid for one are valid for the other. Also, most studies are of adults over the age of 25, do not analyze by age group, and when they extend to younger ages, still tend to omit children and adolescents. The studies that do exist of the young often only look in passing at stress, and with deficient methodology.

An issue that arises in young adults is the extent to which increased numbers of life events may reflect a more generally unstable lifestyle prone to self-induced life change, and itself rooted in personality. A number of papers have hinted at this, and detailed acquaintance with some young suicide attempters does suggest a generally chaotic and impulsive life. The same issues can arise in relation to life events and other disorders. One way to tackle them is by followup studies using recovered patients as their own controls (10) to rule out the possibility that as many events might occur at any other period, irrespective of onset of disorder. Brown's methodology of independence of events (3) should control for this element but it is hard to make the judgment of independence from personality. Interpersonal arguments and separations, which are common in young suicide attempters, often reflect contributions from both sides of the relationship.

Studies of Suicide Attempts and Recent Life Events

The literature on recent life events mainly involves suicide attempts, in samples unselected by age, but usually with large representation of young adults. Studies are summarized in Table 1. (Tables appear at the end of this chapter.) Four studies have made comparisons with general population controls. In one study of adolescents aged 14 to 18, Jacobs (11) compared suicide attempters and normal controls for events over lifetime. The time periods nearer the attempt showed an excess of events, particularly in the weeks or months before the attempt, when there were more break-ups of relationship, illnesses or injuries, and pregnancies.

Among studies of adults, Paykel et al. (12) interviewed suicide attempters for life events in the six months before the attempt. Comparisons were made with matched general population controls and with matched depressives who were interviewed for the six

months prior to onset. Suicide attempters reported four times as many events as in the general population and one and a half times as many events as did depressives in the period prior to onset. There was a marked peak of events in the month before the attempt, and often in the week before. The excess over general population controls involved most types of life events.

Cochrane and Robertson (13) used a less satisfactory method, a self-report checklist, and studied only male subjects. This study did undertake separate analysis of subjects under 25. Total stress scores for the year before the attempt and the number of life events were much higher in depressives than matched general population controls, and the excess was equally apparent in the two samples: under 25 and over 40 years of age. It particularly involved unpleasant events and disrupted interpersonal relationships.

Isherwood et al. (14) also used a modified Holmes-Rahe methodology. Suicide attempters showed much higher stress scores than general population controls or a second control group of drivers involved in automobile crashes.

Several studies have made comparisons with patient control groups. Only one study examined life stress and suicidal behavior in children, and life event methodology was limited. Cohen-Sandler et al. (8) compared 20 children admitted to an inpatient psychiatric unit because of suicide attempts and threats with depressed, nonsuicidal children and with nondepressed children admitted to the same unit. Life events over the whole of the life span were ascertained from the case history charts, a method that might be vulnerable to unreliability in the original recording. Mean stress scores increased over developmental periods, particularly in the suicidal sample. In the twelve months prior to admission, the suicidal sample had experienced higher stress scores than either control group. The suicidal group had experienced more death of a grandparent, separation, divorce, remarriage and hospitalization of a parent, psychological trauma, broken homes, and peer acceptance change.

Among studies of adult suicide attempters not restricted in age, Paykel et al. (12) found that suicide attempters had experienced more events than depressive controls, particularly in the month before the attempt. This excess was confined to threatening event categories: Undesirable events, events scoring as more stressful in a scaling study, or events outside the control of the patient. Slater & Depue (15) compared depressives who made moderately serious suicide attempts with other depressives. In the year preceding the attempt, particularly between onset of depression and the attempt, there were higher rates of independent events and of exit events involving departure of someone from the immediate social field of the subject. Luscomb et al. (16) used a self-report inventory to study male suicide attempters admitted to Veterans Administration hospitals and patients with no history of suicide attempts. Using a number of events and scores for perceived stress, frequency-of-events rated high in stress, exit events, desirable events, and undesirable events, the researchers found some differences, with a particularly high rate of exit events. However, differences were confined to subjects over 35 and, most markedly, those over 50; the differences were not present in those 19 to 34 year olds.

O'Brien & Farmer (17) compared life events in the six weeks before interview of suicide attempters who had taken overdoes of medication, compared with young people visiting general practitioners for various complaints. Most life events were much more frequent in the suicide attempters. Patients were followed up at three months and a year. At three months, there was no decrease in life event rates, but at twelve months there was a decrease. This was in the only study in which subjects served as their own controls, confirming that not all the life event elevation before the attempt was due to unchanging life style.

Three studies have been limited to separa-

tions, both recent and early. Levi et al. (18) examined actual threatened disruptions of interpersonal relationships in the preceding year among suicide attempters, patients with suicidal thoughts, and nonsuicidal patients. Suicide attempters experienced more separations than the nonsuicidal group, whereas those the patients with suicidal thoughts were intermediate. In a replication study of working class subjects, Stein et al. (10 found more recent separations among suicide attempters than psychiatric controls. Greer et al. (10) found that disrupted interpersonal relationships in the last six months were more common in suicide attempters than in psychiatric or medical controls.

One study (21) using a multiple regression analysis found that life stress on the Holmes-Rahe scale related significantly to suicide intent, but a study in adolescents (22) failed to find this.

In some other relevant, uncontrolled studies, Power et al. (23) found that severe events, ascertained over a six month period, peaked in the month before a suicidal attempt, but nonsevere events did not. Suicidal intent, assessed subjectively and objectively, correlated with total life event stress, but lethality of attempt did not. Katschnig (24) found a peak of threatening events in the three weeks before the attempt.

In controlled study, but of a less recent event, Birtchnell (25) found that more psychiatric patients with a recent suicide attempt had experienced death of a parent in the preceding one to five years, than in nonsuicidal psychiatric controls.

In a controlled comparison, Paykel et al. (26) studies suicidal feelings in the general population. Subjects reporting suicidal feelings in the last year experienced more life events, particularly undesirable events.

Studies of Completed Suicide and Recent Life Events

A small number of studies have examined completed suicide, depending usually on interview of relatives. Studies are summarized in Table 2. None of the studies have specifically addressed youth suicide, and most samples have been over 24 years. Bereavement, of a parent or spouse, is an event which can usually be ascertained accurately. Bunch (27) interviewed informants concerning bereavement in the previous five years in suicides and general population controls. There was a significant excess among suicides in the last two years. The difference particularly involved deaths of mothers and spouses. Men appeared more vulnerable to loss of a mother (especially if unmarried). MacMahon and Pugh (28) used death certificates to compare timing of deaths from suicides and other causes in widows and widowers. Suicides showed a clustering in the few years following death of spouse, and particularly in the first year.

In a third study in general population, Hagnell and Rorsman (29) compared recent events among suicides from the prospective Lundby cohort study, matched nonviolent deaths, and general population controls. Seven of 20 suicides experienced stressful life events in the two weeks before death, compared with none of the people who had natural deaths. Viewed over the year before death, the suicides showed more changes of living conditions, work problems, and object losses than the normal controls, and more object losses than the people with natural deaths, for whom work was not relevant because of the nature of their terminal illness. Some of the events in the suicides appear to have been consequences of psychiatric illness, rather than independent events.

Other studies have used psychiatric patient controls. Humphrey (30) studied male suicides, homicidal offenders, and patients hospitalized with neurotic disorders but with no suicidal or homicidal histories. The study examined losses over a lifetime rather than purely recent ones. Excluding early losses, the suicides had significantly more evidence of student, occupational, marital, and parental loss than did the neurotic patients; homicides tended to be intermediate. Information on neurotic patients was obtained

from hospital charts, which might not be comparable with the psychological autopsies on the suicides.

Pokorny & Kaplan (31) interviewed relatives of psychiatric inpatients at a Veterans' Administration hospital, patients who subsequently committed suicide. Suicides were more likely to have had adverse life event between discharge and suicide than patients who, over a comparable time period, did not commit suicide particularly when scores during the hospitalization had been high on a measure of defenselessness, mainly reflecting depressive content.

Borg and Stahl (32) also compared psychiatric patients who committed suicide (in varying time periods up to two years following presentation) with matched psychiatric controls. There were no significant differences for the individual life events analyzed from case notes, and overall, the controls had experienced more events, although the suicide victims had reported more deaths.

Fernando and Storm (33) undertook a similar comparison. They found a significantly greater frequency of losses in the last year; these included divorce, separation, illness or death of a first degree relative or friend, and loss of job.

Murphy et al. (34) in an uncontrolled study also found that alcoholics who committed suicide tended to have recent loss of close interpersonal relationships. Humphrey et al. (35), examining the sequence of events in case histories of former psychiatric patients who committed suicide, identified a characteristic sequence starting with drinking problems, followed by difficulties with family, sex, friends, and work. This sequence was regarded as reflecting the lifestyle of the suicide, suggesting alcohol problems leading to gradual social deterioration.

Magnitude of Effect

It has often been pointed out that the recent life events implicated in psychiatric disorder, although stressful, usually fall short of major catastrophes. Separation, divorce, and death are no uncommon in the general population; together, they form the end of all marriages. Case control studies ignore base rates. In circumstances where the causative event is common and the disorder uncommon it is obvious that most event occurrences are not followed by disorder. Suicide attempts and suicide are rare occurrences in the general population; in children, they are even rarer. Their predictability from any kind of single causative factor is recognized to be low (36).

In studies of life events, conventional estimates of magnitude of effect depend on the time period used, since there is a consistent tendency for differences between subjects and controls to diminish as time periods are extended retrospectively further back. The effects of life events are most marked soon after the event and decay with time. This fact renders difficult comparisons with long-acting factors such as demographic risk factors or early loss. Further problems are the tendency of different studies to use different time periods, different ways of assessing event stress, and analyses that are sometimes categorical and sometimes quantitative. Findings also vary with the type of event analyzed, precluding a single summary index.

One useful epidemiological measure of magnitude (37) is the relative risk of disorder in those exposed to a causative factor and those not exposed. An approximation, the relative odds, can be used in case control studies. Applying this measure to studies of psychiatric disorder (37) suggests values of around 6.0 for the risk of depression in the six months following the more stressful classes of life event, with considerably lower values of 2.0-3.0 for schizophrenia. Values fall off considerably with extension back of the time periods.

Table 3 gives relative odds for suicidal acts, from studies using general population controls which report data in a suitable form for computation. For suicide, values range from 4.6 to 6.5, but for periods of one to two years: for suicide attempts, from 6.0 over 6 months to 10.0 over 1 month. In general, these sug-

gest effects that are higher than for depressive onset.

Overall, these effects are moderate in magnitude, suggesting an important effect but very far from an overwhelming one. A comparison is provided by acute infectious diseases where risks of disorder are high early after exposure then fall off rapidly. Using this comparison, risks are dramatically lower than for disorders such as chickenpox after exposure in those who have not acquired immunity, but comparable to tuberculosis, where there are many modifying factors (38). If effects were summated over a lifetime in suicide, they would be higher for persisting associations, such as demographic variables and, personality, than for recent life events, although in short periods the life event effect can be dominant (39).

There has been considerable study of interactions with potential modifying factors such as social support in depression (3,38), but relatively little similar study in suicidal behavior. Slater and Depue (15) found poorer social support in suicide attempters than controls, but much of this was due to prior exit events. A rich literature relates social isolation to suicidal behavior, although it is not so clear the extent to which some of this association might reflect personality and previous psychiatric illness, and the extent to which it acts specifically as a modifying factor to the consequences of recent life events.

Conclusions Regarding Recent Stressful Life Events

There are few studies of recent life events and youth suicidal behavior that use rigorous methodology. Including all studies irrespective of subject's age, findings are that life events strongly and consistently precede suicide, attempted suicide, and suicidal feelings. For suicide attempts, four studies, one of adolescents, also show stressful life events more common than in the general population; such life events are more common in attempters than in depressives, in mixed psychiatric patients, and in medical patient controls. One of the comparisons with other psychiatric patients was in children and one in young adults; another found differences only among older and not younger adults. Various stressful events are involved. One flaw in existing studies is that few have considered separately events that are independent, in the sense of not previously being caused by the psychiatric disorders which may precede suicidal behavior. The one study that did so found that effects of events and bereavement, one event involved, is almost always independent. Lifestyle effects are not ruled out, but one study did find a fall-off of events on followup, supporting a clustering at onset. It cannot be excluded that lifestyle contributes to the events even if they do cluster at onset: even if this were the case, the events nevertheless may be pathogenic in their own right. Effects are moderate in magnitude, higher than for other psychiatric disorders, although predominately short term.

Possibilities for prevention are limited by the rarity of suicidal behavior. Many life events, at least in adults, are inevitable consequences of the life cycle and interpersonal relationships, and cannot easily be prevented. However, as will be seen in descriptive studies of children and adolescents reviewed in a later section, some events may be consequences of living in very disturbed family settings and might be preventable. Otherwise, preventive efforts must focus on modifying the consequence of the event. Major events can be used to signal a period of high risk when crisis intervention may be indicated, although in adults, so far, this approach has not proved useful in modifying behavior in adult repeat suicide attempters (40).

EARLY LOSS AND SUICIDAL BEHAVIOR.

Methodology

Studies of early environment and suicidal behavior have mainly concerned loss of a parent in childhood, by death or other causes. Careful controls and matching are required (41).

Rates of childhood bereavement tend to be higher in older subjects, born in earlier decades, as death rates in young adults, who are parents of young children, have declined progressively through this century. Divorce rates, on the other hand, have risen. Death rates also tend to be higher in lower social classes and in certain areas. Higher rates of childhood bereavement will also be found in conditions associated with greater parental age. Reliable information is difficult to obtain. Finlay-Jones et al. (42) found that only parental death and marital breakup were reported reliably in an eight-month test-retest study: these made up only one-third of reported childhood separations.

Childhood bereavement effects are generally assumed to be mediated environmentally, but could indicate common genetic influences on parent and child, such as suicide in affectively disordered parents. For loss in other ways, such as marital separation and divorce, the influence of personality patterns becomes more plausible. Parental chaotic lifestyle may contribute much to early marital breakdown and even early parent death, and could well represent genetically inheritable traits manifested in the next generation both in lifestyle and in suicidal behavior. Tsuang (43) found that, among families of schizophrenic and manic depressives, risk of suicide in relatives was higher when the patient had committed suicide.

Retrospective studies of qualitative aspects of early upbringing are even more difficult, in view of the likely retrospective distortions and the limited possibilities for validation. In an elegant study, Wolkind and Coleman (44) showed that recollections of the quality of relationships between parents in childhood varied with the mood state at the time of the interview, whereas reports of separation from parents in childhood did not.

Completed Suicide

The plentiful literature on early loss and depression suggests a weak association between parental death and later depression, a stronger association with parental loss by separation, and a possible association with severity of depression (45,46). Most studies of suicidal behavior deal with suicide attempts rather than completed suicide.

In one of the few studies of completed suicide, Paffenberger et al. (47) used college records and death records of former students at Harvard and the University of Pennsylvania to examine antecedents of 381 suicides and 652 matched controls over a 17 to 51 year followup. An earlier publication (48) had used a smaller sample included in this later analysis. Maternal loss did not predict suicide, but paternal loss by death did so, with paternal loss by separation showing a trend at 10 percent significance. The effect of paternal death was a relatively small one, with a relative risk of 1.6, only reaching significance by the large sample size, but its specificity and causative importance were reinforced by an absence of any similar effects on accident deaths, another group where familial lifestyle might have been of importance. Roy (49) compared case notes of 30 chronic schizophrenics who committed suicide with 30 chronic schizophrenics who did not. The rates for loss of parent before age 17 by death or separation were closely comparable. Studying patients with recurrent affective disorder, the same author (50) found that more of those who committed suicide had early parental loss than those who did not. Studying 90 psychiatric patient suicides with mixed diagnoses, presumably including some or all of the above (51), he found only a trend at the 10 percent level for parental loss by death or separation before age 17.

Suicide Attempts

Table 4 summarizes a number of studies of suicide attempts and early loss in adults. Only two of these separately analyzed younger subjects under 30. Four studies made comparisons with general population samples. Two of these used medical patient controls. For the purposes of recent life event studies, these are best regarded as a patient control group since there is evidence

that life events may precede some medical disorders and hospitalization. For early loss, there is no similar evidence and it is reasonable to regard medical patients as a normal control group.

Greer et al. (20) compared suicide attempters, nonsuicidal psychiatric patients and medical patients and found significantly higher rates of early separation among attempters, particularly for loss of both parents and loss under the age of 4. Analysis confirms that the differences were significant separately for death and for separation or divorce. Crook and Raskin (52) compared depressed inpatients who had histories of suicide attempts, depressives without such histories, and general population controls. They reported a significant excess of loss in the suicidal group by divorce, desertion or separation, but not by death. Detailed figures were not given. Goldney (53) compared female suicide attempters aged 18 to 30 with a small sample of women attending a community health center. There was no difference for parental death but more loss by divorce and separation. Adam et al. (54) studied suicide attempters and general practice controls. Again, there was a slight but not significant difference for deaths, but there was a significant excess of loss due to divorce and separation. Overall, all four studies confirm that parental divorce or separation is a risk factor for suicide attempts in adults but, with one exception, leave doubtful the impact of parental death.

Other studies have made comparisons with psychiatric controls. Many have not distinguished the type of loss. Farberow (55) reported no difference overall in the incidence of separation in small samples of suicide attempters and nonsuicidal patients but more loss before the age of 6. Moss and Hamilton (56) reported separation in 60 percent of seriously suicidal patients as opposed to 15 percent in other patients, both those who were potentially suicidal and nonsuicidal. Walter (57) studies early loss in patients with suicidal threats or attempts, and in nonsuicidal depressed patients. Early loss was reported in 77 percent of the former and 20 percent of the latter, a remarkably high difference. Bruhn (58) reported more loss in suicidal patients, than in nonsuicidal outpatients or inpatients.

Greer (59) studied patients with neurotic and sociopathic disorder. These with a history of a suicide attempt had more evidence of parental loss for at least 12 months before the age of 18; they had experienced such loss particularly before the age of 55 and more commonly were deprived of both parents. The analyses were significant both in patients under 30 and 30 & over. Reanalyzing Greer's data to examine the nature of loss, loss by death just failed to reach significant (23.5% attempters, 24.3% controls, $p = .06$), whereas loss by divorce or separation was significant (17.3% vs 8.3% $p < .05$). Gay and Tonge (60) found significantly more separations before the age of 15 in new consecutive referrals to a psychiatric department with a history of a suicide attempt than in those without it.

Hill (61) examined case notes of depressed patients, comparing those who had made a suicide attempt and those who had not, for early parental deaths. Overall rates were not much different in the two groups but there was some excess of deaths in certain subgroups: patients of both sexes who had lost their fathers when they were aged 10 to 14 and women who had lost their fathers when they were aged 15 to 19.

Birtchnell (25) studies psychiatric patients with a history of attempted suicide. Pooling data about all parental deaths and illegitimacy, he found more such events had occurred in suicide attempters. This was mainly due to parental deaths than occurred when the patients were age 10 to 19, although this difference failed to reach significance. In a later, similar study (62), he found no differences for loss at any age in childhood or adolescence.

Levi et al. (18) studies the effect of parental separation of six months, comparing psychiatric patients who had made a recent

suicide attempt, who had had suicidal feelings, or who were nonsuicidal. The first group were significantly more likely to have experienced a separation than the third, with the second group intermediate. The differences were particularly distinct when the separation occurred before the age of 7. Stein et al. (19) replicated this study in working class attempters, analyzed separately by sex and race. There were significant differences for loss up to the age of 7 for all four groups, and for loss up to the age of 17 for all except black males, for whom the differences were suggestive and the sample small.

Both these studies also examined separations in the last year and have been included in Table 2. Both sought to examine whether there was a particular aggregation of patients with the combination of early and recent loss, suggesting that early loss acted to sensitize the patient to recent loss. Brown and Harris (3) have presented evidence that this is the case for depression in women, although not all the evidence is consistent. Interactions in these two studies were tested by partitioning the total chi square; in neither study were they significant, although inspection of frequencies does suggest some interaction in the predicated direction. Greer et al. (20) used a different mode of analysis and found both suicide attempters and nonsuicidal psychiatric patients tended to show this pattern but medical controls did not, which would be consistent with an effect in various psychiatric disorders. Some confirmation of an effect was found in an uncontrolled study (63) in which suicide attempters were interviewed about early separation and recent interpersonal loss. There was an association between early and recent loss for females, but not males.

Pooling these comparisons with psychiatric controls, four studies have found more early parental death in adult suicide attempters than in psychiatric controls, while two have failed to find this association. Three studies have found a difference for parental separation or divorce and none have failed to. Among studies not distinguishing cause of separations, and usually including temporary separation, all seven have shown an excess in suicide attempters. There is a clear and strong association with loss by other means and a weaker, but probable, association with loss by death.

Suicidal Feelings

Some additional studies have been made of suicidal feelings. Adam et al. (64) found in students attending a student mental health service that suicidal ideation was associated with loss of a parent by death and divorce or separation. Ross et al. (65) studied a mixed sample of students, medical patients, and state employees, and found that those with suicidal feelings more often reported their parents had separated. Goldberg (66) in an epidemiological community study of 18 to 24 year olds found a significant association with loss of mother before the subjects reached age 16.

Retrospective study of qualitative childhood environment is very liable to selective falsification. Ross et al. (65) found that those with suicidal feelings reported parents who favored siblings, were unstimulating, guilt-engendering, rejecting, and unaffectionate, abusing, and punitive. Goldney (53) found that young women attempting suicide were more likely than normal controls to report parental quarrelling, frequent disagreements with their parents, financial problems at home, poor childhood physical health, and various negative parental characteristics. These findings may say something important regarding subjects' perceptions rather than their real environments.

Studies in Children and Adolescents

Few studies of children and adolescents comparing early loss in suicide attempters and control groups have used adequate samples and methods. In the study already shown for recent life events in Table 1, Cohen-Sandler et al. (8) compared children aged 5 to 14, admitted after making suicidal acts of threats with admitted children who were depressed

but not suicidal, or not depressed. Data were obtained from case histories. When compared with the two other groups, the suicidal children showed, during infancy and preschool years, a higher incidence of separation from parents; during early childhood, more parental divorce; and, during late childhood, more separation and divorce of parents.

However, Jacobs (11) found only small differences between adolescent suicide attempters and general population controls in the incidence of separation or divorce of parents during childhood, with considerable differences for more recent break up.

Stanley and Barter (67), comparing suicidal and nonsuicidal hospitalized adolescents, found that parental loss through separations and divorce occurred in both groups, although more common before age 12 in suicide attempters.

Conclusions Regarding Early Loss

There are few adequately controlled studies of youth suicidal behavior, with no systematic study of completed suicide in the group under 25. The very few studies in adult groups do suggest that early loss characterizes suicides, when they are compared with psychiatric controls.

Regarding attempted suicide, one study of children does show a considerable increase of separation from and between parents, although methodology was not ideal, and other studies provide less support. Studies of adult suicide attempters show higher rates of early loss by separation and divorce than the general population in all studies, but increased parental death in only one of four.

Comparisons between adult suicide attempters and psychiatric controls consistently show more loss in the former when the study examines separation, divorce or loss not distinguished by nature, although in some studies, the differences are weak and selective to certain groups. Studies of parental death also tend to show an excess, but to a weaker degree and with some negative studies. Studies that specify the child's age at time of loss and sex of parent or patient do not report consistent findings.

More controlled studies of children and adolescents are needed. Stronger effects might have been expected if events decay over time; early childhood events are not far in the past for the child, as they are for the adult. Parental loss is also clearly an event of major salience in general terms for the child.

Effects are moderate in magnitude. In adult comparisons with the general population where relative odds are computable from the data given, the figures are: completed suicide and parental divorce or separation, 1.6 (47); attempted suicide and parental death 2.5 (20); attempted suicide and parental divorce or separation, 3.9 (20); 3.8 (54). Although lower than relative odds obtained for recent life events computed over six months, they are impressive for effects acting over prolonged times.

Overall, there is an association between early loss and suicide attempts, more marked than for psychiatric disorder in general and more marked for early loss by separation or divorce than by death. The association with death could be due to parental suicide and genetic transmission of suicidal behavior, since parental suicide is not usually excluded from parental death, but this is unlikely to be of sufficient magnitude to account for the differences. A more plausible explanation might be in an associated risk-taking lifestyle, but there is a prima facie case for regarding the death itself as pathogenic.

Loss for reasons other than death, is likely if permanent, to be due to breakup of parents' marriage. Here, conclusions can be less clear. The effect is larger and more consistent than for early parental death. This might reflect familial lifestyle towards acting-out, whether genetically or environmentally based, rather than causation. However, marital strife that precedes breakup and the subsequent uncertainties of having two separated parents may be more persistently harmful than the major loss itself, even by death.

OTHER STUDIES OF SUICIDAL BEHAVIOR IN YOUTH

The studies reported so far have been predominately of adults, reflecting the paucity of good controlled studies in young adults, adolescents, and children. Studies that lack control groups are unsatisfactory in life event collection or other methodological aspects can supplement these. A selection of studies is reviewed rather than a comprehensive survey.

One recent study is reassuring. Rich et al. (68) (in press) compared 133 completed suicides aged 15 to 29, with 150 aged 30 and over. There was no difference in the number of stresses at the time of death, although the older group had more illnesses and the younger group had experienced more unemployment and legal problems, with more separations regarded as suicide precipitants when present. The presence and salience of stresses is likely to be related to the life cycle. Even in this study only 31 of the suicides were under 25..

There have been many uncontrolled descriptive studies, mostly in adolescents rather than younger children. Shaffer (69) made a detailed study of 31 completed suicides aged under 15. Common precipitants were disciplinary crises, fights with peers and disputes with parents or with friends of the opposite sex, bereavements. Only in 10 percent were there no precipitants. Many suicides took place during a period of absence from school. Most children were living with one or both parents and early loss was not common. Amir (70) studied Israeli suicides aged 10 to 18. Common motives recorded were quarrels with parents, with family members and others. In only 3 percent were motives recorded as unknown. Seventy-six percent came from intact families.

Studies of suicide attempters are plentiful. Toolan (71) reviewed 102 admissions to Bellevue Hospital under age 18 but mostly over age 12. There was a high incidence of broken homes; only 32 were living with both parents, with paternal absence common. Jacobziner (72) reported on 597 suicide attempts in subjects aged 12 to 20 in New York City. There was a high incidence of family disorganization. In 21 percent of the cases, the parents were not living together. The author felt that most attempts were sudden, precipitous reactions to stressful situations.

Barter, et al. (73) studied case notes of 45 suicide attempters under 21. Twenty-three had lost one of both natural parents, and of 21 cases where natural parents were living together, 11 had marital problems. School performance was almost uniformly poor. Fifteen of the attempts grew out of an argument with parents and 14 were associated with a break-up of a relationship. Only in 9 cases did the case notes not indicate a precipitant cause.

Rohn et al. (74) studied 65 adolescents who attempted suicide. Fifty-nine percent came from one-parent families, with prolonged absence of a parent in 11 percent more; 25 percent were not living with either parent at the time of the attempt. Seventy-five percent had very poor school records. Tischler et al. (75) studying 108 adolescent suicide attempters, found that most frequently cited precipitants were family problems (52%), problems with the opposite sex (30%) and school problems (30%). Almost 50 percent reported that at least one of their parents had been divorced. Only 49 percent were living at home with both parents at the time of the event.

These studies were American. Similar findings have been obtained in Britain. White (76) studied 50 adolescents admitted to a general hospital following overdose. Seventy percent were experiencing difficulties with important persons in their environment, 8 percent academic worries, 6 percent concern regarding physical illness. In 10 percent no cause was known to the patient. Fifty percent had undergone separation from parents before the age of 15.

Hawton and colleagues (77,78) studies 50 adolescent overdosers. Family backgrounds were disturbed, 36 percent living with a single

parent and 12 percent with neither parent, higher than national figures. The common problems identified at the time of the overdoses were arguments with parents, problems with school or work, including unemployment and problems with boy or girl friends. Eleven percent had problems with physical health.

Seiden (79) reviewed the literature on the special case of university student stress and suicidal behavior. Most studies find students to have higher suicide rates than their nonacademic peers. The degree to which this is related to academic stress or other self-selection factors is not clear.

Otto (80), in a study of suicidal attempts in children and adolescents related to school problems, concluded that they were of relatively low importance. However, recent suicides in school children in Japan reported in the popular press suggest that findings may be different in a culture in which school children are under considerable academic pressure.

Comparisons with psychiatric controls tend to suggest that these factors are only weakly specific to suicidal behavior, and characterize a variety of disturbed adolescents. Mattson et al. (81) studied 75 suicidal children and adolescents referred as emergencies to a child psychiatry clinic. Only about half came from intact families, 27 having experienced parental divorce or separation, 6 loss of one parent, 8 loss of both. However, this was not different from other children referred to the clinic. The common triggering situations were conflicts with parents and loss of heterosexual love objects, with school problems, sexual conflicts, and pregnancy in a smaller proportion. In the nonsuicidal children these were less common, except for conflict with parents, whereas physical injury and exacerbations in chronic physical illness were more common.

Pfeffer et al. (82) studies 42 children with suicidal ideas, threats or attempts and 16 who were nonsuicidal. There were no differences between the two groups in the type of recent stresses, which were most commonly preoccupations about school failure, disturbed friendships, fears of parental punishment, and school and family crises. Nor were there significant differences in family situations, with high incidences of parental separation, parental absence and abuse home atmospheres in both groups. Comparing delinquent adolescents with and without a previous history of suicide attempts (Miller et al.) (83), found no difference in the incidence of absent parents. However, Garfinkel et al. (84), comparing case record information on 505 suicidal children and adolescents presenting at an emergency room and 505 nonsuicidal cases, found the attempters to show significantly more unemployed fathers, employed mothers, and parents absent form the home.

An English study (85) compared children admitted to a general hospital after overdoses with matched psychiatric outpatient referrals. The suicide attempters showed more family disturbances, with more evidence of poor relationship between child and father or mother, lack of warmth, and discord, but no greater evidence of other stresses such as poor living conditions, migration, stress within the family, stress at school, or other extra familial stress.

Overall, these studies uniformly confirm high rates of early loss, broken homes and precipitant stress in adolescent suicide attempters, but suggest lower rates of broken homes for completed suicides. Stresses particularly center around family problems, break or threat of a break in relationships, and school problems. Physical illness is uncommon as a stressor. The stresses are those which might be expected to loom importantly at this stage of the life cycle.

Controlled comparisons with other psychiatrically disturbed adolescents show similar rates of recent stress and fairly similar rates of family breakdown and early loss, indicating that these phenomena are not highly specific to the suicidal, but characterize the psychiatrically disturbed. The rates are probably above those in the general popula-

tion, although better studies are needed to confirm that.

One issue does emerge clearly: the precipitant life stresses in adolescents are to some extent bound up with the disturbed family backgrounds: both are facets of disturbed families. A second issue often described is the impulsiveness of the suicide attempts, raising the question of how much personality traits of impulsiveness and acting out contribute to the ultimate consequence.

GENERAL CONCLUSIONS

A number of general conclusions and directions for further studies emerge form this overview.

1. There is a dearth of studies that assess the impact of employing careful methodology and controlled comparisons of recent life events in the role of youth suicidal behavior.
2. There are more studies of early parental loss, but even here, there are not many controlled comparisons or attempts to date the family break-up to examine the extent to which the associations depend on recent or earlier family break-up.
3. There are few studies involving completed suicides, rather than suicide attempts. The former is more difficult to study, but the many differences in demographic and epidemiological characteristics of the two populations mandate separate studies.
4. Studies of recent life events in older populations consistently indicate increased rates before suicide attempts and suggest the same for major events, before completed suicides. In terms of relative risks, effects are moderate in magnitude, but tend to be short term, with rates of events in suicide attempters (and other psychiatric patients) converging with those in control groups as time periods are extended retrospectively beyond a year. Suicide attempts probably bear the strongest and most immediate relationship in time to recent life events of any psychiatric disturbances; in particular, they often rapidly follow interpersonal disruptions.
5. Studies of early loss in older suicides and suicide attempters consistently show rates higher than in normal control groups or other psychiatric disorders because of break-up of parental marriage. Relative risks are moderate in magnitude; less than for recent events but apparently long-enduring. For parental death, the effects are less marked; rates are probably raised but only a little.
6. Uncontrolled studies of adolescent suicide attempters and the few comparisons with general population controls suggest particularly high rates both of recent life stress and of earlier family disruptions. Precipitant stresses particularly involve family problems, break-ups of relationships, and school problems. Physical illness as a stressor is uncommon. Recent stresses often appear to arise out of disturbed family settings.
7. Comparisons of adolescent suicide attempters with other psychiatrically disturbed adolescents show only small differences, suggesting that the early losses and disturbed families are relatively nonspecific, and the recent stresses only partly specific.
8. Interpretations of these associations are not fully clear cut. In careful studies of recent life events, it is clear that much of the excess in events is independent of causation by the patients and represents a genuine clustering of external stress before the suicidal act, rather than simply an enduring aspect of lifestyle that would be found at any other time. Nevertheless, generally disturbed lifestyles and, for adolescents, family settings not in their control, do put subjects more at risk of major events.
9. For early loss, the small differences in parental death and considerably larger differences in loss by marital break-up are susceptible to two alternative explana-

tions, both of which suggest that something other than the loss itself is pathogenic. One interpretation is that the findings to some degree reflect a tendency to an acting-out personality and life style, genetically or environmentally transmitted down the generations. The second is that the preceding marital strife and arguments are more disruptive to the child, on a long term basis, than is the loss of a parent itself.

10. Neither recent nor early environment can be regarded as sufficient causes by themselves. They, particularly recent events, clearly interact with other personality variables related to acting-out and impulsive behavior.

11. Implications for prevention are not easy. Partly, this is a general problem in relation to the occurrence of rare consequences, so that most occurrences of a cause will not be followed by disorder. In addition, most of the recent or early events are not preventable. At best, the recent events might serve as signals for high-risk periods when crisis interventions might be attempted.

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CONTROLLED COMPARISON OF LIFE EVENTS AND SUICIDE ATTEMPTS

Controls	Sample Size	Method	Findings
1. General Population Controls			
a) Studies of Children			
Jacobs (1971)	Adolescent attempters N = 31 Control adolescents N = 31	Interview	Excess of events in weeks/months before attempt, particularly break of relationship, physical illness, injury, pregnancy
b) Studies of Adults			
Paykel et al (1975)	Attempters N = 53 Controls N = 53	Interview for recent life events	Excess of life events over six months. Especially last month. Most types of event.
Cochrane & Robertson (1975)	Attempters N = 100 Controls N = 100	Self report checklist scores	Higher stress scores and number of life events over 1 year. Especially unpleasant events, disrupted interpersonal relationships. Equally for under 25, over 40.
Isherwood et al (1982)	Attempters = 150 Controls = 200 Automobile accident drivers = 100	Self report Total stress scores	Higher stress than both control groups. Time not stated.
2. Other Patients			
a) Studies of Children			
Cohen Sandler et al (1982)	Suicidal children N = 20 Depressed N = 21 Other psychiatric N = 35	From case records	Higher mean stress scores separation, divorce remarriage, hospitalization of parent, broken homes, other illness.
b) Studies of Adults			
Paykel et al (1975)	Attempters = 53 Depressives = 53	Interview for recent life events	Attempters experienced more events in threatening classes: undesirable; higher rated stress, uncontrolled.
Slater & Depue (1981)	Primary depressive Attempters N = 14 Depressive N = 14	Interview	Attempters experienced more independent events exits in year before attempt, particularly between onset of depression and attempt.

Table 1.

Controlled Comparison of Life Events and Suicide Attempts (continued)

Controls	Sample Size	Method	Findings
Luscomb et al (1980)	Male attempters N = 47 Psychiatric patients N = 51	Self report Checklist	More events, perceived stress, high stress events exits, desirable, undesirable events. In previous year, no attempter-control differences under age 35.
O'Brien & Farmer (1980)	Overdosers N = 197 General practice attenders N = 152	Interview	Higher rates in previous 6 weeks for most events. Fall off on one year follow-up.
Levi et al (1966)	Suicide attempters N = 40 Suicidal feelings N = 40 Non-suicidal N = 40	Interview Separations only	Attempters experienced more separations in last year. Suicidal feelings intermediate.
Stein et al (1974)	Suicide attempters N = 165 Other psychiatric N = 165	Interview Separations only	Attempters experienced more separations in last year. Significant except for black women where suggestive.
Greer et al (1966)	Suicide attempters N = 146 Other psychiatric N = 148 Medical controls N = 148	Interview only disrupted interpersonal relationships	Attempters experienced more disruption in last 6 months than either groups. Psychiatric controls intermediate.

Table 1 concluded.

STUDIES OF RECENT LIFE EVENTS AND COMPLETED SUICIDE

Study	Sample	Comparison Group	Method	Findings
General Population Controls				
Bunch (1972)	Suicides N = 75	General Population N = 75	Interview of informants. Bereavement only	More loss of parents spouse in previous 2 years. Males, especially unmarried more vulnerable to loss of mother.
MacMahon & Pugh (1985)	Suicides N = 320)	Non-suicidal deaths N = 320	Death Certificates of spouses	Clustering of subject death by suicide in 4 years following spouse death, especially previous year.
Hagnell & Rosman (1980)	Suicides N = 28	Natural deaths N = 25 General population controls N = 50	Sources unclear	More changes of living conditions, work problems and object loss than general population in last year: more object loss than natural death.
Psychiatric Patient Controls				
Humphrey (1977)	Psychiatric patient suicides on followup N = 98 (Males only)	Homicidal offenders N = 62 Neurotic patients N = 76	Psychological autopsy, life histories and hospital charts	More losses, not all recent, than in neurotics. Homicides intermediate.
Pokorny & Kaplan (1976)	Male psychiatric patient suicides N = 20	Patients who did not commit suicide N = 20	Interview with relative relative	More adverse events after discharge, particularly where higher defenseless, probably reflecting depression, during hospitalization.
Borg & Stahl (1982)	Psychiatric patient suicides N = 34	Patients who did not commit suicide N = 34	Case records	No significant diffference although tendency to more deaths.
Fernando & Storm (1984)	Patient suicides N = 22	Non-suicide patients N = 22	Case records	More losses.

Table 2.

RELATIVE RISKS IN COMPARISONS OF LIFE EVENTS IN SUICIDAL AND GENERAL POPULATION SAMPLES

Author	Time Period	Event	Event Rates		Relative Odds
			Patient	Controls	
Suicide					
Bunch (1972)	2 years	Bereavement	7/95	7/150	6.5
Hagnell & Rorsman (1980)	1 year	Work problems	14/28	10/56	4.6
		Object loss	11/28	4/56	8.4
Suicide Attempts					
Paykel et al (1975)	6 months	Undesirable events	32/53	21/53	6.0
	1 month	Any event	37/53	10/53	10.0

Table 3.

Studies of Early Loss in Adult Suicide Attempters

Study	Sample	Comparison Sample	Type of Loss	Findings
General Population Controls				
Greer et al (1966)	Suicide attempters N = 156	Non-suicidal psychiatric patients N = 156 Medical patients N = 156	Death of parent under 15 Separation, divorce under 15	Greater incidence than both comparison groups. Greater incidence than both comparison groups. Particularly under 4, and loss of both parents.
Crook & Raskin (1975)	Depressives with history of suicide attempt N = 115	Non-suicidal depressives N = 115 General population controls N = 285	Death of parent under 12. Loss for at least one year due to separation, divorce, desertion.	No difference. Higher incidence in suicidal.
Goldney (1981)	Female suicide attempters aged 18-30 N = 110	Women attending a community health centre (N = 25)	Death under 16 Divorce, separation	No significant difference. More loss in suicidal.
Adam (1982)	Suicide attempters N = 98	General practice controls (N = 102)	Deaths under 25 Divorce, separation	No significant difference. Significantly higher in suicidal.
Psyciatric Patients Controls				
Farberow (1950)	Suicide attempters N = 32 Suicide threat (N = 32)	Non-suicidal patients (N = 32)	Permanent loss under 19	No significant difference overall. More loss before 6.
Moss & Hamilton (1955)	Seriously suicidal inpatients (N = 50)	Potentially suicidal inpatients N = 50 Non-suicidal patients N = 50	Permanent loss in early life	60% in seriously suicidal vs 15% in each comparison group.
Walton (1958)	Psychiatric patients with suicide attempt or threat N = 60	Non-suicidal patients N = 60	Temporary loss under 15	Significantly more.
Bruhn (1962)	Suicide attempters N = 91	Psychiatric outpatients N = 91 Non-suicidal psychiatric inpatients N = 50	Temporary loss under 15	More loss in suicidal.
Greer (1966)	Neurotic or sociopathic patients with history of attempt N=81	Other neurotic or sociopathic patients N = 385	All loss for 1 year under 15. Death	More loss.. Both over 30 and under 30. More loss ($p < .06$)
Gay & Tonge (1967)	Psychiatric patients with history of suicide attempts N=111	Non-suicidal psychiatric patients N = 382	Separation for at least six months prior to 15	More loss in suicide attempters.

Table 4.

SEXUAL IDENTITY ISSUES

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Study Selection Criteria

In this literature review, it was necessary to create several criteria for selection of studies and for emphasis of certain types of studies.

1. Since much of the literature dealing with sexuality and suicide does not specifically focus on adolescent or youthful populations, it was decided to include all studies dealing with the relationship between suicide and a particular aspect of sexuality. Whereas this decision increased the number of studies to be reviewed, the final result was largely a study of youth suicide. This arose because many studies of sexuality are also studies of the young.
2. Those studies with control groups have been given greatest emphasis. However, single-group studies are also included.
3. Primary emphasis was given to studies of attempted and completed suicide with less attention to suicidal gestures, suicidal ideation, or self-mutilation.
4. Little attention has been given to clinical observations, interpretations, and studies reporting one or two cases.

Homosexuality

The literature clearly and consistently shows that homosexuals of both sexes attempt suicide much more often than do heterosexuals. Saghir and Robins found that 7 percent of their 89 homosexual males and none of the 35 heterosexual controls had attempted suicide (1). The respective percentages among the female groups were 12 (N=57) and 5 (N=43). All four groups generally studied young people in their twenties or thirties. In a much larger study in which the four comparison groups were matched on age, race, and education, Bell and Weinberg found the following percentages of subjects who had ever attempted suicide: homosexual men, 18 percent (N=686); heterosexual men, 3 percent (N=337); lesbians, 23 percent (N=293); heterosexual women, 14 percent (N=140) (2). Similar significant (ANOVA) differences in their histories of suicide attempts have been found in comparing lesbian and nonlesbian female prisoners, although means or percentages were not presented (3).

Turning to studies of clinical populations, one study of 500 psychiatric outpatients found that 50 percent of 12 homosexuals compared with 13 percent of 488 nonhomosexual patients had attempted suicide (4). A 6 to 12 year followup study of these patients reported that two of the homosexuals had committed suicide (5). This suicide rate was 17 times greater than the age- and sex-specific death rate for that State. Another study of 60 homosexual men with a mean age of 20 found that 32 percent had attempted suicide at least once (6). As might be expected, the percentages who had attempted suicide are higher among the clinical than among the nonclinical populations.

The literature also speaks clearly to the nature of suicide attempts by homosexuals, al-

though that differs by gender. Five of the six homosexual male attempters reported by Saghir and Robins had made their attempts before the age of 20 during conflict with family members or within themselves over their incipient homosexuality (1). Five of the seven lesbian attempters had made their attempts during their twenties during a depression following the break-up of a relationship. Bell and Weinberg similarly report that homosexual men in their study generally attempted suicide at an earlier age than the lesbians (2). The homosexual men were more likely to report that their attempts were related to trying to deal with their homosexuality than was the case for the lesbians, whose attempts were more related to the break-ups of relationships.

The above data indicate that the period of coming to an acceptance of one's homosexuality--"coming out"--is a period that may be accompanied by a heightened risk of suicide attempts. The average age of coming out among homosexual men has been found to be 18 or 19; (7,8,9) this seems to coincide with the time when homosexual men are at risk of attempts. Two studies of large nonclinical populations of homosexuals have reported that just under half of the respondents agreed with the item: "Before I came out, the idea that I might be homosexual troubled me a lot" (8,10). In a recent study more intensively analyzing the Bell and Weinberg data, Harry found that, among the homosexual men, being troubled over one's homosexuality during adolescence was related to subsequent suicide attempts (11). Among the men of both sexual orientations, childhood cross-gender behaviors were related to attempts. Among all four study groups, being a loner during adolescence and general adolescent unhappiness were related to attempts. It thus seems that a number of the pre-adult characteristics and experiences of homosexuals may create special difficulties for them and that, for some, suicide may seem preferable to other solutions. Studies suggest that trying to grow up homosexual in a culture organized for heterosexuality likely contributes to many of the problems of these troubled youths.

Confusion Over Sexual Identity

The topic of confusion over sexual identity has been here interpreted to mean transsexuals. Although it could also refer to the case of young homosexuals attempting to accommodate themselves to their sexual orientation, that has been dealt with in the previous section. All except one of the studies dealing with transsexuals and suicide are single-group studies lacking a control group. In the one exception, male transsexuals still living as males had made significantly more suicide attempts than male transsexuals living as females, homosexual psychiatric patients, homosexual nonpatients, and heterosexual nonpatients (12). Also, the two transsexual groups were significantly higher in suicidal thoughts than were the other three groups. The sample sizes in this study ranged from 19 to 25.

Turning to the single-group studies, Walinder reported that 20 percent of 30 Swedish male transsexuals and 8 percent of 13 female transsexuals had made attempts (13). These percentages should be considered minimum estimates because the author only reported attempts documented in hospital records, thereby excluding those not leaving such records. Another study of 72 English transsexuals (55 men and 17 women) reported that 53 percent had made attempts. Four (5.7 percent) had completed suicide (14). Person and Ovesey reported that six of ten male transsexual patients were preoccupied with suicidal thoughts and two had made attempts (15).

Although these studies dealing with transsexuals either lack a control group or do not report means or percentages of those who had made attempts, the percentages available indicate that transsexuals may be at higher risk for suicide attempts than other groups at risk, e.g., homosexuals, and much higher than the general population. As a matter of caution when discussing the attempts of transsexuals, it is important to distinguish between past attempts and threats,

attempts, and self-mutilation to induce a therapist to undertake desired medical actions. Such threats and acts seem to be fairly common among clinical transsexuals. However, as far as possible, such attempts have not been included in the percentages cited above.

Acquired Immune Deficiency Syndrome (AIDS), AIDS-Related Complex (ARC)

Since the phenomenon of AIDS is quite new and since the associated medical prospects are frequently changing, little can be said about the relationship of AIDS to suicide attempts or completions. Approximately 70 to 75 percent of persons with AIDS or ARC are male homosexuals. However, there have been cases reported of both attempts and completions (16,17,18). Also, one homosexual man who had been unsuccessful with suicide attempts devised an interesting–and successful–means: having sex with persons known to have AIDS (19).

With our current medical knowledge of AIDS as a classical terminal illness, one might expect suicide and attempts. If attempts and completions are not directly due to the medical aspects of AIDS, they may also be the indirect result of societal reaction to the individual with AIDS. For example, one homosexual man with AIDS attempted suicide after his employer fired him for having the illness (18). Similarly, AIDS can result in evictions, loss of a lover, and loss of a sex life. AIDS can also effect an involuntary disclosure of an individual's homosexuality to others. Hence, these indirect effects of the illness potentially could enhance the possibility of suicide. No information is currently available on any link between ARC and suicide.

Sexual Inhibition or Promiscuity

Computer searches of the SIEC data base, Psychological Abstracts, and Medline facilities produced nothing on this topic. One study suggested a relationship between promiscuity and suicide attempts in a population of 105 adolescents who were pregnant (20). The 14 (13 percent) who had attempted suicide during the two years following pregnancy were more likely to have had a venereal disease. While the presence of venereal disease indirectly suggests promiscuity, the 14 attempters were also significantly more likely to be single and have a number of other problems. Hence, isolating these girls' sexual activity as a contributory factor in their attempts should be viewed with extreme caution.

Victims of Physical and Sexual Assault

The strongest relationship between suicide attempts and physical abuse was reported in an Australian study comparing 20 suicidal and 50 nonsuicidal children under 14 from a child psychiatric hospital (21). Sixty percent of the suicidal children versus 4 percent of the nonsuicidal had been subjected to parental physical abuse; 65 percent versus 4 percent had also witnessed physical fights between their parents. However since one is more likely to be interested in predicting from abuse to attempts, rather than the reverse, these percentages should be made in the other direction. In that case, the percentage among the abused who were suicidal was 86 versus 14 among the nonabused. Viewed in this way, these data appear to show a massive and significant association between abuse and suicidality. However, this association is very likely an artifact of the clinical populations studied. Suicidal children are probably much more likely than nonsuicidal ones to come to clinical attention with problems. Also, abused children are probably more likely to come to clinical attention than are nonabused children with problems. Children who are both abused and suicidal are thus more likely to come to clinical attention than either the simply abused, the simply suicidal, or children who are neither. Hence, abused **and** suicidal children will be far over-represented in clinical populations and thus suggest an apparent association even when none may exist in the general

population. These data suggest that clinical populations may be very inappropriate for studying the association between two phenomena when **both** of those phenomena are major correlates of, or criteria for, admission to a clinical population.

Another study compared 60 abused children, 30 neglected ones, and 30 nonclinical children (22). Their respective rates of self-destructive behaviors were 41 percent, 17 percent, and 7 percent. The percentage among the abused who had made attempts was 8.5 (figures for the other two groups were not given). Again, since both self-destructive behaviors and abuse are both likely to be brought to either clinical or official attention, the reported associations may well overstate the strengths of the true associations.

The studies of sexual abuse and suicidal behaviors are also from clinical populations. Herman and Hirschman compared 40 women who had had incestual relationships with their fathers, with 20 women who had had seductive, but not incestual, relationships with their fathers (23). The women in both groups were private psychiatric patients. The researchers found that 38 percent of the former and 5 percent of the latter had attempted suicide; the difference was statistically significant. A single-group study of sexually abused girls from 201 families served by a protective service agency found that eight girls (4 percent) from these families had also attempted suicide (24). All attempts occurred when the girls were 14 to 16 years old. Since the families of these girls were generally chaotic and conflictful, it is difficult to attribute direct causality to the abusive behaviors of their fathers. Also, the percentages of attempts in this study and the one previously mentioned (22) are not particularly high when compared with groups discussed earlier. Although there may be a relationship between sexual abuse and suicide attempts, these studies cannot show one.

A study comparing 25 women who had been raped several times with 92 women who had been raped once indicates a possible relationship between suicide attempts and being multiply raped (25). All subjects were from a hospital rape center. The multiply raped women were significantly more likely to have attempted suicide (52 percent vs 16 percent), to be younger, poorer, loners, immigrants to the city, and to have had more psychiatric treatment. Although there may be an association between multiple rape and attempts, attribution of causality here is clouded because of the apparently disorganized histories of the multiply raped victims. Both their suicides and rapes may be symptoms of disorganized personal histories. A suggestive study of 13 young (18 to 23 years) military servicemen who had been raped by other military personnel found that two (15 percent) had made subsequent suicide attempts out of feelings of deflation of their manhood (26). A study of prison sexual violence in New York State men's prisons found that 38 percent of 107 inmates who had received verbal threats to physical assault for sex had made suicidal gestures (27). This percentage was more than twice that among 45 sexual aggressors recorded in inmate files and 17 times that among nonharrassed prisoners. These data provide some presumptive evidence that, at least among young males, being subjected to same-sex sexual harrassment or abuse in situations where there is little escape may precipitate suicide attempts. However, it is possible that those prone to suicide may also be subjected to more threats and assaults.

Pregnancy-Related Suicidality

It is very difficult to conclude anything about the association between suicide and pregnancy because of the diverse types of studies, the varying definitions of the term "pregnancy-related," the lack of adequate controls for age, and the small sample sizes.

1. Types of Studies. The studies divide into those that show the percentage of pregnancies among attempters, those that show the percentage of attempters among the pregnant, those with adequate control

groups, and those of completed suicides.

2. Definitions of "Pregnancy-Related." The definitions include pregnant during a suicide or attempt, postpartum attempts or suicides, belief that the attempter was pregnant, and overdue menstuation. These varying definitions make any conclusions from this literature almost impossible.

3. Controls for Age. Since suicide completers are generally middle-aged to old and both attempters and pregnant women are generally young, controls for age--and fairly precise ones--are mandatory.

The above-listed problems occur in the scientific literature about pregnancy and suicide in many, if not all, possible combinations. Below, we proceed through the most common groupings.

Attempts Among the Pregnant. One study of 105 pregnant girls under 18 at an urban hospital found that 14 (13.3 percent) had attempted suicide at least once during a 2-year followup (20). Clearly, these attempts are postpartum and beyond. The attempters were significantly more likely to be single, Catholic, to have had venereal disease, and to have come from higher socioeconomic areas. This study lacks a control group of adolescent nonpregnant girls.

Pregnancies Among Attempters. Comparing 30 pregnant attempters with 453 nonpregnant attempters from Australia, Whitlock and Edwards concluded that since 6 percent of suicidal women are pregnant compared with 7 percent of women who are pregnant in the population at any given time, pregnancy is not a predictor or inhibitor of suicide attempts (28). In their study, the pregnant women were less likely to be married than the nonpregnant (53 percent vs 41 percent). Teicher found that "Twenty-two percent of all suicide-attempting girls compared to zero percent of control girls were either pregnant or believed themselves to be pregnant" (29,30). It is difficult to determine the sample size on which this 22 percent figure is based because the various publications describing this study leave it unclear as to whether the number in the sample, which was three-quarters female, was 20, 48, or 68.

Pregnancies Among Attempters and Controls. It seems that in only two studies did the researchers bother to obtain a nonclinical control group matched for age with the attempters. Jacobs compared 50 adolescent attempters, of whom 38 were female, with 22 female age-matched adolescent nonattempters (22). Matches were made on age, race, sex, and maternal education. The data showed that 21 percent of the attempters were either pregnant or believed themselves to be at the time of the attempt compared with none of the controls. Since the figure of 21 percent is very close to Teicher's figure of 22 percent in the previous study and since the two authors worked together, it is unclear if they are actually describing different sets of respondents. The 22 or 21 percent figures of these studies are much higher than the figure of 6 percent of attempters who are pregnant reported by Whitlock and Edwards. However, since the former studies include both real and suspected pregnancies while the Whitlock and Edwards study includes only real pregnancies, no conclusions can be drawn.

Birtchell and Floyd compared 107 female attempters with 110 female nonattempters with a control for age (32). Of the attempters, 12.1 percent compared with 2.7 percent among the nonattempters, were either pregnant or overdue in their menstrual cycles. Ten (77 percent) of the 13 pregnant attempters were unmarried. Because the definition of "pregnancy-related" employed in this study includes being menstrually overdue, comparison with the immediately preceding three studies is, once again, impossible.

Studies of Completed Suicide. A study of completed suicides in Minnesota for the years 1950-1965 found that 1 percent (14/1019) of female suicides were pregnant (33). The study reported that suicides per 100,000 population were 16 for men and 4 for women during this period. For pregnant

women, suicides were close to 1 per 100,000 live births (14/92,982). None of these 14 pregnant women were unmarried. The author concluded that pregnancies during suicide were extremely low and that pregnancy served as a protector against suicide. Ten of the 14 pregnancy-related suicides in this study occurred postpartum. While this further reinforces the author's conclusion, it also suggests that the postpartum period may be the time of greatest, although still extremely low, risk. It should be noted from this study that using live births as a proxy for the number of pregnant women is a more accurate denominator than using the total universe of women in the reproductive age range (15 to 45).

A later study disputing the conclusion that pregnancy is an inhibitor of suicide presented data on 8 pregnancy-related suicides among a total of 47 suicides in New Mexico (34). Twelve and a half percent (4/32) of female suicides of ages 15 to 34 were pregnant. This age range was provided by the authors to coincide better with the principal years of childbearing. While the 12.5 percent figure is considerably higher than that from the Minnesota study, the numerator (four) is so low that the percentage is extremely unstable from a sampling viewpoint. It should be noted that all of the eight women who completed suicides were married and that their means of suicide were principally guns and hanging.

Despite the dreary inconclusiveness of the various studies on pregnancy-related suicides, one finding does emerge. Most pregnant attempters are single, whereas most pregnant completers are married (20,29,32,33,34). Also, the means of suicide for the single attempters are drugs primarily whereas the means for the completers are mainly guns and hanging. These data suggest that the two groups are different populations, although with some overlap. Hence, being in a pregnant population at risk of attempt may only marginally affect the risk of completing suicide.

Conclusions

Homosexuality. Homosexuals of both sexes are two to six times more likely to attempt suicide than are heterosexuals. Data on completed suicide do not exist. Kinsey et al. estimated that 10 percent of all males and 1/3 to 1/2 that of females are predominantly homosexual (35,36). However, because Kinsey's data included large numbers of prisoners, Gebhard later revised Kinsey's estimates to 4 percent of white males with at least some college education and 1 to 2 percent among all adult females (37). The data show that these two populations are markedly at risk of attempted suicide during late adolescence and early adulthood.

Confusion Over Sexual Identity. Whereas studies with adequate control groups are lacking, the percentages from the single-group studies strongly suggest that transsexuals may be an extremely high risk group for attempted suicide. Adequate data do not exist for completed suicide.

AIDS. Only case reports exist. However, there are strong reasons to suspect that suicidal behavior may be very common among AIDS sufferers.

Sexual Inhibition or Promiscuity. There has been no research on this topic. If research is undertaken, it is important to attend to the sexual behaviors of both men and women to prevent continued bias on labeling of promiscuous behavior in reference to women only.

Victims of Physical or Sexual Abuse. Although the data on this topic come mainly from single-group studies, there does not appear to be a markedly high rate of attempts among abuse victims. The two groups of abuse victims in which there might be an elevated rate are women who have been raped on several occasions and men who have been raped or sexually assaulted by other men.

Pregnancy-Related Suicide. The literature on this topic is too conflicting in its findings to conclude anything. However, the two sub-

groups who may be at risk are single pregnant women and married postpartum women. The former group may be at risk of attempts, while the latter group may be at risk of completing.

Recommendations for Future Research

Control Groups. We need control groups to determine whether a given population has a high or low risk for suicide.

Nonclinical Control Groups. While comparing suicidal with nonsuicidal patients is convenient, it can only show that one specially defined population may differ from another specially defined population.

In the case discussed earlier where one examines the association between attempts and some other clinical characteristic, both of which serve as criteria for becoming a clinical patient, it is likely that one may find totally false associations. When introduced to the clinical literature, such associations can mislead others into pursuing, or funding, lines of research that may be ultimately unprofitable, especially if pursued in clinical settings.

Nonclinical Experimental Groups. It would be most desirable to obtain both experimental and control groups from nonclinical populations through conventional methods of survey research. For example, it has been possible to profitably study family violence through survey methods, including even telephone surveys (38,39). Such research was an immense advance over earlier research of family violence based largely on clinical samples. Two major hurdles to conducting survey research on attempted or completed suicide come to mind. First, there is the intrinsic sensitivity of asking persons about the suicidal behaviors of themselves or of other family members. However, since it has proven possible to ask people in survey situations about the crimes they have committed, deviant sexual activities, and family violence, it should also prove possible to ask about suicide. Second, since attempted and completed suicide are infrequent-to-rare events, the difficulty arises of obtaining sufficient numbers of such persons in a general survey to analyze. This difficulty can be overcome by focusing the survey on limited segments of the general population such as high school students or pregnant women. Also, the numbers for analysis can be increased by asking about suicidal behaviors not only of the respondent but also of a limited set of close relatives. This recommendation of survey research does not extend to possible research on AIDS or ARC and suicide since, given the infrequency of both of these phenomena, survey research on this topic without massive and expensive samples becomes impossible. However, given the considerable potential of AIDS as both a direct and indirect cause of suicidal behavior, one would hope that research on the relationship be soon undertaken.

As a concrete example of my proposed form of research, I suggest a survey of the general population which includes a question on sexual orientation. To date this has not been done. Until the 1960s, and especially the 1970s, homosexuality was a topic studied largely by clinicians. Beginning with the works of Evelyn Hooker, there began a continuing stream of studies based on nonclinical samples of homosexuals, the results of which differed much from those reported by clinicians (40). However, all studies of homosexuals to date still involve nonprobability samples, hence, estimates of rates of suicide can only be approximate (41). The time may be ripe for a survey of the general population that includes a question, possibly placed among the demographic items, on sexual orientation. This would permit more accurate, if still imperfect, estimates of the true risk of suicidal behaviors among such populations.

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Risk Factors Potentially Associated with Adolescent Suicide or Attempted Suicide

Risk Factor	Citation	Outcome Variable	Experimental Group	Control Group	Results	Significance Tests*
Homosexuality	Bell, A., Weinberg, M. Homosexualities. New York, 1978, Simon & Schuster, p. 450	suicide attempts	686 gay males, 293 lesbians	337 straight males, 140 straight females	gay men, 18% straight men, 3%; lesbians, 23%; straight females, 14%	X^2
	Clement, C., Ervin, F., Rollins, A., Plutchik, R., Batinelli, C. Epidemiological studies of female prisoners: homosexual behaviors. J. Nerv Mental Dis 1977; 164:25-29.	suicide attempts	27 self-reported lesbians, 27 staff-identified lesbians in prison	27 straight women in prison	lesbians more, but figures not provided	ANOVA
	Harry, J. Parasuicide, gender, & gender deviance. J Health & Soc Behav 1983; 24:350-361.	suicide attempts	Same as Bell & Weinberg above	Same as Bell & Weinberg above	adolescent guilt over sexual feelings related to later attempts	Log-linear analyses
	Martin, R., Cleninger, R., Guze, S., Clayton, P., Mortality in a follow-up of 500 psychiatric outpatients. Arch Gen Psychiatry 1985; 42:58-66.	completed suicides	11 gay male outpatients	488 other outpatients	gays complete more suicides than other patients	X^2, Poisson
	Roesler, T., Deisher, R., Youthful male homosexuality. JAMA 1972; 219:1018-1023.	suicide attempts	60 young (16-22) gay males	none	32% made attempts	none
	Saghir, M., Robins, E., Male and female homosexuality. Baltimore: Williams & Wilkins, 1973; 118:276-277.	suicide attempts	89 gay men; 57 lesbians	35 straight men; 43 straight fem.s	gay men, 7%; straight men, 0%; lesbians, 12%; straight fem.s, 5%.	X^2
	Woodruff, R., Clayton, P., Guze, S. Suicide attempts and psychiatric diagnoses. Dis of Nerv Sys 1972; 33:617-619.	suicide attempts	12 gay male outpatients	488 non-gay outpatients	gay men, 50%' others, 13%	none

Table 1.

Risk Factors Potentially Associated with Adolescent Suicide or Attempted Suicide

Risk Factor	Citation	Outcome Variable	Experimental Group	Control Group	Results	Significance Tests*
Transsexuals	Huxley, P., Kenna, J., Brandon, S. Partnerships in transsexualism, part I. Arch Sex Behav 1981; 10:133-141.	suicide attempts	72 English transsexuals	none	53% had attempted; 4 had completed	none
	Langevin, Paitich, D., Steiner, B. The clinical profile of male transsexuals living as males vs those living as females. Arch Sex Behav 1977; 6:143-154.	suicide attempts	25 transsexuals living as males; 19 transsexuals living as females; 20 gay patients	19 gay non-patients; 24 straight non-patients	both transsexual groups made more attempts than other groups; means, % not given	F-tests
	Walinder, J. Transsexualism. Goteborg, Sweden: Scan University Books, 1967.	suicide attempts	30 male and 13 female transsexuals, all patients	none	males, 20%; females, 6% as recorded in Swedish hospitals	none
	Person, E. Ovesey, L. The transsexual syndrome: primary transsexualism. Am J Psychotherapy 1974; 28:4-21.	suicide attempts	10 male patient transsexuals	none	2 had made attempts	none
	Lockwood, D. Prison sexual violence. New York: Elsevier, 1980.	suicide gestures	107 targets of sexual harassment in men's prisons	45 sexual aggressors in men's prisons	targets more than twice as likely as aggressors to make suicidal gestures	none

Table 1 continued.

Risk Factors Potentially Associated with Adolescent Suicide or Attempted Suicide

Risk Factor	Citation	Outcome Variable	Experimental Group	Control Group	Results	Significance Tests*
Pregnancy-Related	Bamo, A. Criminal abortion deaths, illegitimate Pregnancy in pregnancy. J Obst and Gyn 1967; 98:356-367.	completed suicide	14 pregnant suicides in Minn., 1950-1965	92,982 live births in Minn., 1 950-1965	suicide rate of pregnant women is about 1/100,000	none
	Birtchnell, J., Floyd, S. Further menstrual characteristics of suicide attempters. J Psychosom Res 1975; 19:81-85.	suicide attempts	107 female attempters	110 female non-attempters matched for age	13% vs 3% of controls were pregnant or menstrually overdue	none
	Gabrielson, I., Kiernan, L., Currie, J., Tyler, N., Jekel, J. Suicide attempts in a population pregnant as teenagers. Am J Public Health 1970; 60:2289-2301.	subsequent suicide attempts	105 under 18 pregnant patients	none	13.3% made attempts in 2 years after giving birth	none
	Goodwin, J., Harris, D. Suicide in pregnancy. Suicide and Life-Threatening Behav., 1979; 9:105-115.	completed suicide during pregnancy or postpartum	8 pregnant or postpartum suicides in New Mexico	47 female suicides in New Mexico	17% female suicides are pregnant or postpartum	none
	Jacobs, J. Adolescent suicide. New York: Wiley, 1971; 67-68.	pregnant or believed self to be	38 adolescent female attempters	22 female age-matched controls	21% vs 0% of female controls were pregnant or believed self to be	none
	Teicher, J. A solution to the chronic problem of living: adolescent attempted suicide. In: Schoolar, J. Current issues in adolescent psychiatry. New York: Brunner-Mazel, 1973: 129-147.	pregnant or believed self to be	female adolescent attempters; N = 20 or 48 or 68	22 female adolescents	22% versus 0% of controls were pregnant	none
	Whitlock, F., Edwards, E. Pregnancy and attempted suicide. Comprehensive Psychiatry 1968; 9:1-12.	being pregnant	30 pregnant attempters in Australia	453 nonpregnant attempters in Australia	6% of attempters are pregnant vs 7% of all women in Australia aged 15-45	none

Table 1 continued.

Risk Factors Potentially Associated with Adolescent Suicide or Attempted Suicide

Risk Factor	Citation	Outcome Variable	Experimental Group	Control Group	Results	Significance Tests*
Physical and Sexual Abuse	Ellis, E., Atteson, B., Calhoun, K. An examination of differences between multiple- and single-incident victims of sexual assault. J Abn Psychol 1982; 91:221-224.	suicide attempts	25 women raped more than once; hospital patients at rape center	92 women raped once; also patients at rape center	52% earlier attempts vs 16% in control group	X^2
	Goodwin, J. Suicide attempts in sexual abuse victims. Child Abuse & Neglect 1981; 5:217-221.	suicide attempts	8 children from 201 families with sexually abused daughters	none	4% had made attempts after abuse	none
	Goyer, P., Eddleman, H. Same-sex rape of non-incarcerated men. Am J Psychiatry 1984; 141:576-579.	subsequent suicide attempts	13 young (18-23) servicemen raped by other servicemen	none	15% made subsequent attempts	none
	Green, A., Self-destructive behavior in battered children. Am J Psychiatry 1978; 135:579-582.	suicide attempts	60 battered children	30 neglected children; 30 normal children	8.5% of battered made attempts; sign. difference, but data on other groups not given	ANOVA
	Herman, J., Hirschman, L. Families at risk for father-daughter incest. Am J Psychiatry 1981; 138:967-970.	suicide attempts	40 female patients with paternal incest	20 female patients with seductive fathers	38% vs 5% of controls and attempted suicide	none
	Kosky, R. Childhood suicidal behavior. J Child Psychol & Psychia & Allied Disciplines 1983; 24:457-468.	physical abuse	20 "suicidal" children patients under 14 in Australia	50 other child patients under 14 in Australia	60% had been abused vs 4% of controls; significant	X^2

*Where significant tests are indicated differences were significant at the .05 level.
However, in studies involving more than 2 groups, not all differences among all groups are necessarily significant.

Table 1 concluded.

"MAJOR PSYCHIATRIC DISORDERS" AS RISK FACTORS IN YOUTH SUICIDE

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The aim of this review is to assess whether major psychiatric disorders constitute risk factors in youth suicide. As the data on this matter are limited, we have chosen to present succinct reviews of three different sources of information that can illuminate this relationship, namely: (1) the types of psychiatric diagnoses found among youths who have completed suicide, (2) psychiatric diagnoses among youth who attempted suicide, and (3) the relationship between familial aggregation of suicidal behaviors and familial aggregation of major psychiatric disorders. The limitations of each data source and of each group of studies will be discussed in each section.

Psychiatric disorders and youth suicide

The strongest evidence about the suicide risk posed by psychiatric illness would have to come from **prospective** studies of clearly defined psychiatric cohorts. Ideally, such a study would entail at least two different diagnostic samples; a suitable, psychiatrically unaffected group of controls; and a period of followup sufficient for the outcome of interest (suicide) to occur. Alternatively, a **retrospective** study of a consecutive, unselected sample of young people who had died by suicide could provide data about the incidence of various psychiatric disorders among them. But, the resultant figures are best interpreted against base rates derived from demographically comparable populations. Finally, the retrospective, case-controlled study of select samples of youth suicides could shed light on the contributing role of mental illness. Strictly speaking, however, both the latter approaches identify correlates or associated features of suicide.

Although there has been increasing concern about youth suicide in the United States and other countries (1-5), the evidence about its association with specific psychiatric diagnoses is neither scientifically unassailable nor unequivocal. The scarcity of conclusive data is partly a reflection of the enormous technical, practical, and ethical problems that are inherent in the study of suicide, including the extremely low base rate of its occurrence. Additionally, data from earlier publications cannot be readily interpreted because, in the last 15 years, there have been substantial changes in the use of psychiatric diagnoses in juvenile cohorts. Nonetheless, the available findings are clinically alarming and suggest that major psychiatric disorders play an important role in youth suicide.

Suicide among psychiatrically ill youth: Prospective studies

The mere fact of "patienthood" is apparently

associated with a higher than expected rate of suicide across the age span. Morrison (6), whose database consisted of 12,104 patients (age range not given) treated over an 8-year interval (1972-1980) by a San Diego-based private practice group, computed the cohorts suicide rate by age and sex (controlling for years of followup). As shown in Table 1, the patients had a consistently higher suicide rate than similarly aged males and females in the general county population. This higher rate was most marked for patients aged 19 or younger, who committed suicide at roughly 40 times the expected rate.

There is evidence that suicide among youths is associated with certain major psychiatric disorders more than with others. Welner et al (7) reported on the 8 to 10 year followup status of 77 psychiatric inpatients whose index hospitalization occurred between 1965 and 1968, at a mean age of 16. On followup, a comprehensive interview verified initial diagnoses, according to the Feighner criteria. The data were gathered from the patients, significant others, or records of rehospitalizations. The authors provided the number of cases in each diagnostic group who committed suicide over the followup interval. Using these figures, we computed the number of suicides in a followup year, and then, the portion of each diagnostic group who committed suicide in a year. Then, we multiplied the resultant figure by 100,000 to estimate the **rough suicide rate** per 100,000 diagnostic population per year. Please note that these rates are only "rough estimates" in part, because inpatients may not represent the entire population of cases with a given diagnosis. We realize the shortcomings of this method, but the rates are easier to compare this way.

As Table 2 indicates, schizophrenia, bipolar affective illness, and primary unipolar depression in adolescence were associated with astonishingly high rates of suicide (the table does **not** include the "alcoholism only" diagnosis, because there were only two such cases, nor six others who had a variety of different diagnoses). It is of interest here that there were no suicides among the "antisocial personality" cases, although each had concomitant alcohol and drug abuse and most (7 out of 9) were hospitalized because of "depressive symptoms and suicide attempts."

We used the same computational procedure on data from King and Pittman (8) data who determined the 6-year followup status of 65 consecutively admitted patients (aged 12 to 19). This group was an earlier cohort from the same university hospital that provided cases in the study of Welner et al., with index admissions from mid-1959 to mid-1960. Followup status was ascertained via structured interviews with the patients themselves, adult informants, and/or hospital records. The diagnoses (listed in Table 3) were derived according to symptomatic criteria specified by the authors. On followup, all available data were used to determine the diagnoses. However, the findings were presently only for 51 cases who fell into two general categories: affective disorders ($\underline{n}$ = 26) and "other" disorders ($\underline{n}$ = 25). The one case of suicide was a patient whose diagnosis was "organic brain syndrome." This study is notable because it illustrates changes in diagnostic practices and/or in the actual manifestations of psychopathology. For example, the authors specifically stated that none of the patient met criteria for "addiction and alcoholism." In contrast, in a current inpatient adolescent sample, one is far more likely to

Suicide Rates in a Sample of Psychiatrically Hospitalized Adolescents at 6-Year Follow-up (Adapted from King & Pittman, 1970)

Diagnosis/n	n	Suicide/Year No.	Suicide/Year Rate
Affective disorder (depression/mania)	26	–	–
Schizophrenia/ schizophreniform syndrome	5	–	–
Organic syndromes (OBS, convulsive disorder, Sydenham's chorea)	12	.166	1,388/ 100,000
Sociopathic personality	4	–	–
Other	4	–	–

Table 3.

Suicide Rates in a Sample of Private Practice Patients and in the Corresponding General San Diego County Population
(Adapted from Morrison, 1984)

Age/Sex	Rate/100,000/Year Patients	County Pop.
0-19		
Female	63.05	1.66
Male	173.01	3.99
20-24		
Female	80.61	10.71
Male	205.66	23.17

Table 1.

Suicide Rates in a Sample of Psychiatrically Hospitalized Adolescents
(Adapted from Welner et al., 1979)

Diagnosis at Follow-up (n; $\bar{X}$ age at onset)	Follow-up Length ($\bar{X}$)	Suicide/Year No.*	Rate/100,000
Schizophrenia (13; 14.5 yrs)	8.5 yrs		
Female (7)		.00	—
Male (6)		.235	3,921
Bipolar Affective (12; 15 yrs)	9.0 yrs		
Female (3)		.00	—
Male (9)		.333	3,700
Unipolar, Primary Depression (16; 15 yrs)	10.0 yrs		
Female (10)		.01	1,000
Male (6)		.00	—
Antisocial Personality (9; ?)	?		
Female (4)		.00	—
Male (6)		.00	—
No Mental Illness (8; ?)	?		
Female (6)		.00	—
Male (2)		.00	—
Undiagnosed Illness (8; ?) (probably adjustment reaction)	?		
Female (?)		.00	—
Male (?)		.00	—

? = data not given; *rounded to nearest digit

Table 2.

find the latter conditions than "organic syndromes."

Based on an average of 3 years of followup (up to June 1970) of 227 drug-using adolescent girls who had been admitted to a remand home in London during 1966-1968, Noble et al. (9) assessed the outcome and correlates of this condition. Using those data, Miles (10) computed the cohorts suicide rate as 3,500/100,000/year. However, a careful reading of the original publication reveals this rate to be suspect because the suicides were cited for all admissions commencing in 1964—which was 2 years before the study sample's admission date--and included deaths up to one year after the cut-off date for the study samples followup (p .501). Moreover, the number of all admitted cases was not provided.

We will close this section by noting three other studies which underscore that the likelihood of suicide being detected varies with the length of followup and the nature of sample, including the type of diagnosis. For example, Annesley (11) who described the 2 to 5 year followup status of 362 previously hospitalized adolescents (aged 7 to 18), reported no suicides among them. This was particularly notable because the admission diagnoses were wide-ranging, covering various psychotic disorders, sociopathy (i.e., "behavior disorders"), neuroses, and obsessional states. Likewise, Strober and Carlson (12), who conducted a 3 to 4 year followup of 60, hospitalized, depressed adolescents (diagnosed according to RDC), aged 13 to 16 years, found no suicide among them.

On the other hand, in a highly select sample, followed for a period ranging from 1 to 14 years, 2 out of 28 patients were found to have died by suicide (13). The patients, who had a diagnosis of manic-depressive illness, were specifically examined because their first attack occurred before age 19 at the mean age of 15 (range: 13-18). The patients entered the study as a result of having been hospitalized at a particular institution; the followup took place after the index the admission (mean age at followup: 41 years, range: 23 to 69 years). Again, using our rough computations, and taking the maximal followup interval (14 years), we obtain a frequency of .143 suicides/year in this group of 28, which then yields a suicide rate of 510/100,000/year.

Studies of youth suicides in the general population

The retrospective method of identifying psychiatric risk factors for suicide suffers from numerous constraints, including ascertainment and interviewer bias, incomplete databases, and probable distortions of historic information because of the informants' "need" to explain the suicidal act. Nonetheless, the findings do deserve consideration, although for youth suicides, estimated rates of mental illness are extremely variable, ranging from 92 percent (14) to 12 percent (15). All things considered, psychiatric disturbance seemed more likely to be detected if study investigators used more extensive or systematic information sources.

According to Rich and associates (14), "psychiatric illness is a necessary (but insufficient) condition for suicide." Using the San Diego Coroner's list for the period of November 1981 to June 1983, they located 133 consecutive cases of suicide under 30 years of age. These cases were compared with 150 consecutive cases aged 30 and older, sampled from November 1981 to September 1982. Multiple information sources were used (92% of the sample) to determine the most valid responses to an extensive, structured interview; then, consensual, DSM-III diagnoses were derived. Subsequently examined toxicology reports might be appended to the diagnoses. For our purposes, the interpretation of the findings were constrained because the data were grouped by cases aged "under 30" versus "over 30" and the exact age range was not reported. Although the second paper on this cohort (16), provided an age distribution by 5 and revealed that 44 percent (n = 59) of the 133 suicides were in the 25 to 29 age range, diagnosis data by age were not included. This is problematic because, for example, a particular diagnosis such as cocaine

abuse may be more prevalent among persons 25 to 30 than under 25. Without more specific age by diagnosis data, the exact prevalence of a diagnosis among early adolescent suicides cannot be determined.

Nonetheless, as Table 4 indicates, 92 percent of those "under 30" had psychiatric diagnoses (comparable to 91% of the older cases), and substance abuse was very prevalent (much more so than among the older suicides). According to a subsequent report (16), altogether 53 percent of the younger cases had a diagnosis of substance abuse. Affective disorders were relatively frequent (n = 47), but less than in the contrast group (n= 78), and 52 percent of the "under 30" cases had a past history of psychiatric care. It should be pointed out, however, that the high overall rate of disturbance in this study's cohort included "minor" DSM-III conditions, such as "adjustment disorders" or dysthymia (which has been viewed as a form of "minor" depression). Moreover, the use of multiple diagnoses per case accounts for the large, absolute frequencies in Table 4.

Psychiatric Characteristics of 133 Younger Suicides (aged <30) in San Diego County (Adapted from Rich et al., 1986).

Post-Mortem Diagnoses-DSM-III	N cases with Diagnoses*
Substance Use Disorder	?
Drug Use	88
Alcohol Use	72
Affective Disorders	47
Atypical Depression	32
Major Depression	9
Schizophrenic Disorder	6
Other Psychoses	16
Antisocial Personality	12
Any Diagnosis (92%)	122
Psychiatric Care (%)	
Past	52
At time of suicide	23

*Table does not include all the diagnoses that were listed.

Table 4.

Another methodologically complete study reported a very high rate of "psychiatric symptoms" and a notable incidence of psychiatric contacts among children who killed themselves; unfortunately, no diagnoses were provided (17). In this total population survey of suicides in England and Wales during 1962-1968, there were 30 unequivocal youth suicides (aged 12 to 14). Using coroner, school, psychiatric, and social service records, Shaffer (17) found that 30 percent of the victims (n = 9) had been in contact with a psychiatrist; 20 percent more (n = 6), although not referred to a psychiatrist, were recognized as having "conduct or emotional problems"; and all but 13 percent had "psychiatric symptoms" of the "antisocial," "emotional, affective," or "mixed" (emotional plus conduct) kind.

The foregoing findings were echoed by a recent study that combined the total population survey and case control methods (18). The Jefferson County (KY) coroner's office was used to locate all cases of youth suicides (aged ≤ 19 years) from January 1980 through June 1983; 24 cases (aged 12 to 19) were found, and their families were then contacted. The families of 20 (83%) agreed to cooperate. Extensive questionnaires, checklists, and inventories were used with families, friends, and relatives to determine the victim's psychologic profile. Similar data were collected on matched-pair controls (friends of the deceased). The 20 suicides differed from the 17 controls on the following variables of interest to us: frequent use of nonprescribed drugs or alcohol (70% vs. 29%, p <.02); having exhibited "antisocial behavior," including shoplifting, physical fights, or disciplinary problems in school (70% vs. 24%, p <.003); and having had previous psychiatric treatment (45% vs. 24%, p <.04). However, despite the high rate (65%) among the suicide cases of inhibited/withdrawn/overly sensitive "personality," they did not differ from the case-controls (25%) in this regard.

Although Bourque and associates (19) focused on long-term trends in suicides among females only, the data are useful to us

because they are analyzed by age. In this methodologically careful study, the authors examined the coroner's records in Sacramento County (CA) over a 55-year period; both case ascertainment and data retrieval accuracy were verified. In the final tabulation, data on Asian and Black women were excluded because of the small sizes of these subsamples. The authors appeared confident in their findings particularly because, since the 1950s, the county coroner's staff has been trained to systematically gather data on several psychosocial variables. The variables of interest to this paper included: "despondency," "emotional problems," "alcoholism," or "drinking problem," and prior psychiatric treatments. The data for the most recent 10-year period (1970-1979) are the most pertinent. During that time, 40 females, aged 15 to 24, were identified as suicides, of whom 85 percent had shown evidence of despondency; 45 percent had emotional problems or "unbalance;" 5 percent had recent arrests; 25 percent had prior psychiatric treatment; none had evidenced problems with alcohol.

In contrast, Sathyavathi (15) found a low rate of "mental illness" among children who killed themselves in Bangalore, India, during the years of 1967-1973. In this total population survey of suicides reported to the police (n = 1834), the author found 45 cases aged 14 years old or younger and 351 cases aged 15 to 19; only the findings on the younger aged group were summarized. The records were scrutinized for the presumed "causes" or "motives" of the fatal act. In 10 cases, the cause was "unknown." Categorization of the remaining records showed that in 12 percent, "mental illness was reported as the cause of suicide." Unfortunately, the author had no details as to the nature of the mental disturbances.

Another suggestive set of findings was reported by Marek et al. (20), based on their survey of all documented suicides in Cracow, Poland, for the period 1960-1974. There were 76 cases of youth suicides (aged 8 to 18). Although note is made of "mental disease such as schizophrenia, epilepsy, and characteropathy" (n = 3), as well as drug addiction (n = 3) in the cohort, the manner in which these diagnoses were ascertained and the exact meaning of the terms are ambiguous.

The final total population survey we summarize was conducted in Upper Austria, for the years 1977 to 1979 (21). The families of all 47 "adolescents" (age criteria not given) who committed suicide in the 3-year period were contacted; 29 families were finally interviewed within two to four years of the suicide. Based on a multi-item questionnaire, the deceased youths (aged 9 to 20) had the following attributes: 14\percent (n = 4) had a history of psychiatric treatment ("including two psychoses"); "2/3 had shown behavior disturbances;" 7 percent (n = 2) were "beginning stage" drinkers; and 10 percent (n = 3) were "unmistakably drug addicts."

Unfortunately, an extensive exposition of another cohort (aged 17 or younger) is uninterpretable for our purposes (22). For reasons best known only to the author, the psychosocial data on all official cases of suicidal acts by youths in Israel (for 1963-1966) were combined for the fatal-outcome and nonfatal-outcome cases (n = 21 and n = 343, respectively). We must also take note of a widely cited, mostly narrative-report by Jan-Tausch (23) on suicide among school children in the New Jersey public school system during 1960-1963. Although it was probably the first U.S. survey of its kind, its description of 41 child suicides (aged 7 to 19), did not include information on psychiatric or mental illness. Additionally, the study did use a preselected sample (rather than the general population), although the specific method by which cases were ascertained was not well described.

Table 5 summarizes some of the salient data from the studies we just reviewed. Findings on psychiatric variables (diagnoses, conditions, symptoms) are extremely difficult to synthesize because of the range of linguistic labels used, the lack of definitions, differences in data retrieval methods, and significant changes in "diagnostic habits" across the years.

Suicide Attempts and Psychiatric Diagnoses

Given the scant diagnostic information on completed youth suicides, we decided to examine also the evidence available on the relationship between psychiatric diagnoses and attempted suicide in the same age group. This strategy has been criticized because many attempters never complete suicide (24), and because systematic differences in demographics and diagnosis have been found between attempters and completers in both youth and adults (24 to 27). Nevertheless, it is also true that there is overlap between the two groups. For example, from a prospective viewpoint, suicide attempts among adults also represent a risk factor for completed suicide (28). It is known that up to 75 percent of adults who committed suicide had made previous attempts or threats (29). Attempts also predict future attempts; thus, about one quarter of adults who attempt suicide had at least one previous attempt (30).

The data for youth are similar. As in adults, sex ratios are different for completed and for attempted suicides. For every completed suicide in children and adolescents, there are at least 3 to 4 attempts in boys and 25 to 30 in girls (31). Among adolescent attempters, the male/female ratio is approximately 1:4, but in preadolescence it is 1:1 (31-33). In approximately 9/10 cases, drug ingestion was the method of choice (31,32,34). In two large studies of youth attempters 16 percent and 37 percent of their subjects had made at least one previous attempt, and 6 percent and 17 percent of the samples, respectively, had

Prevalence of Psychiatric Variables Reported in Total or Partial-Population Surveys of Youth Suicides

	Study (by Reference List Number)						
Variable	14 16	17	19	18	15	20	21
Location	U.S.	U.K.	U.S.	U.S.	India	Poland	Austria
Years: 19_	81-83	62-68	70-79	80-83	67-73	60-74	77-79
N described	133	30	40	20	45	76	29
Age range	"<30"	12-14	15-24	12-19	"≤14"	8-18	9-20
Psych. data source:							
records-coroner	X	X	X		X	X	
records-other	X	X		X			
interviews	X			X			X
Psych Rx (%)							
Past	52		25	45			14
Current	23	30					
Mental/emotional problems/illness (%)	92+	50+	45+		12	4	*
Behavior/conduct disturbances (%)		*		70			67
Psych symptoms (%)		87	85	65			
Drinking problem (%)	53++		0	70			7
Drug problem (%)						4	10

Table 5.

made two or more attempts (31,32). More important for this review, in Otto's study (31), child and adolescent attempters who ultimately killed themselves in the 10 to 15 year followup period were more likely to commit suicide in the first two years after the attempt, but the risk continued all through the followup, and repeated attempts constituted a major predictor of suicide in the boys in this sample. The suicide rate on followup in male attempters was 11.3 percent, a 7-fold increase over the control group. In the female attempters, the suicide rate was 3.9 percent, a 2-fold increase over the control group. Followup showed that about 19 percent of the male repeated attempters at intake, versus only 8 percent of those without prior attempts, subsequently completed suicide. The predictive power of early attempts for future suicidal acts has also been reported by Stanley and Barter (35) and by Cohen-Sandler et al. (36) in youth and by Tefft et al. (37) in adults, among others.

There is some evidence that suicidal attempts in childhood and early adolescence may be particularly associated with later suicide. In Otto's study (31), besides the history of repeated attempts for boys, other factors associated with later completed suicide among these attempters were male sex, length of prior functional impairment (which was, in turn, associated with attempts under age 13 years, and with major psychiatric disorders like manic depression and schizophrenia, in both boys and girls), and the use of active (violent) methods. Girls who used active methods in their attempts accounted for only 7 percent of all girl attempters, but appeared unique in that they were also overrepresented among those whose first suicidal attempt occurred before the age of 13; they were more likely to have left a note and to have attempted suicide by hanging than by overdose. This divergence between intent and lethality has also been found among suicidal prepubertal children with major depression (38). It is apparent that pre- or peripubertal attempts may carry the highest risk for future suicide completion. Unfortunately, good prospective diagnostic studies focusing on very young attempters cannot be found in the literature.

Psychiatric characteristics of youth who attempt suicide

Bergstrang and Otto (39) collected charts on 1727 patients under the age of 21 years who had presented to all hospitals in Sweden between 1955-1959 for attempted suicide. Evidence of parental mental illness (28%), parental alcoholism (15%), and father's absence (44%) were characteristics of the group. Otto (40) reexamined a probably representative subsample of 484 cases that yielded enough information to make a psychiatric diagnosis. Neurotic-depressive reaction was diagnosed in 30 percent of cases, neurosis in 23 percent, schizophrenia in 12 percent (19% in boys and 9% in girls), manic depression in 5 percent, and psychopathy in 13 percent (18% of boys and 11% of girls). Only primary diagnoses were considered. In an attempt to delineate a presuicidal syndrome in children and adolescents, Otto (41) could only ascertain that during the 3 months before the attempt, the symptoms of some mental disorders--namely, anxious and depressive neurosis, schizophrenia, and manic depression--had worsened considerably in about 50 percent of patients with these diagnoses. Personality characteristics showed much less change during the preattempt period. In a 10 to 15 year followup of the original sample (31), the investigators selected a control group matched for age, sex, and geographical birth site. Attrition rate of the attempter sample was only 10.4 percent. The attempters on followup had committed more legal offenses. Mental conditions in military health classifications were 10-fold higher (53%) in the attempters. Unfortunately, no systematic analysis of the predictive power of psychiatric diagnosis for suicide outcome was provided.

In a cross-sectional study based on chart reviews from a pediatric emergency room (ER), Garfinkel et al (32) identified 505 children and adolescents who had made 605 suicide attempts, and compared them with

505 nonsuicidal patients who had come to the same ER at the same time. Prior substance abuse, past history of psychotherapy, and current (not specified) psychiatric diagnoses (most frequent symptoms were dysphoric affect (55%) and aggressiveness and hostility (41%)) were significantly more common in the attempters. The families of the attempters had significantly higher rates of history of mental illness (especially drug and alcohol abuse), suicide, paternal unemployment, group or foster placement, and absence of father. Only 36 percent of the attempts were judged to have carried a moderate or high danger (criteria not provided). These were associated with family history of suicide and current psychiatric symptoms, although this analysis included 100 patients twice and it is therefore flawed. After a followup for up to 9 years, 8 of the 505 attempters had died by hanging, overdose, or motor vehicle accident, while the 5 deaths in the control group were due to medical disease.

Brent et al. (34) also used chart reviews to study the characteristics of 131 consecutive suicide attempts by 126 children and adolescents presenting in a pediatric emergency room between 1978-1983. The median age was 14 years. A bimodal distribution was noted, with approximately one-third of attempts noted to be medically serious, which usually involved a high degree of planning and use of a psychotropic agent (rather than an over-the-counter agent) (34). The following variables were associated with a medically serious attempt: male sex, family history of affective disorder, high suicidal intent, and a diagnosis of affective disorder, either in isolation or associated with substance abuse. The following distribution of diagnoses were found: affective disorder (39%), conduct disorder (26%), substance abuse (23%), and adjustment disorder (26%). Many of the patients had multiple diagnoses. Multivariate analysis of these data suggests the existence of two groups of attempters: **a dysphoric, affectively disturbed, hopeless group** whose lethality is very much a function of intent, and **an impulsive group** whose lethality is very unpredictable. In fact, the class of agent ingested was the most important variable to predict the medical seriousness of the attempt in this impulsive group.

Strober (42) compared 250 suicidal inpatient youths aged 10 to 18 years with an equal number of nonsuicidal inpatient controls matched for age, socioeconomic status, and sex. From a diagnostic point of view, emotional, neurotic and conduct disorders (depression was "hidden" within these two categories, according to the author) were more prevalent in the suicidal group, although statistical significance levels are not reported. Alcoholism was only present in the suicidal group (5%). But Carlson and Cantwell (43), in a sample of 102 clinically referred children and adolescents, found that suicide attempts occurred with and without the syndrome of depression. Attempters did not differ from nonattempters in any particular diagnostic category.

Several studies have included only adolescents. In such studies, "neurotic" depression, conduct or personality disorders, and alcoholism, are the most common psychiatric diagnoses (44,45). As new assessment methods become more generally used, several reports have emphasized the relationship between suicidal attempts and major depression in adolescents (34,46-48). All these papers have also emphasized the increase in alcohol and drug abuse as an associated diagnosis to major depression, and also as a precipitant to the attempt. A similar point has been made by McKenry et al. (49) and by O'Brien (50). One study found a 5-fold excess of patients with epilepsy among attempters, of whom 60 percent were under 30 years old. Phenobarbital was the most frequent overdose (51). Brent (52) replicated this finding recently in adolescents, indicating further that 8/9 epileptic attempters were receiving phenobarbital as their main anticonvulsant. Studies of adolescent delinquents show similar agreement. Depressive symptomatology and suicidal behavior were found to be associated among 48 delinquent girls aged 13 to 18 years. All 23 girls with his-

tory of suicidal attempts were rated as moderately or severely depressed. In turn, depression and suicidality were mainly associated with antisocial and neurotic personality patterns. Some of the girls showed no suicidality in spite of marked depressive symptomatology (53). Alessi et al. (54) reported similar findings with a sample of incarcerated adolescent delinquents of both sexes. Those with major affective disorders or borderline personality disorders presented the highest suicidality and committed the most serious attempts. But there also is substantial evidence that various other characteristics (i.e., externalizing symptoms, impulsivity and borderline personality) may also be related to suicidality in the absence of an affective syndrome (34,55-57,17).

Studies of only preadolescents with suicidal behavior had to address suicidal threats and ideation, especially those with a definite plan, because actual attempts in this age group are rare. Evidence suggests that suicidality before 13 years may constitute a very high risk for later suicide (31). Myers et al. (58) compared chart reviews of 61 suicidal and 287 nonsuicidal preadolescent inpatient children. Depressive disorders were present in 30 percent of suicidal children and only 3 percent of the controls. This was the only diagnosis for which the rate significantly differed between the two groups. Other variables that differentiated the groups were family history of suicidal behavior and abuse of the mother (usually by the father). In a series of uncontrolled studies, Pfeffer et al. (59,60,61) have repeatedly found that prepubertal children with suicidal ideation, threats or acts, frequently present symptoms of depression, hopelessness and low self-esteem, psychomotor activity, conduct disorder, and that the parents present suicidal behaviors and/or depression. Ryan et al. (38) found that among prepubertal major depressive children, 46 percent present with persistent and severe suicidal ideation involving at least a concrete suicidal plan. Kazdin et al. (62) found that hopelessness related more closely than depression to suicidal intent in prepubertal inpatients, a finding similar to that for adults, whereas hopelessness has been shown to be the key link between depression and suicidal behavior (63) and also predicts later suicide in samples of depressive patients (64).

Therefore, it appears that affective disorders, alcoholism, and other drug abuse play the same central role in regard to suicidal attempts among youth, as they do in completed suicide in youth and in the rest of the age spectrum. Schizophrenia appears more related to suicide than to attempts, whereas personality diagnoses may relate more to attempts. The primacy of unipolar and bipolar affective disorders and alcoholism, as well as schizophrenia and schizoaffective disorder, as the diagnosis most often associated with adult suicide has been known since the 1960's (65–70). But there appears to be no doubt that there is also a prominent component of irritability, aggression, impulsivity, borderline features, and conduct disorder among seriously suicidal young people, which is similar to findings in adults (71-73). It should be noted that many of these symptoms are by no means inconsistent with the diagnosis of an affective disorder (74) and especially bipolarity (75). Further refinement of diagnostic instruments and improvements in clinical skills to diagnose mixed bipolar illness in adolescents, which probably is the commonest presentation of bipolarity in adolescents, are likely to bring about further advances in the clinical characterization of this aggressive-impulsive subgroup. Nevertheless, it is also likely that a subgroup of impulsive suicidal adolescents will remain outside the major classical diagnostic categories. Their nosology and biology will require further study.

Familial patterns of suicidality and psychiatric disorders

It is clear that suicidality cuts across several psychiatric diagnoses, the most frequent being bipolarity, nonbipolar MDD, alcoholism and substance abuse,

schizophrenia, and perhaps some personality disorders including, borderline and antisocial. In addition, several of the studies previously cited have noted the frequency of suicidal behaviors in the relatives of suicide attempters and victims. Another way to study the relationships between specific psychiatric diagnoses and suicidality is to review their patterns of association in families, to determine if the familial transmission of suicidality overlaps with, or is independent from, the psychiatric disorders just mentioned. This strategy is possible because most of the diagnoses involved, as well as suicidality, have been shown to aggregate in certain families. Although most of the data come from adult studies of affective disorders, the findings are relevant to this review because there is increasing evidence of diagnostic continuity between youth and adults in most of the diagnoses involved, as well as in suicide, and because young adult, probands and relatives, were also included in many of the studies.

Most of the evidence indicates that although some diagnoses (i.e., major affective disorders) and suicide may be associated within families, familial transmission for suicidality and for psychiatric diagnoses are separate and probably independent. Overall, the data suggest that, given a positive family history of suicide, a superimposed major psychiatric disorder constitutes a serious risk factor for suicide.

In a study of adult primary major depressive probands, only age of onset of affective illness and the secondary diagnoses of alcoholism or an anxiety disorder in the proband were independently related to higher familial aggregation for major depression in relatives. On the other hand, suicidality or the presence of any of the following clinical characteristics during major depressive episodes in the proband showed no independent relationship to familial aggregation for affective illness: any of the Research Diagnostic Criteria depressive subtypes, recurrent depression, or hospitalization (76). A chart review of 243 inpatients with a definite family history of suicide in a first or second degree relative, and 5602 inpatients without such family history found that almost half of the index group had attempted suicide, and that more than half had an affective disorder. A family history of suicide increased the risk for suicidal attempts across the following diagnostic categories: schizophrenia, unipolar and bipolar affective illness, dysthymia, and personality disorders (77). Similar findings were reported by Tsuang (78) comparing suicide rates among adult schizophrenics, manics, depressives, and surgical controls. Suicide rates were high for all psychiatric patient groups, and the relatives of patients who had committed suicide had higher risk of suicide than the remaining relatives.

Egeland et al. (79) reported that, among the Amish, 78 percent of all suicides in the last century were accounted for by four extended pedigrees with high density for major unipolar and bipolar affective disorders, which together account for only 16 percent of the Amish population. Nevertheless, other Amish pedigrees with heavy loading for affective illness present no suicidal acts among their members. Similarly, Linkowski et al. (80) in a study of 713 major depressive inpatients found that a family history of violent suicidal behavior was associated with the same in the proband, and the effect was more marked in bipolar women. In a sample of 50 bipolar patients, those with a family history of suicidality also had suicidal attempts, and associated alcoholism in the parents or in the probands increased the risk (81). From another viewpoint, the findings of Murphy and Wetzel (82) point to the possibility that in the presence of a similar family history of suicidal behavior, the presence of affective disorder or alcoholism, or both, in the proband will substantially increase the person's risk of completing suicide compared to cases with other or no psychiatric diagnoses.

CONCLUSIONS

The available figures suggest that the condi-

tion of psychiatric "patienthood" in the adolescent and young adult years is associated with an alarmingly high mortality risk via suicide. This conclusion is inescapable in light of the general population base rates for death-by-suicide for these age groups (83), and in comparison with the suicide mortalities associated with most psychiatric disorders among adults. Using very global and "rough" estimates, psychiatrically disturbed youths may be running a risk of suicide about 200-fold (or more) the rate of their general population counterparts. And psychiatric illness in the young also seems to pose a suicide risk that may be up to five times higher than the rates reported for adult patients (see below).

Although changes in diagnostic practices in child psychiatry and in the use, definition, and meaning of psychiatric labels make it exceedingly difficult to compare the risk value of various conditions, tentative conclusions can be made. The "classic" mood and thinking disorders, namely, affective illness and schizophrenia, are prognosticators of suicide mortality. Because much of the supporting evidence derives from studies of youths with a history of inpatient hospitalization, the implication is that the major factor could be the presence of psychosis. Among the affective disorders, this would further imply that bipolarity in this age groups is likely to be a major factor (12). The addictive disorders may also carry a high risk value, although the study of these conditions has been constrained by the fact that their incidence and prevalence may be far more subject to societal factors than seems to be the case for affective disorders and schizophrenia. Finally, data are scant on the prognostic value of "neurosis" or personality disorders for suicide in the preadult years. In no small measure, the relative absence of such evidence probably reflects long-standing debates about the diagnostic validity of these conditions in juveniles.

Our conclusions about the risk value of psychiatric illness for suicide in the younger years is underscored by the data on the prognostic value of these conditions among adults. This body of information also suggests that "patienthood" is associated with elevated suicide rates; that the risk is probably higher for previous inpatients than outpatients; and that, although the mortality figures even within diagnostic groups vary, affective illness, schizophrenia, alcoholism, and disorders involving drug addiction probably carry the highest relative risk in this regard.

For example, in this recent 5-year followup report of 4,800 consecutive, first-admission VA psychiatric inpatients, Porkorny (84) found a suicide rate of 279/100,000 patients/year. In a similarly recent study, Morrison (85) estimated the suicide mortality among outpatients, using a large private practice sample ($\underline{n}$ = 12,500); the overall rate was found to be 120/100,000/year.

The rates for particular psychiatric conditions are difficult to interpret because of their variability. The variability is especially evident with data that were presented in percentages or frequencies without adjusting for the length of the followup. Miles (10), who, in his comprehensive review of this body of literature estimated the overall risk for several conditions, arrived at 230/100,000/year suicides for depressives; 270/100,000/year for alcoholics; and up to a 3-fold higher suicide rate for adult opiate addicts. However, the variable data bases with which Miles (10) had to contend can be readily illustrated in reference to schizophrenia. Recently reported suicide figures for this diagnosis yield rates ranging from a low of 203/100,000/year (86) to a high of 456/100,000/year (87).

Given the available evidence, therefore, it is difficult to say whether affective illness in adults is associated with a lower, higher, or equivalent suicide risk than schizophrenia, for instance. However, the two most recent studies of unselected adult patient samples give every indication that different conditions make differential contributions to the cohort's overall suicide rates. In Pokorny's (87) sample, for example, diagnosis-specific

suicide rates varied from a high of 695/100,000/year for affective disorder to a low of 71/100,000/year for organic brain syndrome, with other conditions occupying the middle ranges (e.g., 187/100,000 for alcoholism). Likewise, in Morrison's adult outpatient series (85), the suicide rates ranged from 42/100,000/year for "unipolar' affective disorder, through 318/100,000/year for bipolar illness, to the peak of 411/100,000/year for schizophrenia. Suicide rates for "personality disorders" as well as for the "neurosis" have been also estimated. The overall trends suggest that these diagnoses are also associated with elevated risk rates, although by no means as high as those cited above (e.g.,10,85).

In light of the available information on the various disorders in adults, it is more than likely that the major psychiatric illnesses also contribute differentially to the overall rate of suicide among children and adolescents. Furthermore, the diagnostic findings in attempted suicide in youth point in the same diagnostic directions as those for completed suicide, except for a larger overall proportion of cases with "personality disorders." Given the diagnostic problems associated with these conditions, not the least of which is that mixed bipolar illness can be easily missed, even when the patient can be interviewed, it is not unthinkable that this could also occur with post-suicide diagnoses. Thus, identifying a group of child and adolescent suicide attempters who resemble suicide completers may be very useful, not only for therapeutic and preventive purposes, but also because this population may most closely approximate suicide completers. Moreover, from these attempters, we could learn the most about the affective, cognitive, and biological process that characterize the young patients who actually do commit suicide.

Some have proposed focusing on patients who have engaged in suicidal behavior of high lethality and intent, on the assumption that only chance circumstances allowed their survival; however, in adolescent and adult subjects, such "chance" survival may represent lower intent. Although cluster analyses of data on adult suicidal attempters reveals a group who used more violent methods, with more intent to succeed (71), nevertheless, adolescents and adults with the highest intent are still much more likely to kill themselves, thereby removing themselves from prospective scrutiny (64,88,89). However, in prepubertal children, there is a discrepancy between intent and lethality which makes the situation quite different. While suicidal ideation with a plan occurs among prepubertal children with MDD almost as frequently as in their post-pubertal counterparts (46% vs. 49%) (38), the suicide rate among prepubertal children remains quite low (3,17), in spite of its secular increase among adolescents and young adults. Prepubertal children's lack of cognitive maturity and skills necessary to complete suicide probably accounts for the low rates (3,17). Therefore, this age group provides the opportunity to study suicidality naturally untruncated by suicide completion. The findings reviewed earlier, showing that attempts before age 13 seem to carry a bleak prognosis for later suicide, also suggest that prepubertal suicidality may be much more representative of completed suicides and deserve special study. Suicidality of very early onset may enable the selection for future studies of those attempters who are most at risk, as the closest approximation to completed suicides.

This approach would be consistent with the findings by one of us regarding differences in GH responses and REM latency, and in their patterns of association, among suicidal and among nonsuicidal prepubertal children with major depression, both during the episode and in the recovery drug-free state. Such findings may relate to the evidence for the association of a functional CNS serotonin deficit in adult suicides (90-103), which may be familial (102). Furthermore, the evidence for familial aggregation of suicidality is also consistent with higher risk with earlier age of onset, especially if genetic factors are at least partially responsible for such familial transmission (104-106).

It is difficult to integrate the pertinent data on youths who have killed themselves with the information on the prognostic value of psychiatric illness in juveniles. In part, this is a consequence of the methodologic problems posed by the use of coroner's records and "psychologic autopsies." In this ex post facto database, probably the most "hard core" indicator of psychiatric illness is a positive history of mental health care. However, even those figures can be only approximations of the prevalence of mental illness in the cohorts because treatment is mediated by a variety of factors including recognition that a disorder exists, the availability of mental health treatment resources, awareness of such resources, and social influences that determine referral patterns. With the above caveat in mind, we used known rates of treatment referrals for pediatric cohorts to interpret the pertinent data on completed suicide among youth.

In their review of epidemiologic studies, Gould and associates (89) noted that "almost all psychotic children and adolescents are known to some treatment facilitiy." But only approximately 1 percent to 49 percent of "maladjusted" children receive mental health care. If we eliminate figures that included treatment by general medical personnel (e.g., pediatricians), 30 percent is about the upper limit of treated cases among "maladjusted" youths. Turning to information about rates of referral, Costello (107) found that, from about 2 percent to 5 percent of youngsters seen by primary health care providers (pediatricians, family practitioners) are referred to mental health specialists. She also estimated that 50 percent is the modal referral rate for youths who had been definitively identified by their health care providers as having a psychiatric problem.

The reported rates of psychiatric treatment or contact among youths who have committed suicide in the United States and Britain (see Table 5) therefore suggest that these youths were unlike normal pediatric populations, but similar to maladjusted or disturbed juveniles. That is, the portions of youth suicides with known histories of psychiatric care--from one-third to about one-half of the samples--are far higher than the mental health referral rates in the general youth population. But the figures on the suicides are comparable in this regard both to the portion of psychiatrically identified cases who have been referred for treatment and the portion of maladjusted youths who actually received mental health care.

Our conclusions must be viewed in light of the "methodologic" problems that confound a review of this body of literature. First, using conventional referencing methods, it is not possible to access every study of mentally ill youths that may have found suicide among the sample (e.g., 7), because of the way in which the studies were apparently indexed. Second, in some of the available prospective studies of psychiatrically ill juveniles, the absence of data on suicide could mean either that this outcome was **not** observed or that the investigators did not look for it (e.g., 11,108,109). Third, some of the published data are inconsistent, which is most evident in multiple publications regarding the same cohort. For example, the followup time intervals and the sample sizes may be discrepant (6,74) or case frequencies with certain diagnoses may not exactly correspond (14,16). Should it be desirable to conduct a meta-analysis on the reported findings, such methodologic issues need to be taken into account.

In summary, there is significant evidence that major psychiatric disorders constitute an important risk factor for completed and attempted suicides in children and adolescents. The efficacious treatment and care of psychiatrically ill youths may be the most feasible way to alter their risk of suicide.

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PERSONALITY AS A PREDICTOR OF YOUTHFUL SUICIDE

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INTRODUCTION

This paper will summarize the limited available literature on the personality risk factors associated with youth suicide and will outline the methodological difficulties inherent in this line of investigation. Personality disorder research has recently flourished greatly because the Diagnostic and Statistical Manual III (DSM III) provided a separate axis for personality diagnosis and specified explicit criteria defining each of the personality disorders. This has led to the development of reliable semistructured interview instruments to assess personality disorders in adults. Preliminary findings also suggest that personality disorders may influence, in important ways, the presentation, course, biological test results, and treatment response of various Axis I conditions. Thus far, however, there has been very little systematic research on personality assessment in children and adolescents, and there are many inherent conceptual and practical obstacles to any precise determination of the personality risk factors for youth suicide.

We will briefly review personality variables associated with suicide in adults, summarize research on the personality variables associated with youth suicide, and outline a number of the pertinent methodological problems and some of their possible solutions. We will conclude with suggestions for future research, current clinical practice, and prevention. The most interesting question that emerges from this review is the degree to which the personality factors that predict youth suicide are equivalent to factors that also pertain to adult suicide. This question has important theoretical, clinical, and prevention implications.

Personality Predictors of Adult Suicide Behavior

The two DSM III personality disorders most clearly associated with adult suicides, both completed and attempted, are the borderline (BPD) and the antisocial (APD) (1). Suicide rates for several-year followup studies of BPD patients are reported at 4 percent (2) and 7 percent (3); on a 15-year followup, the rate was 7.5 percent (4). Several studies suggest that the comorbidity of BPD with affective and/or substance abuse disorders results in particularly lethal combinations (5-7). Although most self-destructive behavior in BPD patients is probably nonlethal in intent, a substantial portion of BPD patients do eventually die by suicide, usually in young adulthood.

Reported rates of suicide attempts in APD individuals vary considerably (11%-46%),

perhaps because of differences in underlying base rates of APD and of suicide attempts in the samples studied and the fact that most studies did not use DSM III criteria (8-10). It is thus difficult to generalize the findings across studies. It is estimated that 5 percent of APD individuals eventually die by suicide (8-11). APD may also predict for frequent and recurrent attempts (12-14). These may occur in response to anger and frustration in interpersonal relationships and in order to manipulate others (15,16). The comorbidity of APD with affective and/or substance abuse disorders may, as with BPD, result in more frequent and more lethal attempts (6,17,18).

The psychology literature has employed a different strategy to determine the personality predictors of suicide. Rather than assessing the presence of a categorical personality disorder in suicidal individuals or the rate of suicide in those with personality disorder, many psychology studies have measured specific personality dimensions or traits in suicide attempters and/or completers. Attempters and completers appear to be different in their personality and in other characteristics. Attempters have the more disturbed personality profiles and are also more likely to be young, female, to lack an Axis I diagnosis, and to commit public, impulsive, suicidal acts using less serious means (19). Most of the personality dimensions that have been studied apply only to suicide attempters and may not generalize to completers.

The following personality traits seem to be particularly characteristic of suicide attempters: aggression or hostility (20-29), impulsivity (30), social withdrawal or interpersonal difficulties (31-37), low self-esteem (38-45), dependency (21,26,27,46), hopelessness (47-49), external locus of control, rigid cognitive style, and poor problem solving (54). The many studies that have tested the ability of the MMPI to differentiate suicidal patients have been inconsistent (55), and the same is true for studies of the association of hysterical traits and suicide (24,25,56,57,58). Studies using the Eysenck Personality Inventory fairly consistently find high neuroticism, psychoticism, and introversion scores (59-62). The major limitation of available personality dimension studies is that each has tended to assess in isolation only one or a small number of dimensions so that we don't know the degree and direction of convariation among them and the amount of total variance they explain. Dimensional personality trait measures may also be difficult to obtain in ordinary clinical situations.

Recently, a particularly fascinating connection has emerged between the personality dimension of aggressive impulsivity in suicidal and violent individuals and the biological finding of low central nervous system serotonin turnover (63-67). The association holds up in patients with impulsive personality disorder, even in the absence of an Axis I diagnosis of affective disorder (68,69). The serotonin dysfunction appears to represent more a trait than a state condition (70). It has been postulated that a central problem in serotonergic metabolism may contribute to the individual's impulsivity, aggressiveness, and suicidal potential, which then may be released in the presence of clinical depression.

Personality Predictors of Youthful Suicide

This paper reviews the available research literature on personality traits and disorders in adolescent suicide attempters and completers. Most of the literature on personality applies to suicide attempters and may not generalize to completers. The four studies on completed suicides in youth are retrospective and do not utilize standardized personality measures. In studies of attempted suicide, assessments frequently are brief and often are made in crisis settings. Patients in these studies who are not admitted to the hospital are difficult to follow and frequently do not want to discuss their suicide attempt. Assessment of personality occurs at variable time intervals from the attempt and

may be confounded by the presence of an Axis I diagnosis and by stress.

Very few of the studies reviewed have used systematic and rigorous diagnoses of personality disorder since the focus of attention has usually been on Axis I disorders. A variety of different control groups have been used in some studies but not in others. Because suicide is an event with relatively low frequency, there are few prospective studies in the literature. Furthermore, there are extremely few studies of suicide attempters in a population with identified personality disorders. This review focuses on studies using standardized personality measures and assessments with appropriate control groups. The most frequently used method of assessment has been the questionnaire, but issues of reliability and validity are infrequently addressed, and the findings and measures have not been replicated in other studies (11).

Conduct Disorder: Strictly speaking, childhood conduct disorders cannot be considered the exact equivalent of personality disorder since the majority of children who qualify for this diagnosis do not go on to display a pattern of adult categorical disorder (71). Nonetheless, we discuss conduct disorders here because they tend to be relatively stable and are, by far, the sturdiest predictors of adult antisocial personality. The fact that conduct disorder is a major risk factor for both youth suicide and for adult antisocial personality disorder (which itself predicts for adult suicide) suggests that this diagnosis deserves special treatment and preventive attention.

Conduct disorder appears to be strongly associated with both suicide (72-74) and with suicide attempts (75-77). Conduct disorder is much more common among male suicide victims, and the precipitating event for the episode is often a disciplinary crisis. There is a frequent comorbidity of conduct disorder with affective, substance abuse, and borderline personality disorders, and the frequency and lethality of attempts increases with the degree of comorbidity. The few studies reviewed here that have systematically assessed for conduct disorder in suicidal youngsters are supported by the additional studies to be reviewed soon that have found aggressive, impulsive, and irritable personality traits to be more generally associated with suicide.

Borderline Personality Disorder (BPD): Although the construct of borderline personality disorder has not yet been carefully investigated or validated in adolescent patients, there are several interesting preliminary studies suggesting that it is often present and can be reliably diagnosed in adolescent suicide attempters (78-81). It also appears that the comorbidity of BPD and other disorders in adolescents is particularly likely to predict for more frequent and more lethal suicide attempts. Friedman et al. (82) found that among 76 adolescent inpatients, those who met criteria for both BPD and for major affective disorder were the most suicidal. In this same sample, Clarkin et al. (78) found that adolescent suicidal patients were equivalent to their adult counterparts in the prevalence of personality disorders (defined by a duration criterion of one year). Crumley found that BPD was the most common personality disorder in a group of hospitalized adolescents and that this diagnosis usually coexisted with major depression (67%) and/or substance abuse (77%). Alessi et al. (81) found a high prevalence (35%) of BPD in a sample of incarcerated juvenile offenders who would presumably also meet criteria for conduct disorder. The BPD diagnosis strongly predicted for greater frequency, seriousness, and lethality of suicide attempts. The association between BPD and suicide held up in both the Friedman (82) and the Alessi (81) studies even when the suicide item was itself eliminated as a criterion for making the BPD diagnosis, thus removing the risk that the association was merely a tautological artifact resulting from the fact that the DSM III definition of BPD includes one criterion devoted to suicidal behavior. Pfeffer (76) and colleagues found that BPD was the most frequent diagnosis among 48 preadolescent

inpatients who were both assaultive and suicidal.

The place of the BPD diagnosis remains controversial in adult psychiatry and this is even more the case for adolescent patients who have received less systematic personality disorder assessment. Nonetheless, it seems likely that a diagnostic construct tapping characterological instability usefully predicts for suicidal behavior and this can be reliably assessed fairly early in life.

It is of great theoretical interest, and also of practical importance, that antisocial and borderline personality disorders that are most associated with adult suicidal behavior are also, in their adolescent form, (that is, conduct disorder substituting for antisocial) the most common personality disorders predicting adolescent suicidal behavior. Moreover, the personality trait measures associated with suicide are similar in adults and adolescents.

Personality Traits: In contrast to the relative paucity of studies having systematic psychiatric diagnosis, a number of studies have focused on personality traits in suicidal youngsters. The personality traits most commonly found in suicidal adolescents are equivalent to those found in adults and include aggressiveness (83-87), irritability (89-92), low frustration tolerance (83,84), social isolation (83,87,92-98), hopelessness and helplessness (91,104), poor self-concept (90,91,99-101), sexual conflicts (93,101,102), poor problem solving (100,103), resentfulness (88), and external locus control (105). It is of interest that these personality traits (especially aggressiveness, irritability, low frustration tolerance, and resentfulness) are fully consistent with the personality diagnostic categories (i.e., conduct disorder, borderline personality disorder) most often found in youthful suicides.

As is the case in studies of personality dimensions in adults, there have been several major problems in studies of such dimensions in adolescents. Generally, a given study focuses on only a small number of possibly important dimensions so it is impossible to determine the degree to which the various dimensions can vary. Predictors are reported to be significantly different in large groups of suicidal individuals compared with nonsuicidal individuals, but the absolute and comparative predictive powers of the variables for the individual patient are not calculated. Studies of personality traits are usually not coordinated with studies of personality disorders so it is impossible to determine the degree to which these are correlated. Finally, there is the problem of comparison groups. Many studies of personality traits of suicidal individuals compared them to normal controls. Unless subjects are equivalent in their psychiatric diagnosis, it is impossible to determine the degree to which a given finding in the suicidal group is specific to suicide or whether it represents a trait more generally characteristic of psychiatric patients.

METHODOLOGICAL ISSUES

The Ability to Assess Personality in Youth: Before we can confidently determine whether particular personality disorders or personality traits are useful predictors of suicide, we must address the more fundamental question about the degree to which personality assessment is meaningful in the younger age groups. How does personality diagnosis in children approximate that in adults?

The DSM III definition of personality disorder requires an age of onset that occurs by adolescence or earlier and a continuous course throughout most of adult life. The relationship of personality disorder diagnosis in children and adolescents to that in adults is addressed specifically, and in some detail, in the introduction to the DSM III personality disorders section. It is proposed (without any great empirical support) that certain diagnostic categories from the DSM III Infancy, Childhood, and Adolescence section correspond to, and in effect eventually develop into, certain personality disorders (e.g. Schizoid Disorder of Childhood or Adolescence into Schizoid Personality Dis-

order; Avoidant Disorder of Childhood or Adolescence into Avoidant Personality Disorder; Conduct Disorder into Antisocial Personality Disorder; Oppositional Disorder into Passive Aggressive Personality Disorder; and Identity Disorder into Borderline Personality Disorder). The presumption is that the childhood or adolescent condition will be diagnosed if the individual is under age 18 whenever the personality psychopathology has persisted at an intensity sufficient to meet disorder criteria. Adult personality disorders without a corresponding childhood or adolescent category (e.g., hystrionic or paranoid) can be applied in childhood or in adolescence "in those unusual instances in which the particular traits appear to be stable. When this is done there is obviously less certainty that the personality disorder will persist unchanged over time."

Indeed, there are a number of reasons to be concerned that personality assessment may be less stable over time and predictive of future behavior in younger individuals. Since the past is the best predictor of the future in most things, including behavior, it makes sense to assume that the more of the past one has available, the more accurate the prediction will be. One is on statistically safer ground predicting that an individual with 30 previous criminal offenses by age 30 will soon commit more crimes than that a first offense at age 16 will be repeated over and over again. This general threat to the stability of personality assessment in early life is enhanced even further by three more specific confounds (personality/state; personality/role; and personality/developmental) which are also inherent problems in adult personality diagnoses but become especially problematic in assessing youths. We will discuss each of these in turn.

It is well documented that current state factors in adults (particularly the presence of accompanying mood disorder) greatly influence personality ratings by causing retrospectively distorted reporting of previous behaviors. State conditions, especially those that are chronic, may also interact in complicated ways with personality functioning; they may cause personality dysfunction or, conversely, personality dysfunction may predispose to state conditions, or, in many instances each may influence the other. The Axis I/Axis II confound presents major problems in adult personality disorder diagnosis, but there are several reasons to suppose that it is an even more difficult problem in childhood and adolescence. First, the various Axis I conditions have been less clearly and definitively described in younger patients and, in this age group, may be more likely to present in atypical or individual ways (perhaps influenced by developmental factors). Second, children have a less extensive track record on which to decide whether the problems are more state- or more trait-related. This combination of atypical Axis I presentations and a limited Axis II data base makes it doubly difficult to determine with any certainty whether a particular symptom or behavior (say irritability and/or poor conduct) arises from an Axis I syndrome (e.g., depression) or instead represents the early onset of stable personality features that may become manifest, for example, as conduct disorder or, ultimately, as antisocial personality.

The confounding of situational factors and personality disorders is also a problem in adult personality diagnosis but may be even more difficult in childhood because children tend to be more influenced by their social environment and its role expectations. For example, when a youngster presents with a conduct disturbance, it is difficult to determine whether he is responding to a disturbed family environment or to peer pressure or whether this is the beginning of what will become an antisocial personality disorder. In the first two instances, the appropriate diagnosis would be adjustment disorder with disturbance of conduct, with the expectation that the conduct problems will be self-limited if the precipitating stressors are removed. A diagnosis of conduct disorder or personality disorder implies that the behavior is more specific to the individual and likely to be

stable and manifest across different social situations and role expectations.

Developmental changes constitute the third specific confound complicating personality assessment in children and adolescents. It is often difficult to predict prospectively whether a given behavior represents a stage-specific manifestation that the child is likely to "grow out of" or whether it is the beginning of a stable and lifelong pattern of personality functioning. For example, as a group, adolescents in our society are probably more narcissistic, troubled by identity problems, and prone to conduct disturbances than they will be as adults. The diagnoses of narcissistic, borderline, or antisocial personality disorder therefore will be applied prematurely and too liberally if these are based on a small slice of developmentally influenced adolescent behavior. Rather, such diagnosis should be based on a longer and wider strip of life experience beyond the confines of the developmental epoch in which such behaviors are less pathologic and specific to the individual.

Despite all these methodological cautions concerning personality diagnosis in childhood, there is evidence that some personality characteristics consistent across time can be detected fairly early in life. A number of studies indicate that marked individual differences in aggression become manifest early in life (certainly by age 3) and remain stable to a degree that approximates the stability of the I.Q. There is also abundant evidence that the presence of conduct disorders in childhood is uniformly obtained in the histories of individuals who go on to exhibit adult antisocial personality. (Note, however, that the majority of childhood conduct disorder youngsters do not grow up to be antisocial.) (106-111). These data suggest that although many children with conduct disorders "grow out" of them, many others do not. A childhood diagnosis of conduct disorder predicts both for childhood suicide and also for adult antisocial personality. Thus, in the personality areas that most reliably predict youthful and adult suicide, the pertinent personality variables have demonstrated sufficient stability to suggest the value of early detection, treatment, and prevention.

The best, although partial, solution to the methodological problem raised in this section is to develop semistructured personality disorder interviews adapted for children and adolescents. This is analogous to the fairly recent development of specialized Axis I interviews adapted especially for children (KIDDIE SADS). It will be necessary to define more specifically the behavioral criteria for childhood personality disorder as this is not handled with sufficient clarity in DSM III. Personality assessment in children will always be more difficult and less predictive than in adults, but such assessment will improve as it becomes more systematic and as empirical data accumulate.

Possible Relationships Between Personality Variables and Suicide: Establishing a correlational relationship between personality variables and suicide does not alone establish the direction of causality. We will discuss the several possible relationships that may be involved:

a. Definitional overlap: suicidal behavior may form an inherent part of the personality disorder definition, just as suicidal behavior is included within the definition for major depression. For example, DSM III includes reference to suicide within the criteria sets for both the borderline and hystrionic personality disorders. Whenever suicidal behavior is included within the definitional set for a disorder, it is inevitable that there will be some connection between that disorder and suicide. To establish that the relationship is real and not just definitional, one must demonstrate empirically that the criteria set for the personality disorder predicts for suicide even when the suicide item is omitted.

b. Personality disorder directly predisposes to suicidal behavior or to a form of suicide attempt (e.g., if one considers the impulsivity and aggressivity of BPD as a direct cause of suicidal behavior).

c. Personality disorders may predispose to Axis I disorders (e.g., depression), which then independently increase the risk for suicide.

d. Personality disorders may exert an influence on the expression of the Axis I condition so that the suicide risk is increased (e.g., most depressed patients do not suicide; the presence of personality disorder may increase the vulnerability to suicide in depressed patients.

e. Axis I conditions (e.g., depression), especially in chronic presentations, may predispose to behaviors that are indistinguishable from personality disorders or may exacerbate personality characteristics so that they present at the disorder level and/or the combination may interact to increase risk for suicide.

f. Personality traits (e.g., impulsivity or aggressivity) that cut across the categorical Axis II personality disorders may predispose to suicidal behavior.

g. The covariation between suicide and personality disorders may be based on chance or on the covariation of each with some other underlying factor.

A number of different types of studies and analyses are necessary to establish the nature of causality. The first step is to document that the prevalence of personality disorders is higher in suicidal patients compared with nonsuicidal patients, controlling for Axis I diagnosis. This would establish that there is a greater than baseline or chance comorbidity. The degree of independent specific contribution to suicide of the pertinent personality disorders (BPD and APD) can be determined by comparing their rates of suicide with those that occur in other kinds of personality disorder and also comparing the rates that obtain for them with and without comorbid Axis I disorders. Studies should also compare that predictive power of the categorical DSM III disorder system with dimensional measures of pertinent personality traits (e.g., aggressivity).

Attempters vs. Completers: In adults, suicide attempters and suicide completers seem to constitute two separate, but overlapping populations. A previous attempt carries an increased risk of eventual suicide (2% in one year and 10% lifetime), but attempters do not greatly resemble completers in demographic, diagnostic, or personality variables. The relationship of attempters to completers needs to be defined for the child and adolescent populations. The degree to which data on attempters (who are much easier to study) can be extrapolated to completers remains unclear. Moreover, the data gathered after a suicide attempt may not accurately reflect the individual's presuicidal functioning. Studies on personality characteristics in successfully completed suicides will have to depend upon informant methods of data gathering that are now being developed for adult personality assessment. Informant methods also may be very useful for childhood attempters who are not very reliable reporters of their own personality characteristics.

Comparison Group Selection: Many studies attempting to isolate the characteristics of suicidal patients compare them with normal controls. This is a serious methodological limitation, given that factors in the suicidal patients may be secondary to their psychiatric disturbance and not be particularly specific to, or predictive of, suicide. To relate a risk factor specifically to suicide, it is necessary to use a comparison group that is matched on diagnosis (as well as other possibly pertinent variables) so that suicide is the only uncontrolled variable in the comparison. Risk factors may vary by sex and age groups.

Interactions with Environmental Variables: Personality variables usually have been considered in isolation from the environmental variables with which they may interact in important ways. Future studies will have to redress this simplification. It will be necessary not only to tap the personality variables and the environmental variables associated with suicide but also to determine the specific interactions between these variables that

heighten risk (e.g., angry impulsivity in a borderline personality disorder interacting with the loss of love object or the conduct disorder individual who has been caught in a misdemeanor).

Predictive Power: Suicide is a rare event, is associated with many correlates, and may result from heterogeneous causes. It seems unlikely that any variable, or grouping of variables, will ever have a high predictive power for suicide, especially in cross-sectional evaluation. By isolating personality variables associated with suicide, we can probably improve our ability to identify a group of youngsters at high suicide risk who deserve extra treatment and preventive efforts. Assessment is unlikely ever to be very successful in predicting which specific youth is at high risk to attempt suicide in the very near future.

DISCUSSION

Thanks largely to the increased reliability afforded by DSM III, personality disorder research in adults has recently been flourishing and promises to provide increasing clarity on the relationship of Axis I and Axis II disorders and in the interaction of these with suicidal behavior. However, the technical innovations in personality assessment developed for adults have not yet been translated into improved assessments of childhood personality features. Although the diagnosis of personality in youngsters is inherently problematic in the many ways we have outlined, it is likely to improve greatly as research attention turns in this direction. The results of this literature review suggest that the personality features that predict youthful suicide are very closely related to those that are associated with suicide in adults (borderline personality, conduct disorder/antisocial personality, impulsivity, aggression, social withdrawal). This would seem to confirm the continuity of personality factors throughout the life cycle as possible contributors to suicide risk.

Suggestions for Current Clinical Practice: Youngsters who present with conduct disorders and/or the impulsivity associated with borderline personality disorder deserve an especially thorough diagnostic evaluation that specifically assesses for the possible presence of Axis I conditions (e.g., affective disorder and substance abuse). Suicide risk and lethality appear to be highest for patients who present with comorbid combinations of Axis I and personality disorders so that aggressive treatment of the depression and/or substance abuse is crucial in this group. The presence of specific stressors (trouble with the law, loss of love object) that are particularly associated with suicide in personality-disordered youngsters should alert the clinician to increased risk and provide a target for immediate education and intervention. Although effective treatments for conduct and borderline disorders have yet to be documented, certain promising leads deserve further clinical and research attention.

Suggestions for Prevention: Robins and Earls (112) have suggested a promising research design to test the ability of a special prevention strategy to reduce the incidence of conduct disorder. They would select a group of children who have at least a 50 percent morbid risk of developing conduct disorder (i.e., those who have at least one antisocial parent). Since some of the origins of conduct disorder may occur early (prenatal exposure to neurotoxins and distress, postnatal trauma and illness, and parental deprivation) and since the earliest manifestation may occur during the preschool years, the preventive intervention would be designed for early delivery. The sample would be selected from pregnant women with antisocial disorder. The intervention aim to offset known risks for conduct disorder by providing adequate prenatal and pediatric care, offering high risk infants a special curriculum to increase language and social skills, and providing training and support of the parents. The research design would include randomization to a special developmental center or to a no-intervention control group. If the intervention were suc-

cessful, Robins and Earls would expect significant differences to be evident by age 3 and that these would be substantial through age 10. Positive results detected at this point would presumably reduce the longer term risk of antisocial personality and also of youthful adult suicide, although such determination would require additional longitudinal study. This strategy for studying the effects of primary prevention for conduct disorders would appear to be feasible, cost-effective, and likely to have an impact on youthful suicide rates.

Suggestions for Future Research: The most immediate need is to develop methods to assess childhood personality disorders and personality traits. Available personality definitions and assessment instruments designed for adults have been developed only recently and must now be adapted for use in youngsters. The stability and predictive power of childhood personality measures and their relation to Axis I conditions must be determined empirically. Once assessment problems have been addressed, it will be important to evaluate treatment and prevention programs.

CONCLUSIONS

Personality disorder diagnosis has only recently achieved reliability, and empirical studies have only just begun to demonstrate the predictive power of personality variables. Thus far, almost all the available research has been conducted among adults, and we must recognize that personality assessment in childhood and adolescence is difficult and subject to inherent limitations. Nonetheless, it is fascinating that the very same personality variables that are associated with adult suicide are also associated with youth suicide, suggesting that preventive efforts focused on personality variables should be targeted to early identification, treatment and prevention, in high risk populations. Interventions that are effective in reducing personality risk factors are likely to reduce the suicide rates, not only in youthful populations but also in these same populations as they grow older. It seems crucial to develop programs of prevention and treatment to counteract the disturbing cohort effect for conduct and affective disorder that may be responsible for the increasing rate of suicide in younger age groups.

Specific conclusions derived from our review include:

- The personality predictors of youthful suicide are equivalent to the personality predictors of adult suicide.
- There is stability of adolescent personality diagnoses into adulthood.
- Conduct disorder and borderline personality disorder are the most important personality disorder risk factors for adolescent suicide.
- Certain dimensional personality and cognitive traits (e.g., aggressivity, impulsivity, hopelessness, social isolation) may be important predictors, perhaps cutting across categorical personality disorder diagnosis.
- The comorbidity of Axis I and personality diagnosis increases the frequency and lethality of attempts.
- There may be a contributory role of a family history of antisocial behavior, substance abuse, and/or affective disorders to suicidal behavior.
- Comorbidity plus family history may increase lethality (both through genetics and environmental reinforcers).
- There is a need for better personality measures and assessments for children and adolescents.
- There is a need to establish whether the biological (particularly serotonergic) correlates of personality and suicidal behavior found in adults also apply to adolescents.
- It is necessary to determine how personality disorder/traits interact with other risk factors (i.e., family history, biological abnormalities, lack of social

supports, other psychosocial risk factors, presence or affective disorder) to increase risk for suicidal behavior.

- Perhaps most important of all is the possibility that programs of primary and secondary prevention that succeed in reducing the morbidity of personality disorders in the young may thereby reduce not only the youthful suicide rate, but also the rates of adult personality disorders and the rates of adult suicide.

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SUBSTANCE USE AND ABUSE: A RISK FACTOR IN YOUTH SUICIDE

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INTRODUCTION

This paper reviews the relationship between the use and abuse of substances and adolescent suicidal behaviors. Before presenting the actual data, it is important to address some relevant problems of definition.

For purposes of this overview, childhood and adolescence extend to age 24, although the majority of studies have focused on people 19 years old or less. Suicidal behavior can include intense thoughts of wishing to be dead; attempts or "gestures" can relate to any level of deliberate self harm; while completion of suicide requires documentation through a coroner's report or interviews with "significant others."

Alcohol and substance use connote intake of these drugs without associated major life problems (1,2). Information about use is distinct from data on alcoholism or drug abuse which relate to heavy intake of drugs or alcohol and documentation of serious and persistent related life problems (1,5). Unfortunately, in many studies specific criteria are not clearly stated.

Also of central importance to this discussion is the definition of psychiatric disorders. Many of the earlier studies set forth no rigorous criteria for the syndromes being described. The more recent investigations often use the Research Diagnostic Criteria (RDC) or the Third Diagnostic and Statistical Manual of the American Psychiatric Association (DSM III) (4,5). Reflecting these more rigorous and reliable classifications, whenever possible emphasis is placed on findings from current studies.

Discussions of behavior associated with substance abuse, however, must go a step further in classifying subjects. In the course of misuse of drugs or alcohol almost all types of behavioral aberrations can develop, including severe states of anxiety, depression, acute psychoses, and severe confusion (1,2,6). Using diagnosis to indicate prognosis and to help in selection of treatment, it is important to attempt to establish a hierarchy of problems. One approach is to differentiate between primary and secondary illness (3,7). A primary psychiatric label is assigned when an individual fulfills criteria for that disorder and has no major preexisting psychiatric problem. An example would be an adolescent who met the requirements for drug abuse and who had no antisocial personality disorder (ASPD), major depressive disorders, schizophrenia, etc., prior to the onset of severe drug related difficulties. A secondary label is assigned when an individual meets criteria for a disorder only after another

major psychiatric illness was present. An example of this phenomenon is the man or woman with an ASPD (e.g. the onset prior to the age of 15 of pervasive antisocial difficulties) who, at age 18, went on to develop severe alcohol-related life problems; this is a case of primary ASPD and secondary alcoholism and the prognosis is likely to be that of the personality disorder, not alcoholism (6,8-10).

With these caveats in mind, we turn to a discussion of some risk factors associated with adolescent suicidal behavior. Section II briefly reviews the prevalence of suicide attempts and completions among young people in order to place into perspective the data that follow. Section III reviews the direct relationship between substance use or abuse and suicidal behavior, emphasizing the application to adolescents. Section IV looks at indirect associations between substance use or abuse and suicidal behavior as they relate to other primary diagnoses including ASPD, borderline personality, affective or depressive disorders and schizophrenia. This includes brief comments on the ties between suicidal behavior and substance abuse in adolescents and family environment or family history of psychiatric disorders. Finally, Section V synthesizes the information and offers some clinical and research implications.

THE EPIDEMIOLOGY OF SUICIDE ATTEMPTS AND COMPLETIONS

The following discussion distinguishes between the prevalence of suicide attempts and completions. Within each section, information is first given regarding rates in the general population, and this is followed by figures among adolescents. Each section concludes with data on changes in the rate of these phenomena over the years.

Attempts

About 10 percent (10,000/100,000/yr) or more of people in the general population reported suicidal feelings over the prior year, including 2.5 percent who had more intense thoughts (11-13). Counting all age groups, actual suicide attempts are observed at a rate between 100 and 800/100,000/yr, with women age 15 to 24 years standing out with the high figures shown in Table 1 (12,14,16). In men, the 15 to 24 year olds also predominate, but in each age group the actual rates are about half those seen in women (12,14,15,17-22).

Since the peak age for suicide attempts is between 15 and 24 years old (14-19), it is not surprising that a number of studies have focused specifically on the attempt rate for

Suicidal Behavior by Sex and Age per 100,000/yr (12-15,17,19,22,30,31)

	ATTEMPTS		COMPLETIONS	
Age	Male	Female	Male	Female
<15	26	92	<1	<1
15-24	423	786	16	4
25-44	267	598	24	10
45-64	152	257	26	14
65+	70	41	33	11

Table 1.

children and adolescents. Looking first at more anecdotal data on children who have sought help, it has been estimated that 3 percent of a consecutive series of young people coming to private practice or psychiatric outpatient settings had ever attempted suicide. The same is true for 10 percent to 30 percent of adolescents coming to emergency rooms, and the rate of attempts increases to between 10 percent and 50 percent among young psychiatric inpatients (18,20-22). These figures are probably inflated because of the troubled nature of the populations observed.

The high prevalence of suicide attempts in any age group, including adolescents, is not a new phenomenon (13,16,17,23-25). Most of the literature focuses on more anecdotal reports; between 1972 and 1980 there was a 5-fold increase in adolescents seen for suicide attempts in a Louisville, Kentucky psychiatric hospital (26), and an almost doubling of adolescent suicidal behavior was seen between 1970 and 1975 in a New Haven, Connecticut emergency room (14).

Suicide Completions

Suicide completion is a much rarer phenomenon than suicide attempt. The ratio between the two depends upon the definitions used, but is at least 10 to 1 (17,27), and could be as high as 100 or more to 1 in some groups (28,29). There is, however, an important connection between attempts and completions, because as many as 50 percent or more of completers have attempted suicide in the past (27).

As shown in Table 1, overall about 15 people per 100,000 of the general population died by suicide in 1980, with a male preponderance of between 2 or 3 to 1, and a peak rate for men age 65 or older (15,30-33). As infrequent as completed suicide is in the general population, it is even less common among adolescents. However, self-inflicted death has long rated as the third leading cause of mortality in this otherwise healthy group, especially for youth with histories of psychiatric care (18,21,34,35). Despite isolated cases of apparent short-term "epidemics" of suicidal behavior among young people (36), completed suicide is especially rare for children under age 15 (15,30,35).

The prevalence of suicides in the United States and Canada appears to have been stable during the 1950s (20,32). However, as reported for attempts, suicidal death began to increase in the 1960s. The overall rate in 1961 was 5/100,000/yr for men and 1 for women in Alberta, Canada; almost double the figures from 1951 (32). Self-inflicted death rose to 25 and 5 for the two sexes by 1971, on to approximately 32 and 5 by 1976 (32). In general, the U.S. suicide rate rose from 5.2 to 13.3/100,000/yr from 1960 to 1980 (31). Other investigators have also documented an increase of at least two- to three-fold between 1960 and 1980 (18,30,31,37,38).

SUBSTANCE USE/MISUSE AND SUICIDE RISK: A DIRECT ASSOCIATION

Alcohol and drug use and violent death (accidents, homicide, and suicide) are potentially related in a number of ways (39-41). Drugs of abuse, especially brain depressants (e.g. barbiturates, antianxiety drugs, and alcohol) and brain stimulants (e.g. amphetamines, cocaine, weight reducing products) can impair judgment, increase levels of impulsivity, and are capable of producing severe mood disturbances, including temporary, intense and suicidal depressions (1,6,42). Any substance of abuse can also exacerbate a preexisting state of psychopathology, including increasing the level of hallucinations or delusions in psychoses, enhancing anxiety, and increasing levels of depression (1,6,43-45). The following sections briefly review information on the association between substances and suicide attempts or completions in general (Section A), as well as in adolescents (Section B).

Alcohol, Drugs, and Suicide Attempts: A General Discussion

One obvious association between substances

and suicide is the use of alcohol or drugs as vehicles for the suicidal act. Historically, drug overdoses of prescription or over-the-counter drugs have been a favored mechanism in suicide attempts, especially overdoses with brain depressants in women (14,46). The use of drugs as the mechanism of attempt by young people is equally strong. In one consecutive series of 505 adolescents and children seen in a pediatric emergency room for a suicide attempt, 88 percent had used drug overdose, as had 78 percent to 100 percent of suicide attempting youth reported in other samples (1,22,47-49), although some authors have reported lower rates (30,31).

In any age group, intoxication with alcohol or drugs often immediately precedes suicidal behavior (17,39,50-52). In some instances, this relates to suicide attempts among alcohol or drug abusers, but in others it reflects the use of substances as part of the attempt itself or in an effort to "screw up enough courage" to carry it out. In any event, one study reported as many as 70 percent of male and 40 percent of female suicide attempters had consumed heavy doses of ethanol before the act, with average resulting blood alcohol concentrations (BACs) of almost 150 milligrams per deciliter (mg/dL) for the men and over 100 mg/dL for the women (12). Alcohol was found to have "contributed to the death," through perhaps impaired judgment or exaggerated mood swings as well as through effects on vital systems, in more than half the autopsied cases in one study in Washington, D.C., and more than two-thirds of the suicides in another study in New York City (61,62).

There is ample documentation of a high suicide rate among substance abusers themselves. At entrance into an alcohol treatment program, at least 20 percent of alcoholics report histories of suicide attempts (53). Prospective followup of identified alcoholics have revealed a three-fold or higher increased rate of suicide completion (41,54,55), with Miles estimating a lifetime rate as high as 15 percent (56).

The association with violent death extends to drug abusers as well, with at least 15 percent admitting to past suicide attempts. The estimated lifetime suicide completion rate among some types of drug abusers exceeds 10 percent (1,53,56-59), including a four-fold increased rate over the general population among amphetamine abusers, as well as a high of suicide among cocaine and heroin addicts. Drug abusers who express extreme feelings of depression or hopelessness may be at exceptionally high risk (60).

Considering the lifetime rate of suicide completion among substance abusers, it is not surprising that studies of patients who have committed suicide have noted that a high proportion have a history of substance misuse. Using rigorous criteria, 20 percent to 50 percent of suicide attempters or completers were found to be drug abusers, while between 15 percent and 50 percent of completed suicides in several studies were alcoholics (27,33,63-68).

In summary, from the studies in the general population and focusing on all ages there appears to be a close relationship between alcohol and drug use or abuse and suicide. The association is supported by followup studies of alcoholics or drug abusers, evaluations of the characteristics of suicide victims, and followup evaluations of psychiatric patients.

Alcohol, Drugs, and Suicidal Behavior Among Adolescents

Analyses of data for adolescents also document a close association between substances and suicide, as outlined in Table 2 (35,69,70). This conclusion is supported by studies of suicidal youth, evaluations of substance abusers, and through observation of young psychiatric patients.

Adolescents who fulfill criteria for drug abuse or who have relatively heavy drug intake patterns have an increased rate of death overall, including high rates of suicide. A 10-year followup of two groups of teenagers (one from the general population and the second identified because of prior drug use) revealed a two- to seven-fold increased death

rate among boys with histories of drug misuse, and an almost two-fold to eight-fold increased death rate among girls (71). Approximately half of this increase in death rate was from suicide.

The relationship between drugs, alcohol, and suicide in young people is corroborated when populations identified because of suicidal behavior are evaluated. Patel reported that among suicide attempters age 12 to 19 years old, 41 percent of the boys and 19 percent of the girls had been drinking immediately before the attempt (13), and Garfinkel found a ten-fold higher rate of recent alcohol or drug use in 505 adolescent attempters than for controls (22). Shafii noted "frequent use of nonprescription drugs or alcohol" among 70 percent of the 20 teenagers who committed suicide in the Louisville area between 1980 and 1983 (26), while almost half of the suicides aged 15 to 19 in Erie County, New York, had alcohol in their blood (50). The study of suicides under age 30 in San Diego found that more than 75 percent abused drugs or alcohol, including between a third and a half for whom these diagnoses were the primary illnesses (31). Among those with drug problems in the San Diego sample, 79 percent had abused marijuana, 45 percent cocaine, 34 percent amphetamines, and about 25 percent each had abused opiates, sedatives/ hypnotics, or hallucinogens. There was an average of three to five substances abused per individual.

The association between suicidal behavior and drugs is just as strong among adolescent psychiatric patients. Robbins and Alessi studied 33 teenage psychiatric inpatients who had histories of prior suicide attempts, looking for the relationship between alcohol or drug use and suicidal behavioral (18). They used an analysis of correlation that evaluates the degree to which two factors change at the same time (the higher the correlation, the greater the similarity in change). A history of alcohol abuse correlated with the number of past suicidal "gestures" at a 0.42 level ($p<.001$), accounting for 25 percent of the variance or range of the number of gestures in this group. Similarly, the correlation between alcohol abuse and the seriousness of past attempts was 0.35 ($p<.01$), and alcohol problems correlated with the level of medical seriousness at 0.36 ($p<.01$). Overall, the association between a history of alcohol abuse and the occurrence of a suicide attempt was 0.28 ($p<.05$). A history of drug abuse correlated with the number of suicide "gestures" at 0.32 ($p<.05$), and with the medical seriousness at 0.26 ($p<.05$). Those authors conclude that "substance abuse in depressed adolescents appears both to increase the risk of multiple attempts and to add to the medical seriousness of the attempt."

Suicidal Behavior and Substance Abuse in Adolescents are Linked
(13,18,22,26,30,31,50,71)

Among heavy substance users:	Four fold increased suicidal death rate
Among adolescent suicide attempters:	Ten fold increased substance use 30 percent drank before attempt
Among adolescent suicide completers:	70 percent used drugs frequently 50 percent had alcohol in blood 75 percent fit criteria for drug or alcohol use disorders
Among young psychiatric patients:	Suicidal behavior and substance abuse correlate

Table 2.

Several factors complicate the interpretation of these data. First, adolescence and early adulthood are ages of maximal alcohol and drug use (1,72-74). Second, as discussed by Weissman (75) people with multiple problems are more likely to seek care than those with one problem alone. Therefore, substance users who also have depressive symptoms and multiple life crises are the ones most likely to be identified and to be a part of studies. The apparent close association between substance use and suicidal behavior in treated groups might not completely generalize to substance users in the general population.

In summary, there is much evidence connecting alcohol and drug use with suicide attempts and completions in both adults and adolescents. This includes an increased prevalence of alcohol and drug use prior to suicide attempts, a marked increase in risk for suicide attempts and completions among drug and alcohol abusers, an overrepresentation of drug and alcohol abusers among suicide attempters, and a correlation between suicide attempts and a history of drug or alcohol abuse among psychiatric patients.

MORE INDIRECT EVIDENCE CONNECTING DRUGS AND ALCOHOL WITH SUICIDAL BEHAVIOR

Section I described how careful psychiatric diagnostic labels can give important clinical information on a patient's probable prognosis and treatment needs (1,3). To meet these goals, however, it is necessary to distinguish between primary disorders and those illnesses that develop only after another preexisting psychiatric problem was established (secondary illness). This is especially important for alcohol and drug abuse, because the prognosis and rehabilitation needs can be quite different for primary and secondary misusers (1,6,9,45).

This section highlights a number of primary psychiatric disorders in which both suicidal behavior and substance abuse are common problems. Thus, an important association between substance abuse and suicidal behavior is mediated through personality disorders and psychiatric illnesses that can be seen in adolescents and that sometimes run in families.

Personality Disorders

Over the years, attempts have been made to use clear-cut criteria to outline psychiatric disorders for which good followup data are available (3-5). Unfortunately, with one or two exceptions, the progress for personality labels has been less impressive than for the other categories of the DSM III.

Personality disorders in general are likely to be associated with suicidal behavior. Anecdotally, character and behavior (or personality) disorders are among the most frequent diagnoses for soldiers or sailors with suicide attempts (17,19,29,76). Among psychiatric patients with histories of self-harm, between 35 percent and 80 percent are noted to have some type of personality disorder (21,77-79), although few studies used objective criteria to identify the personality problem involved.

It is probable that the specific label of the antisocial personality disorder (ASPD) is closely tied to suicidal behavior. The diagnostic framework for this problem has changed over the years, evolving from the psychodynamic concept presented by Cleckley (80) to a more precise constellation of symptoms outlined by Robins and colleagues and adopted (with some modifications) by the DSM III (5,81,82). As presently used in most studies, the label of ASPD connotes an individual with antisocial problems in multiple life areas beginning prior to the age of 15 and continuing into adulthood; these are problems that cannot be explained solely by alcohol or drug use histories. Subjectively, these individuals are likely to be impulsive, have difficulty conforming to the expectations of others and learning from mistakes, and show impairment in establishing long-term relationships.

Approximately 80 percent of ASPD patients

have a history of alcohol abuse and associated serious problems (6,83,84), and these men and women carry an elevated risk for drug related pathology as well (82-86). ASPD patients are also more likely than the general population to attempt and complete suicide (1,35,68,83). One in four have history of suicide attempts, and during a 5- to 6-year followup, 5 percent had died by suicide (53,87).

Two other personality disorders appear to be associated with both substance abuse and suicidal behavior. First is the DSM III syndrome of somatization disorder that grew out of a concept of hysteria and Briquet's disease (3,5,88,89). Patients with this disorder are usually women who at an early age develop somatic complaints in multiple body system, including numerous conversion symptoms (neurological symptoms other than pain with no known medical basis). Severe mood swings are common and suicide attempts occur at a much higher rate than in the general population (3,89,90). Women with this disorder may have a 15 percent prevalence of concomitant use of substances for "recreation" or use outside of normal prescribing practices (89). Therefore, considering the relatively early age of onset, this may be a second example where substance misuse and suicidal behavior are tied together through a separate primary illness.

Finally, an early onset personality disorder characterized by severe mood swings and an inability to handle life stress has been described as the "borderline personality" (91,99). Subjectively, these patients share many characteristics with individuals with ASPD or somatization disorder, demonstrating impulsiveness and frequent mood swings. In addition to an increased rate of suicide attempts, these men and women are also more likely than the general population to misuse alcohol or other drugs (93,94).

Major Psychiatric Disorders

The most frequently reported diagnoses associated with suicidal behavior are affective illnesses, usually unipolar or bipolar major depressive disorders or, in the earlier studies, "depressive neurosis." An affective disorder is seen in 50 percent to 65 percent of adult suicide attempters (19,20,53,100,103), as well as in between 55 percent and 95 percent of suicide attempting adolescents and children (18,22,93,104). The association between suicide completion and depressive illness is also high for all ages, with about half of suicide completers noted retrospectively to have had major depressive disorders (64,101,105). Synthesizing this information, Miles projects that the life-time risk for completed suicide among major affective disorder patients is at least 15 percent (56).

Another psychiatric illness with an elevated risk for suicide attempt and completion appears to be schizophrenia. This diagnosis is especially important in young people because the onset of the process is usually in the teens or twenties (3). While definitive conclusions are jeopardized by the marked variation in diagnostic criteria utilized in different studies, it appears that 12 percent to 15 percent of adolescent or adult suicide attempters have schizophrenia (20,21), while 3 percent to 10 percent of suicide completers fulfill criteria for this disorder (64,101,105).

This section is included both because each of these problems is a risk factor in suicidal behavior, and because secondary substance abuse during the course of these disorders can exacerbate symptoms (1,6). As many as two-thirds of manics and one-third of severe depressives escalate their drinking while ill, a problem that could intensify depressed feelings and impulsiveness and might increase suicidal behavior (45). Similarly, schizophrenics who increase intake of brain depressants or stimulants are likely to experience a worsening of their poor judgment and psychotic thinking (107,108). Finally, it is possible that heavy drinking or drug use might exacerbate mood swings or intensify almost any major medical disorder (1,109).

Substance Misuse, Suicidal Behavior and the Family

The previous subsections have documented

that few adolescents who attempt or complete suicide are free of major psychopathology. This finding impacts on two other observations: the high prevalence of family instability and the high rate of psychiatrically ill relatives among suicidal young people.

During the 1970s it was common for authors to emphasize the observation of broken or chaotic homes among suicidal youth (19,101,105). Interpersonal difficulties were often named as an immediate precipitant for suicide attempts in adolescents (19), and many of these young people were reported to have observed suicidal behavior within their immediate families. Indeed, there is evidence that self-destructive acts run in families (111). For example, one evaluation of 243 psychiatric inpatients concluded that those with a family history of suicide were more likely than their coevals to have themselves attempted suicide (50 percent vs 22 percent, $p<.0001$) (110).

Few clinicians doubt the interaction between suicidal behavior, chaotic homes, and a family history of suicide attempts or completions. The causal nature of the relationship is, however, less obvious. Not only are most children raised by their parents, but they also get their genetic material from them. Considering the close relationship between suicidal behavior and psychiatric illness described in the prior sections, if the major psychiatric disorders associated with suicide are themselves genetically influenced, then part of the familial nature of suicidal behavior could relate to genetic factors increasing the predisposition towards similar illness in parents and children.

Three of the disorders carrying the highest lifetime risk for suicide attempts and completions do each appear to be genetically influenced. The importance of biological, genetic factors in alcoholism is supported by the familial nature of this disorder, the 60 percent to 80 percent rate of concordance for alcoholism in identical twins of alcoholics compared to a risk of approximately 30 percent for the fraternal twins, as well as the four-fold increased risk for alcoholism in sons and daughters of alcoholics adopted away close to birth and raised without knowledge of the biological parent's problem (112-114). Similarly, family, twin and adoption studies indicate that major depressive disorders (especially bipolar, manic depressive disease) are also genetically influenced (115,116), and the data supporting the probable importance of genetic factors in schizophrenia are equally impressive (116). For at least one of these disorders (alcoholism), the greater the number of alcoholic relatives and the more severe their problem, the greater the probability of an earlier onset and more intense course for those children who develop the disorder (117,118).

Thus, there is another level of association between substance misuse, psychiatric disorders, and suicidal behavior in children and adolescents. Alcoholism or other illness in parents are relatively common findings among suicidal children and teenagers (110), it is possible that substance abuse or psychiatric disorders in these parents might have contributed to the increased rate of broken homes and chaotic childhood lifestyles for young people; these children may have a high risk for early onset of the disorder itself (117,118). Therefore, the suicidal behavior in these children may sometimes reflect their own early onset of illness associated with disordered mood or judgment.

In summary, substance abuse or psychiatric disorders in parents could contribute to the suicidal behavior in young people in at least two ways. First, some of the self-destructive problems in these children could have been influenced by the models set by the rearing parents, as well as the child's reaction to the anger and frustration engendered by the behavior of the ill parent. Second, some of the suicidal behavior observed in the children may reflect the inheritance of a predisposition towards the genetically influenced illness itself, with concomitant suicidal risk associated with the disorder and not just the specific childhood environment.

SUMMARY AND CONCLUSIONS

This paper has presented data and also attempted to stimulate thought and discussion. The emphasis has been on the potential contribution of alcohol and drugs to suicidal behavior in children and teenagers.

There is an important relationship between substance use or misuse and violent behavior in adults. Controlled substances and/or alcohol are frequently used as the means of attempting self-harm (especially among younger women), and alcohol is often taken as a prelude to the suicidal act, thus contributing to impaired judgment and impulsivity. Also, the lifetime risk for completed suicide appears to be 15 percent among alcoholics and about 10 percent for drug abusers.

It is not surprising, therefore, that the association between substance intake or abuse and suicidal behavior is also observed in adolescents. Whether studied in the general population or among groups in treatment, substance abusing young people have a significantly increased rate of self-inflicted death; youth identified because of their suicidal behavior frequently use and abuse nonprescription drugs and alcohol; and there is a close relationship between substance misuse patterns and the number and severity of suicide attempts.

Suicidal behavior early in life is also associated with substance problems in more indirect ways. Diagnoses such as the ASPD and "borderline personality" carry high risks for both self-harm and substance misuse. It is also probable that heavy drinking or drug use during major depressive episodes or in the midst of other psychiatric problems can exacerbate problems and might contribute to a suicide attempt or completion in these high risk individuals. A third indirect association between substance abuse and self-harm relates to the probable importance of genetic factors in the development of alcoholism and early onset psychiatric disorders. Thus, for example, children of alcoholics are more likely than the general population to observe suicidal behavior in their parents, more likely to suffer chaotic homes during childhood, and themselves have a genetically increased risk for both suicidal behavior and substance misuse.

From this review it is appropriate to conclude that, through both direct and indirect mechanisms, intake and abuse of substances is a potentially important risk factor in suicidal behavior early in life. The relationships between these substances and self-harm is rather complex, and careful data collection will be required if we are to understand more about this clinically relevant association.

It is possible to speculate about some of the clinical implications of the data reviewed in this paper. First, through numerous direct and indirect mechanisms, adolescent alcohol and drug abusers have an elevated risk for suicide attempts and completions. Second, whatever the mechanism, children of alcoholics and of patients with depressive or schizophrenic disorders may themselves be at elevated risk for suicide attempts and completions. The same may be true for children of drug abusers, although less data is available to substantiate that conclusion. In working with these families the potential dangers for self-harm in children should be recognized, A third clinical implication of the data comes from the recognition that almost all substances of abuse are likely to exacerbate preexisting emotional or psychiatric disturbances. Therefore, heavy intake of any of these controlled substances or alcohol may be important risk factors increasing the suicidal propensity of young people in crises, as well as those with major psychiatric disorders or personality disturbances. Efforts aimed at minimizing the risk for suicide should include educating young people and their families about the need to refrain from intake of all substances of abuse during times of mood swings or anger. Finally, physicians must learn to be careful in prescribing psychotropic agents or drugs of potential abuse to teenagers with emotional or

psychiatric disturbances because there is evidence that in many instances the suicidal overdoses involve prescribed drugs (119).

The research implications of this review are also apparent. Studies of suicidal behavior in adolescents should rigorously document drug and alcohol use patterns in the recent past, evaluate individuals for major primary and secondary psychiatric disorders including those related to substance abuse, and document the presence of these problems in first-degree relatives. Investigators must also take care to not assume that an association between two factors (e.g., a suicide attempt in a child and alcoholism in a parent) proves that it is the disturbance in the home environment that caused the attempt. While the environmental stressors probably contribute greatly, other important avenues of influence must also be considered. For example, it is possible that children of alcoholics may themselves have inherited (or acquired through *in utero* damage) problems of impulsivity, hyperactivity, or a propensity to misuse substances with subsequent mood swings, anger, and frustration in their own lives.

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METHODS AS A RISK FACTOR IN YOUTH SUICIDE

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In this paper we will consider methods of suicide as a risk factor. Although other risk factors already discussed in this conference may be more important than methods as precipitants and precursors of suicidal behavior, none is more important than methods when it comes to the risk of death. Some methods lead to almost certain death while other methods are more uncertain as to outcome and they portend more reversibility and rescuability. We have seen a recent rise in youth suicide, especially with regards to completed suicide. Is this increase in completed suicide due to an overall increase in suicidal behavior or is it due to the fact that youths who engage in suicidal behavior are using more lethal means of self-destruction? A better understanding of methods may provide us with an answer to this question, as well as providing us further insights into the dynamics of youth suicide and possibly offering some clues for prevention.

How do adolescents and young adults kill themselves? Overall, those in the 10 to 24 age range most frequently kill themselves by firearms and explosives, with guns being the most prominent means. The second most frequently used method of suicide is by hanging, strangulation, or suffocation. Self-poisoning by ingesting solid and liquid substances is the third most frequent method of self-destruction. (Holinger, 1978). Although there are few major differences in choice of method between black and white youths, there are some distinctives. Proportionately more black males than white males hang themselves or die by jumping from high places or drowning, whereas relatively more white males use firearms or die utilizing carbon monoxide. White females are more likely to hang themselves than black females. Overall, a higher proportion of females to males poison themselves irrespective of race. (Fredrick, 1984). It is interesting to note that suicide statistics in the United States are not kept for children under 10 years of age. This implies that suicide is not seen as an option for young children by those collecting such information.

Paulson at UCLA disputes this fact. Studying children who were seen at the UCLA Neuropsychiatric Institute from 1970 to 1974, Paulson found 34 children ages 4 to 12 who demonstrated suicidal behavior--mostly suicide threats and attempts. The mean age of his sample was 8.2 years. Suicidal behavior in this age group involved more self-abuse and bodily mutilation than self-poisoning. Examples of self-abuse were cutting, stabbing, burning, and jumping either from high places or in front of moving vehicles. Children exhibiting the most mutilating assaults on themselves frequently came from highly disorganized families and were also the children with the highest ideational violence. It is interesting to note that Paulson did not find significant gender differences in ideational violence among his young subjects. (Paulson et al., 1978).

Pfeffer also studied suicidal behavior among younger children. In investigating children ages 6 to 12 who were inpatients in the child psychiatry unit of the Bronx Municipal Hospital and who demonstrated some type of

suicidal behavior, she found that jumping was the most frequent choice of these young attempters. Out of the 42 subjects in her study, jumping was chosen by 38 percent of the children. Of those remaining, 25 percent chose self-poisoning, 19 percent burned themselves, 13 percent cut themselves, and 6 percent ran into oncoming traffic. (Pfeffer et al., 1979). In a subsequent study of 65 children admitted to the child psychiatry unit of New York Hospital Westchester she also found jumping from high places to be the most frequent method and this was found in 25 percent of the cases. (Pfeffer et al., 1982).

Although jumping is a frequent method for these very young attempters, self-poisoning should not be overlooked. McIntire and Angle discovered an interesting phenomenon when investigating reports from 50 poison control centers in the United States and the United Kingdom. In the 6 to 10 age range, self-poisoning was more frequently found among males (63%) than females (37%). This is the opposite of what they found in their older group of children, 11 to 18 where self-poisoning by females far exceeded that by males. This same gender differences can be also found among adult self-poisoners where the number of females exceeds males. McIntire and Angle offered no explanation for the difference they found, but they did conclude from their study that self-poisoning in a child over the age of 6 is rarely accidental. (McIntire & Angle, 1971b). It should also be noted, however, that completed suicide for these very young children is rare.

Hawton & Goldacre studied cases of self-poisoning in a population of young people ages 12 to 20 years who were admitted to hospitals in the Oxford area of England. They also noted that self-poisoning was higher for females than for males at all of these ages. (Hawton & Goldacre, 1982). It would have been useful if the investigators had included the younger children from ages 6 to 12 in their study to see if the reverse male to female phenomenon that McIntire found could have been replicated in such a large sample and in another country.

There is general agreement that incidents of self-poisoning become more frequent as children increase in age. There is less agreement as to what substances they ingest. Hawton compared adolescent self-poisoners to adults and found that adolescents more frequently ingested non-opiate analgesics and less frequently took psychotropic drugs. The use of alcohol as an adjunct factor in an overdose was found less frequently among adolescents than among adults. This was especially true in the younger groups of children. Most young children tended to ingest drugs found around the house rather than drugs specifically prescribed for them. (Hawton, 1982). Hawton also found that the ingestion of psychotropic drugs increased as the females in his study became older, but the same was not true for the males studied. Fredrick (1984) reported that barbiturates and tranquilizers were the most frequently ingested substances for completed suicides among 15 to 24 year olds in 1979. Goldney in looking only at female self-poisoners ages 18 to 30 found that anti-depressant medications were often ingested as overdoses. This was especially true for attempts judged to be highly serious both from the standpoint of medical lethality and the ratings from the Beck Intent to Die Scale which was given to these 109 women in the study. (Goldney, 1981). One might conjecture that younger children are more likely to ingest substances found around the home. As children grow older they may be in psychiatric treatment and receiving medication which is available to them if they decide to overdose.

The reasons given for choice of method are always of interest. Some suicide behavior is well thought out and the methods selected well in advance. Other suicides are impulsive and the person may turn to the nearest perceived lethal substance at hand. To the extent that the choice is rational, there was an interesting study conducted by Marks with approximately 700 college students. The mean age of his respondents was 19.5 years. He asked the students to rank order nine

means of self-destruction according to their acceptability and to suggest which methods they thought were used most often by males, by females, and why. Both males and females in his study ranked self-poisoning as the most acceptable. Firearms were ranked higher by men than by women. Women were more likely than men to cite "lack of pain" as the reason for their choice. In citing additional reasons, "availability" and "knowledgeability" were associated with self-poisoning for females; with firearms for males. Similarly, "efficiency" was related to self-poisoning for females and to firearms for males. (Marks, 1977).

Although self-poisoning is the frequent choice of the adolescent suicide attempter, it ranks third in the causes of suicidal deaths in the 10 to 24 year old population. Most young people who succeed in taking their own lives do so with guns and explosives. For young people ages 15 to 24 the rate of suicide by firearms increased 97.1 percent from 1966 to 1975 while the rate of suicide by other means increased 72.4 percent for the same period. The significantly large increase in death by firearms may reflect the 14.5 percent increase in the availability of legal handguns during that same time period (Seiden & Freitas, 1980, Boyd, 1983).

To what extent, then, is availability a determining factor in the choice of a method of self-destruction? There has been considerable discussion as to the availability of a method, both as a determinant for choice and as a possible way to reduce suicidal behavior, such as gun control. Marks and Abernathy (1974) minimize physical availability as a determinant. The most available methods are not those most frequently employed. For example, rope with which to hang oneself is more readily available than firearms, yet firearms are more frequently used. Obviously, however, availability is a necessary precondition in the choice of a method.

There is evidence that when a certain method becomes unavailable some persons wishing to suicide will switch to another means. Lester and Murell (1982) found that States with stricter gun-control laws had lower rates of suicide by firearms but higher rates of suicide by other means. However, in an earlier report, Lester and Murell (1980) found that the total suicide rate was lower in States with stricter gun-control laws. Thus it is possible that when firearms are less available, persons turn to other methods which may leave more time for intervention.

Marks and Abernathy (1974), in trying to explain both gender and individual differences in choice of method, have posited a sociocultural perspective of differential socialization which takes into account not only availability but several other factors which also influence such a choice. Marks and Abernathy respond negatively to what they term the "psychological perspective"--a perspective which suggests that the difference in choice of method solely reflects a difference in intent to die. This perspective implies that the higher incidence of handgun use in male suicides indicates that males are more intent on killing themselves.

Marks and Abernathy argue against this psychological perspective on several grounds. For instance, if it were correct, then we would expect to find different methods employed by female attempters than female completers. However, the use of poisons is high in both groups. Furthermore, one would expect those areas of the country in which the more deadly methods, e.g. firearms, are preferred to also have the highest suicide rates. However, such is not the case.

Marks and Abernathy have identified at least three factors beyond availability which may influence the choice of a suicide method. The first of these is the sociocultural acceptability of the method. Certain methods have greater or lesser acceptability within the internalized social and cultural norms of the individual, and this will be reflected in the choice of a method. Examples of this may be reflected in the distinctives mentioned earlier between young black and white males and between young black and white females. The second factor is the person's knowledge

of the methods. A person is more likely to employ a method with which he or she is knowledgeable and familiar. The third factor is personal or social accessibility. For example, heroin may be physically available from a street supplier but socially inaccessible because of the person's social standing as a police officer. In this example heroin would be a less likely method for an overdose.

Research by McIntosh & Santos (1982) also supports the idea that selection of a method is dependent upon a constellation of sociocultural factors. They found that no generalization could accurately describe the range of suicidal behavior displayed by various sex, racial, or ethnic groups. Although they did not specifically study youth suicide or break down their sample by age, their point is most applicable to our discussions of youth suicide in this conference. We must be careful not to draw overgeneralized conclusions about youth suicide methods without more closely examining the various sociocultural influences on these young men and women and how these influences might differ by age, sex, social position, cultural background, geographical location and personal history. Much more research is needed to understand the selection of suicide methods by youth.

One important factor influencing gender preferences for suicide methods may be "anticipatory socialization." (Marks & Abernathy 1974). Traditionally boys have been exposed to and encouraged to participate in violent games and activities to a greater degree than their female counterparts. An example would be the game of cops and robbers. This may account, in part, for the greater incidence of firearm use by males. One could speculate that changing role definitions for women may account for the increase in the use of firearms in female suicides. It is interesting to note that the majority of young women in the U.S. Army who suicide (73%) do so predominantly with firearms (Datel & Jones, 1982). Taylor & Wicks (1980), while supporting the sociocultural perspective, find no evidence that certain groups of women who prefer firearms to other methods are any more "liberated" than those women who prefer poison or some other means of self-destruction. Liberation is probably a poor choice of terms. Changing role definitions does not necessarily imply liberation. Location within the social structure is a better term than liberation and fits within the sociocultural perspective. Changes in traditional role expectations are pervasive in our society and its culture and this needs to be taken into consideration when explaining gender changes in patterns of suicidal behavior.

There are important implications to be drawn from the sociocultural perspective with regard to suicide methods and youth. The most important is the need to determine what sociocultural factors differentiate youths and adolescents from the adult population. Are different methods more or less available to youths than to adults? Are certain methods more culturally acceptable to youths? How do these sociocultural factors vary by age within the youth population? There is no specific research in this area though it is clearly needed. We recommend research which will clearly differentiate between adults and youth and carefully examine the influence of sex, age, geography, cultural values, social status, intent to die, familiarity and availability of methods, and how these factors relate to the choice of self-destructive methods in these populations.

Some suicidal methods obviously carry more risk of death than others. Because of this, clinicians are apt to use nominal classifications when they discuss the relative lethality of a suicidal act. Words like "gesture," "moderate lethality," and "serious suicide attempt" are still used when talking about a person's suicidal behavior. However there are many suicide attempts of intermediate lethality which cannot be dichotomized easily into "gestures" and "serious" attempts. This is especially true in the area of self-poisoning.

In 1972, Weisman and Worden developed a scale known as the Risk-Rescue Rating Scale

in an attempt to describe and quantify lethality in suicide attempts. (Weisman & Worden, 1972). This scale is based on the assumption that the probability of death is substantially influenced by what a person does to himself and the context in which he does it. Any suicide attempt entails a calculated risk. But because any attempt must also take place in a psychosocial context or within a specific set of circumstances, survival may depend upon the resources for rescue as well as upon the specific form of the attempt. Jumping off a high bridge into the river beneath has similar risk to physical damage whether it is done at 3 p.m. or 3 a.m. However, rescue factors are different in the early morning hours when it is dark and there are fewer people around. The Risk-Rescue Rating Scale assesses five factors of risk and five factors of rescue and enables the clinician or researcher to quantify the lethality of implementation in any suicide attempt.

There are other scales similar to the Risk-Rescue that look at the relative seriousness of methods. Recently, Smith, Conroy, and Ehler at the Menninger Foundation created a nine-point interval scale for assessing the relative lethality of a suicide attempt. (Smith et al., 1984). This is a well developed scale and their updated toxicity chart is an improvement over the older one developed by Sterling-Smith and used by Weisman and Worden.

The ability to quantify a suicidal act by looking at methods in context is valuable from several standpoints. First, you can compare one group of suicide attempters with another. We know for example that young females more frequently use self-poisoning than young men, but young men do poison themselves. Even though there is less self-poisoning among males, is the lethal level of their attempts higher than for females? Using a scale like the Risk-Rescue Rating could help answer this. We presently know the types of methods used by youth in different age categories and the percentage of use for various methods varies widely for different age groups and possibly for youth in various social sub-cultures and geographic locations. Being able to rate methods within their context and to be able to scale the observations would clearly aid in our attempt to understand youth suicide across the age cohorts.

Second, such a rating scale also helps one to assess relative lethality for a person who has made multiple attempts. It is well known that those who have made previous attempts are at higher risk for completed suicide. Rating each attempt with the same scale enables one to see whether lethality is ascending, decending, remaining the same, or forming some other pattern. In one study Worden found that one could predict the lethal level of subsequent attempts in adults by rating previous attempts in combination with various other demographic information. (Worden & Sterling-Smith, 1973).

A third use for a lethality rating scale is to better understand the complex issue of intent to die. Measuring intent is often very difficult. Patients do not always give an accurate account of their intent to die from an attempt. There are both conscious and unconscious factors that lead to distortion. Patients may say one thing when taken to the emergency room and have a totally different story a day later. Also, ambivalence is present in most people trying to hurt themselves. On the extreme ends of the spectrum intent to die is rather easy to discern. The young girl who ingests 25 aspirin and immediately tells her mother is clearly in the low lethal range. The young man who takes a gun into the remote woods and shoots himself in the head is obviously in the high lethal range. These are obvious. But there is a whole range of behaviors that fall into the middle ranges of lethality and using a rating scale that looks at methods in context would be very useful in future studies of youth suicide to better understand the issues of intent especially in those falling into the middle ranges of lethality.

In any discussion of youth suicide methods one should not overlook automobile accidents as suicide equivalents. In the 1970s we

did a study of automobile fatalities in the greater Boston area under a grant from the Department of Transportation. One part of the study investigated the human factors associated with these accidents. A number of these fatal accidents involved young drivers from 18 to 25 years of age. Our retrospective analysis, fashioned after the psychological autopsy, revealed a number of probable suicides especially in cases involving young men who died in single car accidents. (Sterling-Smith, 1976).

What are the implications and recommendations from our investigation into youth suicide methods? There are several:

- Although the numbers may be few, suicide statistics should be gathered on children under 10 years of age.
- In the U.S. Vital Statistics we were able to find methods by age and methods by sex but not methods by age by sex. We recommend that statistics be made available in this fashion.
- The extant literature on youth suicide with regards to method has several shortcomings. There is a lack of control studies. These are necessary so that we might determine more accurately to what extent youth suicide differs by age and from the adult population.

  For example, are different methods available to youth than adults? If so, at what ages and how does this discrepancy arise?
- We believe that the selection of a self-destructive method depends upon a constellation of sociocultural factors. However, just what and how these factors are has not been well documented. There is a need for well developed studies that will identify what social factors are influencing the choice of method for the youth population and how these factors might differ by sex, by age, and from the adult population. It is also important, once these factors have been isolated to know how they might be changing. This would have implications both for prevention and for prediction of future trends.
- We also believe that methods should be studied in context. If those who are collecting data on youth suicide methods would use one of the existing scales that accounts for the context of the event, we would have a better grasp on the relative lethality for various age, sex, and ethnic groups as well as important distinctives between methods chosen by youth as compared to adults. This would greatly enhance our understanding and take us beyond our current state of listing methods only in the grossest of forms.

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STUDY	N	AGES	POPULATION	FINDINGS
Goldney 1981	109 Females	18-30	Women admitted to large city general hospital for self-poisoning.	—There was no significant correlation between age and intent to die. (Beck Scale) —There was a significant correlation between intent to die and seriousness of the attempt. —Many of the serious attempts involved anti-depressant medications.
Hawton	50	13-18	Admissions to Oxford General Hospitals.	Compared to adult self-poisoners, adolescents more frequently took non-opiate analgesics and less frequently took psychotropic drugs. Alcohol was less related to overdoses among adolescents than in adults, especially in the younger groups. Most of the drugs used were found around the house and not prescribed specifically for the patient.
Hawton & Goldacre 1982	682	12-20	General Hospital admissions, Oxfordshire 1974-79	Self-poisoning was higher for females then for males. Of frequent use were analgesics and anti-pyretics, the use of which increased by age for males and decreased by age for females. The use of psychotropic drugs increased as the women got older but such was not true for the males.
Holinger 1978	unknown	10-24	U.S. vital statistics completed	<table><tr><th></th><th>Poison</th><th>Gas</th><th>Hanging</th><th>Firearms</th><th>Other</th></tr><tr><td>10-14</td><td>5%</td><td>0%</td><td>46%</td><td>47%</td><td>3%</td></tr><tr><td>15-19</td><td>13%</td><td>7%</td><td>19%</td><td>55%</td><td>3%</td></tr><tr><td>20-24</td><td>13%</td><td>8%</td><td>16%</td><td>55%</td><td>0</td></tr></table>—The smaller number of self-poisoning in the 10-14 age may be due to listing such behavior as "accidental." —Firearms, Gas, and Hanging were used most frequently by males; self-poisoning was not frequently used by females.
McIntyre & Angle 1971(A)	1,103 35% M 65% F	6-18	Reports from 50 poison centers in U.S. and U.K., 1968-1969.	—75% of the poisonings were suicide related. —Self-poisoning was higher among males than females in the younger ages (6-10) but the order was reversed in the older group (11-13). —Self-poisoning among blacks decreased with age while it increased with age for caucasians. There is speculation that the older blacks may have looked to other means than poison.
McIntyre & Angle 1971(B)	1,103	6-18	Reports from 50 poison control centers in U.S. and U.K.	<table><tr><th></th><th>Male%'</th><th>Female%</th></tr><tr><td>6-10</td><td>63%</td><td>37%</td></tr><tr><td>1-13</td><td>31%</td><td>69%</td></tr><tr><td>14-16</td><td>28%</td><td>72%</td></tr><tr><td>17-18</td><td>39%</td><td>61%</td></tr></table>—As in adults, self-poisoners are more frequently female. —Self-poisoning in a child over 6 years of age is rarely accidental. —Sedatives (barbiturates, non-barbiturates, & Tranquilizers) were used most frequently by all age groups. The next most used drug was aspirin which was used in a quarter of all cases.
Marks 1977	600 M=268 F=332	Mean age was 19.5 yrs.	College Students from South and Non-South	In ranking preference for method of suicide, both sexes ranked self-poisoning the most desirable. Firearms were ranked higher by men than women. Women were more likely than men to cite painlessness for their choice of method. Men were more likely to choose methods because of their accessibility or efficiency.

Table 1.

STUDY	N	AGES	POPULATION	FINDINGS
Paulson 1978	34 M=23 F=11	Mean age=8.2 yrs.	Seen at UCLA Neuropsychiatric Institute 1970-1974	Documented suicide attempts involved more self-abuse and bodily mutilation than self-poisoning. Self-abuse involved cutting, stabbing, burning and jumping in front of moving vehicles or from high places. Although there were no sex significant differences in ideational violence, there was a significant relationship between family disorganization, violent ideation, and a mutilating assault.
Pfeffer 1979	42	6-12 Mean age=9.0	Bronx Municipal Hospital, Child Psyc. in-patient.	Jumping was the most frequent choice of attempters (38%), followed by self-poisoning (25%), burning (19%), cutting (13%), and running into traffic (6%).
Pfeffer et al. 1980	13	6-12		Although jumping was the most frequent ideation or threat, only one jumped in front of traffic. Of the remaining 12, there was 1 self-poisoning, 1 stabbing, 2 hangings, and ??
Pfeffer	65 M=48 F=17	6-12	Children admitted to the child psychiatry unit of New York Hospital, Westchester March 1979-June 1981	Jumping from high places was the most frequent method used and it was used in 25% of all cases.
Shaffer 1974	30	12-14	Completed suicides in England & Wales 1962-1968.	—Most frequent method used was carbon monoxide. —More males than females hanged themselves. —More females than males used self-poisoning.
Selden & 1980	unknown	15-24	National statistics??	The rate of suicide by firearms increased 97.1% from 1966-1975 while the rate of suicide by other means increased 72.4% for the same period. The significantly large increase in death by firearms may reflect the 14.5% increase in the availability of legal handguns during the same time period.

Table 1 concluded.

NEUROTRANSMITTER MONOAMINE METABOLITES IN THE CEREBROSPINAL FLUID AS RISK FACTORS FOR SUICIDAL BEHAVIOR

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Introduction

The idea that brain biochemistry may contribute to a person's decision to take his own life is fairly recent. In a bibliography (1) of research on suicide published between 1958 and 1967, only five out of 1267 titles deal with biochemical subjects. Suicide has been conceived of as an exclusively human behavior, which presupposes intentionality and a concept of death, and whose biological background is remote and irrelevant.

Recently, however, two lines of study have suggested that some instances of suicidal behavior may indeed have biological correlates, which obtain not only in conjunction with depression, but even perhaps when no depressive disorder is apparent. Two clusters of biological factors have emerged that tend to correlate with suicidal behavior, namely variables associated with a neurotransmitter, the monoamine serotonin (5-hydroxytryptamine, 5-HT), and variables associated with certain neuroendocrine functions. This paper will review the evidence for a relationship between serotonin and suicide attempts or completed suicide.

Biochemical Methods

The biochemical investigation techniques used in the field almost entirely derive from studies of depressive illness. They include studies of brain tissue obtained at autopsy, and measurements in cerebrospinal fluid (CSF), blood platelets and plasma, and urine. Monoamines and their precursors, catabolizing enzymes, and degradation products have all been measured; and hormonal processes thought to be controlled by monoamine neurons, and the reaction of the various systems to challenge, have been studied. This review will focus on measurements of CSF concentrations of monoamine metabolites, particularly the serotonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA) and the dopamine metabolite, homovanillic acid (HVA).

Cerebrospinal Fluid Measurements as an Indicator of Brain Events

CSF metabolite concentrations have been widely studied to clarify the turnover of the monoamines in the brain. The advantage of the CSF studies is that spinal fluid is comparatively easily obtained with little discomfort to the patient--usually by means of a lumbar puncture (LP), a routine procedure in neurological investigations.

There are disadvantages as well. The concentration of the metabolites of serotonin and dopamine, 5-HIAA and HVA, depend, *inter alia*, on the subject's sex and age (2-4),

and on body height (5-7). The dependence on body height is presumably due to an active removal from the CSF of the acid metabolites as they flow from the brain ventricles down to the lumbar sac where the CSF is sampled. The concentrations of 5-HIAA and HVA decrease along the route of the CSF from the cerebral ventricles to the lumbar sac (8-9). A concentration gradient is seen even within the small volume usually drawn at lumbar puncture (10-12).

Metabolite concentrations also vary seasonally (7,13), and with the time of the day (14). Most important for clinical studies, the concentrations of 5-HIAA and HVA are drastically altered by treatment with certain psychotropic drugs. Many antidepressant treatments lower CSF 5-HIAA (4,15-19), and neuroleptic drugs usually increase HVA (20-23). Some factors of importance for the concentrations of 5-HIAA and HVA in lumbar CSF are summarized in Table 1. (Tables begin on page 207.)

Clearly, when groups of subjects are compared, confounding factors must be controlled or taken into account, as their influence is sometimes substantial and may lead to erroneous conclusions. Thus, if consistently more CSF is drawn from one group than from another in a comparative study, the average concentration of 5-HIAA and HVA will naturally be lower in the group from whom less CSF was taken. On the other hand, a true difference in concentration may be hidden if, for instance, control subjects are taller on the average than experimental subjects. The difference in average CSF 5-HIAA between depressed patients and healthy controls of equal stature, is numerically smaller than the difference between tall (>180 cm) and short (>160 cm) subjects, irrespective of whether they are healthy or depressed (7).

The concentration of a transmitter metabolite in the CSF is at best an indirect measure of the turnover of the parent amine in the brain, and it has been argued that, for example, 5-HIAA concentrations reflect events in the spinal cord, rather than in the brain (24). However, the recent finding by Stanley and coworkers (25) of a strong correlation between 5-HIAA concentrations measured *post mortem* in the frontal brain cortex, and in the lumbar spinal fluid, supports the contention that CSF 5-HIAA indeed reflects brain events; interestingly, the correlation between HVA in brain and in CSF was lower and was not statistically significant.

The concentration of the acid monoamine metabolites in the CSF is a function not only of their production rate, but also of their removal by an active transport mechanism from the cerebrospinal space. That the transport mechanism can be blocked by means of probenecid, has been taken advantage of in attempts to obtain more valid estimates of transmitter turnover (26). The probenecid technique has been described in detail by van Praag et al. (28). The probenecid technique, while removing one source of error, introduces other problems, however. With lower concentrations of probenecid, the blockade of the transport mechanism is incomplete, and may vary within individuals because of differences in probenecid metabolism. Higher probenecid concentrations often cause nausea and vomiting, and may also alter central neurotransmitter turnover.

One of the advantages with the probenecid technique is that concentrations of the monoamine metabolites are increased, which places less heavy demands on the analytical methods. With the very sensitive methods available today, concentrations in the nanomole range can be measured with satisfactory precision, and most investigators rely on baseline measures of the metabolites rather than on probenecid-induced accumulation.

Measures of Suicidal Behavior

In comparison with the advanced biochemical methods used in the studies to be reviewed, the approach to measuring suicidal behavior has been much less sophisticated. The reason for this is probably that, rather

than being designed to deal with suicidal behavior, most studies were focused on depressive illness and relied on procedures developed for measuring severity of depression. Diagnostic inventories and depression rating scales often contain an item dealing with suicidal ideation and tendencies, and such ratings have been used in some studies.

In other studies, the occurrence of 'suicide attempts' has been related to the biological variables. While some studies use more or less explicit, operational definitions of the term **suicide attempt**, others do not even attempt a definition. Although, in very few studies, ratings have been made of intent and lethality of a suicide attempt, heuristically the most useful classification seems to be according to the method used in the attempt (active, violent, or passive, nonviolent)-- perhaps because of its high reliability.

The time span involved also varies from one study to another. Some investigators have considered the incidence of any suicide attempts in the patient's history, while others have focussed on attempts during the current illness episode. In the former approach, the biological measures are assumed to be stable over time, a controversial assumption which will be discussed later.

Only a very few investigators have examined the possible predictive value of biological variables for ultimate suicide--understandably so, considering the low base rate of suicide and the time and cost of the investigation.

None of the available studies has dealt with the question of youth suicide. Although there seems to be little reason to believe *a priori* that a correlation between a biological variable and suicidal behavior would be limited to a certain age group, the issue remains to be empirically examined.

CSF 5-hydroxyindoleacetic acid (5-HIAA)

In a study of possible clinical correlates of CSF 5-HIAA in depressed patients, Asberg et al. (29) unexpectedly found patients with low concentrations of the serotonin metabolite to represent an increased incidence of suicide attempts (defined as any deliberate, self-inflicted injury, regardless of the lethality risk involved, that the patient had thought to entail a death risk).

The findings of previous research by van Praag and Korf (30) and Asberg and coworkers (4,31) (see also Gibbons and Davis (32)) had indicated that the concentrations of the metabolite were bimodally distributed in depressed patients, suggesting the existence of a biochemical subgroup of depressive illness characterized by disturbed serotonin turnover. In the study by Asberg et al. (29), 40 percent of the patients with low CSF 5-HIAA concentration had attempted suicide during their current illness, as compared with 15 percent in patients with normal 5-HIAA. Moreover, the attempts were of a more determined nature with a preference for active, violent methods in the low 5-HIAA patients, whereas those in the high 5-HIAA groups were confined to drug overdoses. Two deaths from suicide occurred during the study period, both in low 5-HIAA patients.

The relationship between CSF 5-HIAA and suicidal behavior was confirmed by Agren (33), who studied depressed patients and measured suicidal behavior by means of the suicide behavior scales in the Schedule for Affective Disorder and Schizophrenia (SADS). These scales do not differentiate suicidal ideation and suicidal acts. In the Asberg et al. (29) study, low CSF 5-HIAA was not correlated to suicidal ideation, only to suicidal acts. Argren's choice of method may thus have weakened the correlation, which nonetheless was statistically significant.

These early studies did not take into account the relationship between CSF 5-HIAA and such interference factors as sex and body height. Men tend to have lower CSF 5-HIAA concentrations than women, and they are also more prone to use violent methods if they attempt suicide. The sex factor could, however, be ruled out in a subsequent confirmatory study by Traskman et al. (34), who

adjusted for interference factors by analysis of covariance (ANCOVA).

More recently, the relationship between 5-HIAA and suicide has been confirmed in Dutch depressed patients studied by van Praag (35), who found a highly significant increased incidence of suicide attempts in patients with low probenecid-induced accumulation of 5-HIAA. The association between 5-HIAA and a violent mode of the attempt was not confirmed, however.

In a British study of depressed patients, Montgomery and Montgomery (36) also found more suicide attempts in patients with low CSF 5-HIAA concentrations (using the cut-off point between "low" and "normal" 5-HIAA suggested by Asberg and coworkers (31)).

Among depressed patients in India, Palaniappan and coworkers (37) found a significant correlation between CSF 5-HIAA concentrations and suicidal tendencies estimated by scores on the item Suicide in the Hamilton Rating Scale. A rating scale index of suicidal tendencies was also used by Leckman et al. (38), who found an association with 5-HIAA which was confined to patients with disturbed reality testing.

Banki and coworkers (39) found a relationship between low CSF 5-HIAA and suicide attempts in Hungarian female patients, a relationship that was confined to those who had used active methods. Lopez-Ibor et al. (4) (1985) reported a relationship between suicide attempts and low CSF 5-HIAA in Spanish patients, irrespective of the method used in the attempt. A further confirmation in Swedish patients was provided by Edman and coworkers (41), using the same methods as in the original Asberg et al. (29) study.

There are also, however, some nonconfirmatory studies. Vestergaard and coworkers (42) mention that among depressed patients studied by them, suicide and suicide attempts were equally frequent in individuals with low and high CSF 5-HIAA. Since they do not provide any further information, their data have not been included in Table 2, which summarized the relevant studies.

A well-designed, nonconfirmatory study was performed by Roy-Byrne and coworkers (43), who studied American patients, most of them more or less treatment-resistant, referred to a research center specializing in the study of depressive disorders. No significant relationship was found between CSF 5-HIAA and suicide attempts (over the individual's lifetime), possibly owing to the high proportion of bipolar (manic depressive) patients in the group. Suicidal unipolar patients tended to have lower CSF 5-HIAA than had nonsuicidal unipolars, but the number of such patients was too small for statistical analysis. The biological correlates of suicidal behavior may thus differ between bipolar and unipolar disorders, a conclusion also reached by Agren (44).

Another difference between the study of Roy-Byrne et al. (43) and those of Asberg et al. (29) and Traskman et al. (34), is that the former considered suicidal behavior over the patient's entire life span. In the Asberg et al. (29) study, the significant association with CSF 5-HIAA was restricted to suicidal behavior during the index illness episode. The discrepancy suggests that CSF-HIAA values may not be stable over time in suicidal individuals, a possibility that will be discussed in further detail below.

Only about half of those who commit suicide are retrospectively diagnosed as having suffered from a depressive syndrome, as suggested from the thorough psychological autopsies performed by Beskow (45) and Asgard (in preparation). Several groups have studied the relationship between suicide attempts and CSF 5-HIAA in other diagnostic categories. Traskman et al. (34) found CSF 5-HIAA concentrations to be lower in **nondepressed** suicide attempters (mainly patients with personality disorders and minor affective disorders). Brown et al. (46-47), studying two groups of men with **personality disorders**, found more subjects who had made a suicide attempt at some point in life among those with low CSF 5-HIAA.

van Praag (48), and Ninan and coworkers (49), found a similar association in **schizophrenia.** This finding is somewhat against the odds, considering the report by Sedvall and Wode-Helgodt (5) that a subgroup of schizophrenic patients (those with a family history of the disorder) have abnormally high concentrations of the metabolite. Both suicide studies are well-designed with carefully selected, matched controls. Patients with a depressive disorder superimposed on their schizophrenia were deliberately excluded from van Praag's (48) study. Roy et al. (51), however, found no difference in CSF 5-HIAA concentrations between chronic schizophrenic subjects who had attempted suicide at some time during their life, and those who had not made such attempts. Lower CSF 5-HIAA concentrations were, however, reported in suicidal patients with schizophrenia than in nonmatched controls by Banki et al. (39), who also found similar relationships in **alcoholism** and **adjustment disorder.** The bulk of the evidence would thus seem to support the notion that potential for suicidal behavior is reflected in low concentrations of CSF 5-HIAA-- even when no major affective disorder is apparent.

CSF Concentrations of Homovanillic Acid (HVA)

The average concentration of the dopamine metabolite, HVA, in CSF is reduced in depression (52-53), and more consistently so than is CSF 5-HIAA, to which HVA is nevertheless strongly correlated. Whether the correlation between the two metabolites is due to their sharing the same transport mechanism, or to a functional connection between the parent amines is not known. A functional connection would seem to be indicated because of the consistent finding that, in addition to reducing 5-HIAA, drugs that interfere with serotonin turnover--such as the antidepressants clomipramine (54), zimeldine (19), and citalopram (55)--change HVA concentrations in CSF, while having no known direct effects on dopamine neurons.

Low concentrations of HVA in suicidal depressed patients have been reported by Traskman et al. (34), by Montgomery and Montgomery (36), by Palianappan (37), and by Roy et al. (56). In the Roy et al. (56) study of 27 depressed patients, the association between low HVA and suicidal behavior was much stronger than that between 5-HIAA and suicide, which did not reach statistical significance. In his 1980 study, Agren (33) found no association between HVA and any of the SADS suicide scales. In Agren's later (44) and larger patient group, he reports an association between low HVA and the lethality of suicide attempts made prior to the current episode.

Banki et al. (39), on the other hand, found suicide attempts to be less clearly related to HVA than to 5-HIAA. In particular, their depressed patients who had taken drug overdoses had significantly higher HVA than had nonsuicidal patients, whereas HVA was low in attempters who had used violent methods.

The studies of HVA in CSF in relation to suicidal behavior are summarized in Table 3. Interestingly, none of those who have studied nondepressed groups have reported any association between CSF HVA and suicidal behavior. Thus, Brown et al. (47) found no association in their patients with personality disorders. Leckman et al. (38) report no association in their diagnostically heterogeneous group, and Traskman et\al. (34) found an association only in those of their patients who fulfilled research criteria for a diagnosis of depressive illness. Ninan et al. (57) found no association in their schizophrenic subjects. A possible interpretation of the findings would be that CSF concentrations of HVA are related to suicidal tendencies, but only in conjunction with a depressive illness. Studies of patients with bipolar depressive illness would seem to be particularly interesting in the context.

Noradrenaline and 4-hydroxy-3-methoxy-phenylglycol (HMPG)

In contrast to the evidence relating suicide to serotonin, the relationship with noradrenaline is less clear. In depressed patients, Agren (33) reported a negative correlation between suicidal tendencies and the CSF concentration of the noradrenaline metabolite, 4-hydroxy-3-methoxy-phenylglycol (HMPG). Brown and coworkers (46) found a positive correlation in subjects with personality disorders, which was not reproduced in their study (47) of borderline patients.

In two studies of mixed diagnostic groups, Ostroff and associates (58-59) measured the ratio between noradrenaline and adrenaline (the NA:A ratio) in urine and found a relationship between a low ratio and suicidal behavior. Within a group of suicide attempters, Prasad (60) found the NA:A ratio to be significantly lower in those who used violent methods in the attempt.

Other Substances in the CSF: Cortisol and Magnesium

The relative robustness of the association between CSF 5-HIAA and suicide tendencies has inspired investigators to examine the correlations with other biological markers than the amine metabolites. Traskman et\al. (6l) thus measured cortisol concentrations, but found no abnormality in suicide attempters. Depressed patients, on the other hand, had significantly higher CSF cortisol than had healthy control subjects.

Banki and coworkers (62) found a relationship between suicide attempts and low CSF concentrations of magnesium. There was a strong positive correlation between CSF magnesium and CSF 5-HIAA. Interestingly, magnesium concentrations in CSF are strongly correlated to CSF melatonin concentrations (63). Melatonin in plasma may in turn be related to suicidal tendencies. Beck-Friis and coworkers (64) reported that nocturnal serum melatonin concentrations, known to be decreased in depression (65-66), were closer to normal in suicidal, than in non-suicidal depressed patients. Melatonin production is dependent on prevalent lighting conditions and thought to be regulated by beta-adrenergic neurotransmission. Serotonin is a precursor of melatonin, although little is known of any correlation between the concentrations of the two compounds in humans.

Post Mortem CSF Measurements in Suicide Victims

The concentrations of monoamines (serotonin, dopamine, noradrenaline and adrenaline) after death by suicide were measured in suboccipital CSF by Kauert et al. (67), who somewhat unexpectedly found increased serotonin concentrations in the suicide victims. Their finding has, however, received support from preliminary findings by Arato et al. (68), who report significantly higher concentrations of 5-HIAA in lumbar and suboccipital CSF obtained post mortem from suicide victims.

The CSF autopsy studies are summarized in Table 4, which also contains summaries of some studies of monoamines and metabolites in brain tissue from suicide victims. The post mortem CSF findings may prove crucial for our understanding of how alterations in serotonin transmission predispose to suicidal behavior--that is, if they can be confirmed and are not due to any of the sources of error that mar autopsy studies of suicide victims (such as delay between death and discovery of the body, the influence of drugs, mode of dying and agonal state).

Prediction of Suicide from CSF Measures

Those who commit suicide and those who merely attempt it differ notoriously in many important respects, even if there is an overlap between the two populations (69). In several studies, subsequent mortality from suicide among suicide attempters has amounted to about 2 percent within a year after the attempt (70). Although this is a

considerable increase in suicide frequency over that of the general population, suicide is a rare event even in this group.

Estimating suicide risk so as to be able to take appropriate precautions is one of the most difficult tasks of the practicing psychiatrist, and many attempts have been made to create rating scales and inventories for the purpose. Most of these have not been very successful (71-72), which may be due, at least partly, to the low base rate of suicide and other statistical problems (73).

Among a well-known risk group for suicide, namely patients who have made a suicide attempt, those with low CSF 5-HIAA were 10 times more likely to die from suicide than the remainder (34) (see also Table 5). Roy et al. (56) reported a relationship to exist between low concentrations of HVA in the CSF and subsequent suicide in depressed patients, regardless of whether previous attempts have been made. These findings suggest that inclusion of biological variables in the clinical assessment of suicide risk might increase its precision.

To judge from the studies published so far, there is fairly consistent evidence that low concentrations of CSF 5-HIAA are associated with an increased rate of suicide attempts, and may be a risk factor for suicide in individuals with a psychiatric history. There is also evidence relating low HVA concentrations in the CSF to suicide, although so far only in depressed individuals.

Among the many questions raised by these findings, a few will be discussed here: how do the CSF risk factors correlate with other potential biological risk markers; what can be inferred about the processes whereby a disturbed serotonin system may predispose to suicide; and how this knowledge can be applied in preventing suicide.

Correlations Between Possible Biological Risk Factors

Apart from the 5-HIAA concentrations in CSF, a series of biological markers related to serotonin have been reported to be disturbed in depressive illness. Among them are the concentrations of the precursor, tryptophan, in serum and its ration to other amino acids transported by the same mechanism (74), the binding of the antidepressant drug imipramine to specific sites in blood platelets (75-76), the uptake of serotonin by the platelets (77-78), and the concentrations of serotonin in platelets and plasma. The urinary output of 5-HIAA, on the other hand, is of little interest since it is strongly influenced by diet, varies from day to day, and is uncorrelated to CSF 5-HIAA (79).

So far, there are very few studies of other serotonin-related markers in relation to suicidal behavior, and little is known of the interrelations between them. These relationships need to be clarified, both with a view to understanding their physiological significance and for practical diagnostic purposes.

Interestingly, there are no clear-cut relationships between imipramine binding and serotonin uptake in depressed patients (80). These two possible serotonin markers may thus reflect different aspects of serotonin function. The relationships reported between CSF 5-HIAA and platelet MAO activity have not been consistent (81-82).

Monoaminergic neurons are known to be involved in the chain of events resulting in the release of many hormones, including cortisol. The details of this have not yet been worked out, but the data from the Meltzer et al. (83) study of 5-hydroxytryptophan-induced release of cortisol strongly suggest a functional connection between the serotonin system and HPA axis.

The available human data do not, however, show any negative correlations between markers of the serotonin system and the hypothalamus-pituitary-adrenal axis, such as might be expected if they reflect an identical risk factor for suicide. Thus, CSF concentrations of cortisol and of 5-HIAA have been shown to correlate positively, though weakly (61), or not at all (62,84). Both Carroll et al.

(85), and Banki and Arato (86), found a positive correlation between postdexamethasone cortisol and 5-HIAA. Interpretation of the results of Carroll et al. (85) is, however, complicated by the fact that spinal fluid was drawn after the administration of dexamethasone, which raises CSF 5-HIAA concentrations (87).

Among other potential markers of serotonin, the ratio of l-tryptophan to other neutral amino acids was positively correlated to postdexamethasone cortisol (88), whereas vmax of serotonin uptake into platelets (which is reduce in depression) tended to be negatively correlated to an abnormal DST (89). Preliminary reports suggest that the 5 hydroxytryptophan-induced cortisol release may be related to CSF 5-HIAA (90).

Gold and coworkers (91) report an inverse correlation between CSF 5-HIAA concentrations and the magnitude of the increase in thyroid stimulating hormone (TSH) reaction to administration of thyrotropin releasing hormone (TRH). The negative correlation between CSF 5-HIAA and the TRH/TSH-test also appears in a study by Banki and coworkers (39), where it is compatible with their finding of more normal TRH/TSH- responses in suicidal than in non-suicidal patients.

Stability of CSF Concentrations of 5-HIAA over Time

Related to the question of the usefulness of biological markers as risk factors for suicide, is their stability over extended periods.

Unfortunately, CSF studies of recovered depressives are rare. Such patients are often maintained on drugs for extended periods, and those who are not, even if available for lumbar puncture studies, may well be non-representative of the depressed population.

A further complication in followup studies is that most serotonin-related variables also seem to vary seasonally. Seasonal rhythms have been shown for the serotonin concentration in the human hypothalamus (92), for the platelet serotonin uptake (93-94), and for the platelet 3H-imipramine binding (95-96). There is some evidence that a seasonal rhythm, very similar to that observed for serotonin in the hypothalamus, may also exist for CSF 5-HIAA (7).

The evidence from four published followup studies of depressed patients (52,97-99) is summarized in Table 6. 5-HIAA concentrations in CSF appear to remain fairly stable over limited periods in normal subjects, and in depressed patients re-admitted for relapse of depression (99). Recovered depressives, whose concentrations are normal during illness, also remain stable over prolonged periods, whereas in depressives with low 5-HIAA during illness the concentration sometimes increases with recovery, though it remains in the low range in most cases.

A possible interpretation of available data is that there is a subgroup of depressed patients, characterized by concentrations of CSF 5-HIAA that are not only low but also less stable over time. If this type of unstable serotonin system is associated with an increased vulnerability to illness, and with a further decrease in release during illness, the emergence of bimodal distributions in diseased populations is easily explained.

In line with the 'instability' hypothesis, are findings from two patients in whom repeated lumbar punctures were made, and who subsequently committed suicide (Asberg and coworkers, in preparation). In both cases, there was a substantial reduction in CSF 5-HIAA from one puncture to the next. The above-mentioned finding by Arato et al. (68), of higher CSF 5-HIAA in CSF from suicide victims than in controls may also be in line with an instability hypothesis.

Low CSF 5-HIAA - a Vulnerability Marker?

Low concentrations of 5-HIAA in CSF occur not only in depressed and suicidal people, but also in perfectly healthy subjects (53). This suggests that low CSF 5-HIAA is not a marker of the state of depression, but rather

an indicator of vulnerability. Supporting the vulnerability hypothesis, van Praag and de Haan (100) found an increased incidence of depressive illness in relatives of patients with low CSF 5-HIAA, compared with those of patients with normal 5-HIAA concentrations. This finding is reminiscent of the observation by Sedvall and coworkers (101) that CSF 5-HIAA concentrations were lower in healthy subjects with a family history of depressive illness than in healthy subjects without such antecedents. Preliminary data from twin studies by Sedvall and coworkers (102) further support familial involvement in CSF concentrations of the monoamine metabolites.

Serotonin, Aggression and Suicide

If serotonin transmission is permanently low or unstable, it is conceivable that this may be manifested in other ways than in suicidal tendencies. The often quite unpremediated, impulsive and violent character of may of the suicide attempts in low 5-HIAA patients gave rise to the suggestion (29) that they might have difficulties in controlling aggressive impulses. The hypothesis was supported by the association known to exist between aggression in animals, and serotonin turnover (summarized by Valzelli (103)), as well as the links between anger and suicide proposed by classic psychoanalytical theory (104-105).

'Aggression' is a somewhat nebulous concept. The word has many meanings, and some aspects of aggression are hardly amenable to empirical study. Aggression, in the sense of verbal threats or violent acts aimed at causing injury to others or to oneself, has, however, been studied in suicidal individuals. Thus, Weissman et al. (106), found that excessive hostility was characteristic of suicidal depressed patients, and Brown et al. (47), found more overt aggressive behavior in subjects who had made suicide attempts.

One of the strongest predictors of suicide is murder. In Great Britain, a 30 percent suicide rate is reported among murderers after the act. The risk of suicide is greatest in those cases where the victim is a spouse (107). (In the United States, the suicide rate among murderers is lower, around 4 percent according to Wolfgang (108).)

Several investigators have tested the hypothesis that aggression dyscontrol is the link between serotonin turnover and suicidal behavior. Brown and associates (46) found a life pattern of aggressive behavior in subjects with personality disorder and low CSF 5-HIAA.

Further support for a relationship between serotonin and violence came from three studies of murderers. Linnoila and coworkers (109), found lower CSF 5-HIAA in violent offenders whose crimes were unpremediated. Lidberg et al. (110), found lower CSF 5-HIAA in homicide offenders who had killed a spouse or a lover than in those who had killed someone of less emotional significance (usually a drinking buddy). Lidberg and coworkers (111) also found very low CSF 5-HIAA concentrations in three cases, where suicide attempters had killed, or attempted to kill, their children.

A relationship between serotonin and aggressive behavior in alcoholics was also found by Branchey et al. (112), who studied the ratio of tryptophan to other neutral amino acids in serum. They found significantly lower ratios, compatible with a deficiency of brain serotonin, in those subjects who had been arrested for assaultive behavior than in other alcoholics or in nonalcoholic controls.

Suicide and the Biology of Personality

Interestingly, some personality features that seem to be prominent in patients who attempt suicide, are also associated with CSF concentrations of 5-HIAA. These personality features often reflect impulsivity and problems in the handling of anger. In normal people, low CSF 5-HIAA appears to be associated with vitality, social dominance and easily aroused anger, as shown by Zuckerman et al. (82), and Schalling et al. (in preparation). In psychiatric patients, low

CSF 5-HIAA has also been associated with high vitality, self-reported impulsivity and psychopathy- related features (47,113-114), and with high hostility and anxiety in ratings based on Rorschach protocols (115). Correlations with HVA, when reported, are generally parallel those with 5-HIAA, but are weaker.

Implications for Suicide Prevention

Their association with a heightened risk of suicide suggests that markers of serotonin may be valuable in a clinical context. Low concentrations of CSF 5-HIAA in suicide attempters, for instance, were connected with a 20 percent mortality from suicide within a year, which suggests that the combination may be one of the strongest suicide predictors hitherto identified. The number of false positives is, however, still very large.

Although it seems likely that CSF determinations might help in the assessment of suicide risk, there are problems in applying the technique in a clinical setting. Owing to the many factors that influence CSF concentrations of 5-HIAA and HVA, the spinal tap procedure must be standardized to an extent that is rarely practical in a busy clinic. Furthermore, the patients must be hospitalized overnight, and most difficult of all, they must have been off antidepressant and neuroleptic drugs, and lithium, for several weeks prior to the puncture.

Usually, the spinal tap is easily tolerated by the patient, and the post LP headache that afflicts about a third of the subjects is not a major problem. The procedure sometimes appears to pose greater problems for the psychiatric staff, who may feel that it is too "medical" and out of tune with the type of therapeutic relationship they wish to establish with the patient.

Thus, though there is an obvious need for new, more easily accessible markers of the state of the serotonin system, in centers with access to the relevant analytical procedures, routine spinal taps may nevertheless be a real help in clinical management.

A better understanding of the biological and psychological links between serotonin turnover and suicidal behavior might also open up new approaches to the prevention of suicide. Serotonin transmission can be controlled, with drugs or amino acid precursors, and possibly by dietary changes, and it would seem important to test such treatment regimens in patients with a high suicide potential. It is also possible that an increased understanding of the psychological processes that are controlled by serotonin neurons could be used to develop more specific psychotherapeutic techniques than has hitherto been possible.

CONCLUSIONS

In a number of studies, a relationship has been shown to exist between low CSF concentrations of the serotonin metabolite 5-HIAA and an increased incidence of suicide attempts in psychiatric patients. Although most studies deal with depressed patients, there is fairly strong evidence that this relationship exists in other disorders as well, particularly in personality disorders and possibly also in schizophrenia. Some reports suggest that bipolar (manic-depressive) disorder may be an exception.

Low concentrations of the dopamine metabolite HVA may also be associated with suicide attempts. Although this may to some extent be accounted for by its correlation with 5-HIAA, there is probably more to it, since unlike 5-HIAA, the association may be confined to depressive disorder.

Both markers have been associated with an increased frequency of ultimate suicide, but there is a need for further prospective studies.

Low CSF concentrations of 5-HIAA may reflect a low serotonin output, or possibly a low stability serotonin system, which may in turn be a vulnerability factor. In most individuals with low CSF 5-HIAA, this vulnerability will never be manifested in a suicide attempt. A suicide attempt is unlikely to occur unless the individual finds himself

in a situation which he conceives of as desperate, or when he is without hope for the future. Adverse events may have created this situation, or the individual's perception of the situation may be colored by depressive illness. Previous experience of adverse events (e.g., during childhood) is liable to render the interpretation of current adversity more ominous. Whether this state of affairs leads to a suicide attempt, is to some extent determined by the quality of the person's social support network, which may attenuate the effect of adverse events, or render the sufferings of depressive illness more tolerable.

A low-output serotonin system (or perhaps even more likely, a low-stability one) might render an individual more vulnerable to self-destructive or impulsive action in time of crisis. This characteristic of the serotonin system may have a genetic basis, or it may be acquired.

Although little is known of the processes linking serotonin with suicidal behavior, there is some evidence that personality features such as impulsivity and difficulties in handling aggression may be important intervening variables.

CSF measures are currently used as an aid to suicide risk prediction in some highly specialized clinical settings. They appear less likely to be useful on a larger scale, because of the need for strict standardization of the procedure. An important research task would seem to be to identify other markers of the serotonin system that can be measured repeatedly over time in large groups of subjects.

The potential for treatment and prevention of suicide remains to be explored.

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Some factors of importance for the concentrations of 5-HIAA and HVA measured in lumbar spinal fluid samples.

Factor	Possible control measure
Subject's age and sex (2-3,6)	Matched controls or ANCOVA
Subject's body height (5,6)	Idem
Physical illness, e.g. Parkinson's disease (116), multiple sclerosis (117), adult coeliac disease (118) and hydrocephalus (119)	Physically healthy subjects
Drug treatment (4, 15-23)	Drug-free subjects
Time of day (14)	Samples always drawn at the same time
Time of year (7,13)	Patients and controls matched for season
Diet a	Fasting subjects or controlled diet
Physical movement (120)	Bed rest prior to lumbar puncture
Subject's position at lumbar puncture b	Same position always used
Amount of CSF drawn (122)	Same amount always drawn
Handling and storage of samples	Identification procedures for all samples
Analytical method (123-125)	Best available method

a. It cannot be excluded that a diet particularly rich (or poor) in monoamine precursors might influence the metabolic concentrations. Thus underweight anorexia nervosa patients have significantly lower CSF 5-HIAA than weight-recovered and long-term weight-recovered anorectics. (126)

b. Siever et al. (10) report that the concentration gradient of CSF 5-HIAA was cost in the decubitus position. Gateless et al. (127), on the other hand, found similar gradients in sitting and lying patients.

Table 1.

Studies of CSF 5-HIAA in Relation to Suicidal Behavior

Author	Subjects	CSF sampling and analysis	Confounding factors	Measure of suicidality	Result
Asberg et al. 1976 (29)	68 hospitalized depressed patients	standardized; GC-MS	not controlled	attempted or completed suicide within index illness episode	low 5-HIAA in the 15 attempters, particularly those using violent methods
Brown et al. 1979 (46)	22 men with personality disorder	standardized; fluorometry	not controlled	lifetime history of suicide attempt	lower 5-HIAA in the 11 suicide attempters
Agren 1980 (33)	33 depressed patients	standardized; GC-MS	not controlled	SADS suicidality scales	negative correlation between 5-HIAA and suicidality scores
Traskman et al. 1981 (34)	30 suicide attempters (8 major depressive, 22 other psychiatric disorders excluding schizophrenia and alcoholism), 45 healthy controls	standardized; GC-MS	controlled by ANCOVA for age, sex and body height	recent attempted or completed suicide	5-HIAA lower in both categories of attempters than in healthy controls
Lackman et al. 1981 (38)	132 psychiatric patients, several diagnoses	standardized, after probenecid; fluorometry	not controlled	item suicidal ideation or nurse rating scale	negative correlation with suicidal ideation in the 76 psychotic patients
Brown et al. 1982 (47)	12 patients with borderline personality disorder	standardized; GC-MS	not controlled	life time history of suicide attempt	lower 5-HIAA in the 5 attempters
Montgomery and Montgomery 1982 (36)	49 patients with endogenous depression	not reported	not controlled	history of suicidal act	more attempters among patients with low CSF 5-HIAA
van Praag 1982 (35)	203 depressed patients	standardized, after probenecid; fluorometry	not controlled	recent suicide attempt	significantly more suicide attempters among patients with low CSF 5-HIAA
Palaniappan et al. 1983 (37)	40 hospitalized depressed patients	LP procedure not fully described; fluorometry	not controlled	suicide item in the Hamilton Rating Scale	negative correlation between CSF et 5-HIAA and suicide score
Agren 1983 (44)	110 depressed patients	standardized; GC-MS	not controlled	SADS suicidality scales	low 5-HIAA associated with recent or current suicidal ideation

Table 2.

Studies of CSF 5-HIAA in Relation to Suicidal Behavior

Author	Subjects	CSF sampling and analysis	Confounding factors	Measure of suicidality	Result
Roy-Byrne et al. 1983 (43)	32 bipolar, 13 unipolar patients in different phases of illness	standardized; fluorometry or HPLC	not controlled	lifetime history of suicide attempt	no association with 5-HIAA in bipolar patients
van Praag 1983 (48)	10 nondepressed schizophrenics who attempted suicide in response to imperative hallucinations, 10 nonsuicidal schizophrenics, 10 controls	standardized, after probenecid; fluorometry	matched for age and sex	recent suicide attempt	lower CSF 5-HIAA after probenecid in suicide attempters
Banki et al. 1984 (39)	141 female inpatients (36 depressed, 48 schizophrenic, 35 alcoholic, 24 with adjustment disorder; 45 previously reported)	standardized; fluorometry	adjusted for age and body height by ANCOVA	recent suicide attempt	negative correlation with 5-HIAA in all diagnostic groups, particularly with violent attempts
Ninan et al. 1984 (49)	8 suicidal, 8 nonsuicidal schizophrenic patients	standardized; HPLC	matched for age, sex, and physical characteristics	lifetime history of suicide attempt	lower 5-HIAA in suicide attempters
Lopez-Ibor et al. 1984 (40)	21 depressed patients	standardized; fluorometry	controlled	suicide attempt, suicidal ideation rated on the Hamilton Scale and the AMDP system	more attempts and higher suicidality scores in patients with low 5-HIAA
Roy et al. 1985 (51)	54 patients with chronic schizophrenia	standardized; HPLC	adjusted for age and body height by ANCOVA	lifetime history of suicide attempt	no difference in 5-HIAA between 27 attempters and 27 non-attempters
Edman et al. 1986 (41)	7 suicide attempters with various psychiatric disorders, 7 healthy controls	standardized; GC-MS	matched for sex, age and body height	recent suicide attempt	lower 5-HIAA in attempters
Roy et al. 1988 (56)	27 depressed patients, 22 healthy controls	standardized; HPLC	adjusted for sex and age by ANCOVA	lifetime history of suicide attempt	lower HVA in the 19 attempters

Table 2 concluded.

Studies of CSF HVA in relation to suicidal behavior

Author	Subjects	CSF sampling and analysis	Confounding factors	Measure of suicidality	Result
Brown et al. 1979 (46)	22 men with personality disorder	standardized; fluorometry	not controlled	lifetime history of suicide attempt	no correlation reported
Agren 1980 (33)	33 depressed patients	standardized; GC-MS	not controlled	SADS suicidality scales	no significant correlations
Traskman et al. 1981 (34)	30 suicide attempters (8 major depressive, 22 other psychiatric disorders excluding schizophrenia and alcoholism), 45 healthy controls	standardized GC-MS	controlled by ANCOVA for age, sex and body height	recent attempted or completed suicide	lower than controls in depressed attempters, nondepressed attempters similar to controls
Leckman et al. 1981 (38)	132 psychiatric patients, several diagnoses	standardized after probenecid; fluorometry	not controlled	item suicidal ideation on nurse rating scale	no correlation reported
Brown et al. 1982 (47)	12 patients with borderline personality disorder	standardized; GC-MS	not controlled	lifetime history of suicide attempt	no correlation
Montgomery and Montgomery 1982 (36)	49 patients with endogenous depression	not reported	not controlled	history of suicidal act	more attempters among patients with low CSF HVA
Palaniappan et al. 1983 (37)	40 hospitalized depressed patients	LP procedure not fully described; fluorometry	not controlled	suicide item in the Hamilton Rating Scale	negative correlation between CSF et HVA and suicide score
Agren 1983 (44)	110 depressed patients	standardized; GC-MS	not controlled	SADS suicidality scales	low HVA associated with high lethality of suicide attempts prior to present episode
Banki et al. 1984 (39)	141 female inpatients (36 depressed, 46 schizophrenic, 35 alcoholic, 24 with adjustment disorder; 45 previously reported)	standardized; fluorometry	adjusted for age and body height by ANCOVA	recent suicide attempt	higher HVA for drug overdose case within the depression subgroup, otherwise no clear cut association
Ninan et al. 1985 (57)	8 suicidal, 8 nonsuicidal schizophrenic patients, matched for age and sex	standardized; HPLC	matched for sex, age and physical condition	lifetime history of suicide attempt	no difference in HVA between the two subject groups
Roy et al. 1985 (51)	54 patients with chronic schizophrenia	standardized; HPLC	adjusted for age and body height by ANCOVA	lifetime history of suicide attempt	no difference in HVA between 27 attempters and 27 non-attempters
Roy et al. 1986 (56)	27 depressed patients, 22 healthy controls	standardized; HPLC	adjusted for sex and age by ANCOVA	lifetime history of suicide attempt	lower 5-HIAA in the 19 attempters, although the difference was not statistically significant

Table 3.

Some Controlled Studies of Monoamines and Their Metabolites in Brain Tissue and Cerebrospinal Fluid from Suicide Victims

Author	Subjects	Tissue	Result (concentrations in suicide victims compared to controls)
Shaw et al. 1967 (128)	22 suicides, 17 controls	Hindbrain	5-HT lower
Bourne et al. 1968 (129)	23 suicides, 28 controls	Hindbrain	5-HT similar, 5-HIAA reduced, NA similar
Pare et al. 1969 (130)	26 suicides, 15 controls	Brainstem, caudate, hypothalamus	5-HT reduced, NA and DA similar
Lloyd et al. 1976 (131)	7 suicides, 5 controls	Six raphe nuclei	5-HT lower in nuclei raphe dorsalis and centralis interior, 5-HIAA similar
Cochran et al. 1976 (132)	19 suicides, 12 controls	Several brain areas	5-HT similar
Beskow et al. 1976 (133)	23 suicides, 62 controls	Several brain areas	5-HT similar after adjustment for difference in postmortem delay; NA, DA, 5-HIAA and HVA similar
Owen et al. 1983 (134)	7 suicides, 18 controls	Frontal cortex	5-HIAA similar
Korpi et al. 1983 (135)	30 schizophrenics (50 % dead from suicide), 14 nonschizophrenic suicides, 29 controls	Several brain areas	5-HT lower in hypothalamus in non-schizophrenic suicide victims 5-HIAA and TRY similar
Kauert et al. 1984 (87)	60 suicides and controls	Cerebrospinal fluid	5 HT, NA, NM higher, DA and A similar
Arato et al. 1986 (88)	Not stated	Cerebrospinal fluid	5-HIAA higher

Abbreviations: 5-HIAA = 5 hydroxyindoleacetic acid, 5-HT = 5 hydroxytryptamine (serotonin), A = adrenaline, DA = dopamine, HVA = homovanillic acid, NA = noradrenaline, NM = normetanephrine, TRY = tryptophan.

Table 4.

Mortality from Suicide within One Year after Admission to Hospital in Some High Risk Groups

Patient category	Number	Percentage suicides
Patients admitted to intensive care unit after suicide attempt	45	2%
Patients admitted to a psychiatric clinic after a suicide attempt, CSF 5-HIAA above 90 nanomol/L	42	2%
Ditto, CSF 5-HIAA below 90 nanomol/L	34	21%

Data on suicide attempters admitted to the psychiatric department of the Karolinska Hospital derive from the studies by Asberg et al. (29), Traskman et al. (34), and Edman et al. (41). Data on patients admitted to the intensive care unit of the same hospital after a drug overdose are given for comparison.

Table 5.

Changes in CSF 5-HIAA after Recovery from Depression

Author	Type of 5-HIAA measure	N	Interval between examinations	Results
Coppen et al. 1972 (97)	Baseline 5-HIAA	8	3-59 w	Stable over time
van Praag 1977 (98)	5-HIAA after probenecid	50	6 mo	2 % of patients with low CSF 5-HIAA during illness normalized; the rest remained stable
Post et al. 1980 (52)	5-HIAA after probenecid	11	several months	Stable over time
Traskman-Bendz et al. 1984 (99)	Baseline 5-HIAA	11	2-7 yr	Increased concentrations at follow-up in patients whose levels were low during illness; stable in the remainder

Table 6.

POST MORTEM STUDIES OF SUICIDE

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Suicide is a major cause of death in the United States for the adolescent and young adult population. In the 13- to 24-year age range, it ranks as the second leading cause of death. Furthermore, a dramatic increase in the adolescent suicide rate has occurred in the last 15 years. In an effort to counteract this growing rate, recent research has begun to focus on the identification of youths "at risk" for suicide and prevention of suicide. These studies, which are few in number, have principally investigated personality, psychosocial and diagnostic factors. However, suicide research on adults, focusing on the same factors has had limited success and the suicide rates have not been significantly reduced. Predictors are typically overinclusive and identify many individuals as "at risk" who never commit suicide. Furthermore, the association of these predictors with suicide is too weak to have much utility in the clinical setting. Thus, the traditional approaches to identifying suicide risk have been inadequate. Therefore, while psychosocial and diagnostic factors are important to examine in the adolescent and young adult population, the study of suicide in this age group may benefit from an alternative approach that takes into account neurochemical factors. To date, there have been no studies of the neurochemistry of suicide in adolescents.

The purpose of this paper will be to review the post mortem biological findings in the field of suicide. This review will include critiques of studies that have examined enzymatic findings, concentrations of biogenic amines and their metabolites, and the findings from studies that have employed the more recently developed technology of receptor binding.

The advantages of human post mortem neurochemical studies must be balanced against those disadvantages inherent in these investigations. In post mortem research numerous confounding variables may contribute to inconsistencies within a study or across studies. In this review, we will assess the impact of some of these variables (e.g., age, post mortem interval, and regional brain dissection) and describe their impact on several of the neurochemical measures described.

There are several lines of evidence that suggest an association between serotonin and suicidal behavior (2).

Because of the involvement of 5-HT in suicide and because 5-HT is a substrate for monoamineoxidase (MAO-A), Mann and Stanley (6) thought it would be of interest to conduct a post mortem study of this enzyme in a series of suicide victims.

Two previous studies had examined post mortem MAO activity in suicide victims. One study reported no differences in MAO activity compared with controls (7). A second study found reduced MAO activity in patients where the suicide was associated with alcoholism (8). Both these studies, in contrast to the study of Mann and Stanley (6), included a significant proportion of patients who had died by carbon monoxide or drug overdose that may have altered

neurochemistry and employed a single substrate concentration, a method that is less informative and less sensitive than enzyme kinetic studies.

Mann and Stanley (6) assayed MAO-A and B in the frontal cortex of 13 suicides and 13 controls using labeled 5-HT and phenylethylamine (PEA) as substrates for MAO-A and B, respectively. The suicide victims we studied generally died by determined and violent means, with the exception of one overdose. There were no significant differences between the suicide and control group with respect to factors such as age, sex and post mortem interval.

The results of this kinetic study show no significant difference between the groups for either substrate (5-HT or PEA). There was a significant positive correlation between age and MAO-B Vmax for both groups. There was no correlation between post mortem interval and MAO enzyme kinetics.

The series of suicide victims included in this study are distinguishable from those of other studies of brain MAO in as much as those who died by overdose were largely excluded, thereby avoiding the potential problem of drug effects contaminating the results. Other studies have suggested that MAO activity was reduced in alcoholic suicides but not in non-alcoholic suicides (8). The data suggest that the reported lowered brain MAO activity in alcoholic suicides, if confirmed, may be related primarily to alcoholism rather than to suicidal behavior.

In many of the post mortem studies, which have measured the concentration of 5-HT or its principal metabolite, 5-Hydroxyindoleacetic acid (5-HIAA), it is important to point out that some diagnostic information was available for the suicide victims. These data indicate that approximately 50 percent of the suicide victims were diagnosed as endogenously depressed: the remaining cases carried a variety of diagnoses including schizophrenia, personality disorders, alcoholism, and reactive depression. These diagnostic groupings are consistent with a number of studies that have made a retrospective diagnostic analysis of individuals who have committed suicide (9-11). In general, these studies found that in addition to the diagnosis of depression, individuals classified as schizophrenic, alcoholic, and having personality disorders were also represented. Thus, it is of both theoretical and practical importance to note that suicide victims typically represent a diagnostically heterogenous group of individuals. With regard to biochemical findings within this population, the diagnostic heterogeneity suggests that differences in neurochemistry may be more related to suicidal behavior rather than to depression per se.

It should also be mentioned that none of the studies described below had youth suicide as their focus.

A total of 11 studies have investigated the concentration of 5-HT, 5-HIAA, or both in several brain regions of suicide victims (12-22). In addition to measurements of the serotonergic system, 3 of the 11 studies also report findings for the noradrenergic and dopaminergic systems.

With regard to findings reported for the serotonergic system, 7 of 11 studies have reported significant decreases in the levels of 5-HT, 5-HIAA, or both. In general, decreases were noted in the area of the brain stem (Raphe Nuclei) and in other subcortical nuclei (e.g., hypothalamus). Lloyd et al. (15) measured 5-HT and 5-HIAA in Raphe Nuclei of five suicides and five controls. Three of the five suicides had died by drug overdose. They found no significant difference in 5-HIAA levels between the two groups. There was, however, a significant reduction in 5-HT levels for the suicide group. Pare et al. (14) determined norepinephrine, dopamine, 5-HT, and 5-HIAA levels in suicide victims who had died by carbon monoxide poisoning. They found no significant difference between the two groups for norepinephrine, dopamine, and 5-HIAA. They did report a significant reduction in brainstem levels of 5-HT, for the suicide group. Shaw et al. (12) found lower

brainstem levels of 5-HT in suicide victims compared with controls, a statistically significant difference. However, it should be noted that about half of the suicide group died by barbiturate overdose and the other half died by carbon monoxide poisoning.

More recently, Korpi et al. (17) reported significant decreases in the hypothalamic concentration of 5-HT of suicide victims compared with nonsuicide controls. Similar findings were reported by Gillin et al. (16). They noted that 5-HT levels were significantly lower in the hypothalamus of suicide victims compared with controls.

Three studies have reported significant reductions in the levels of 5-HIAA in suicide victims. Bourne et al. (13) measured norepinephrine, 5-HT, and 5-HIAA in the hind-brain and found significantly lower levels only for 5-HIAA. Beskow et al. (18) measured dopamine, norepinephrine, 5-HT, and 5-HIAA in brainstem areas of suicide victims and controls. They noted significant reductions in 5-HIAA levels for the suicide group. The results of these studies are summarized in Table 1. (Tables and figures appear at the end of the chapter.)

In many of the foregoing studies, factors such as death by overdose or carbon monoxide poisoning, extensive post mortem delay, and lack of age-matched control groups figure significantly in the interpretation of these findings. These variables may also account in part for the lack of uniformity of findings among the post mortem studies. In addition to these potential sources of error, the levels of monoamines and their metabolites are known to be influenced by factors such as diet, acute drug use, alcohol, etc. While it is possible to control for the acute influence of these factors in CSF studies, for obvious reasons this is not the case in post mortem assessments. In an effort to minimize the impact of the aforementioned variable, we decided to examine a system--receptor binding--which has been shown to be generally nonresponsive to these acute influences.

Binding studies have shown that changes in the number of sites (or their density) can be induced by either chronic exposure to a chemical agent (e.g., antidepressants) or deprivation of the particular amine by its removal (e.g., lesioning). Recently, binding assays that appear to be associated with pre-(imipramine) and post-(spiroperidol) synaptic 5-HT neurons have been developed (23,24). Imipramine binding sites have been characterized in platelets and various regions of the brain. Some of the experimental evidence linking imipramine binding with 5-HT is that (1) radioautography studies of 3-H imipramine binding sites show distribution similar to serotonergic terminals (25); (2) chemical and electrolytic lesions of the Raphe nucleus cause a significant reduction in serotonin level and in the number of imipramine binding sites (26); (3) the use of an irreversible ligand results in reduced 3-H imipramine binding and serotonin uptake (27); (4) the potency of antidepressant drugs to inhibit serotonin uptake is significantly correlated with their potency to inhibit 3-H imipramine binding (28); (5) serotonin is the only neurotransmitter known to inhibit (^{3}H) imipramine binding (28,33); and (6) there is a similar pharmacologic profile between brain and platelet (^{3}H) imipramine binding sites (27).

The clinical significance of imipramine binding was provided by the studies of Langer and coworkers who reported decreases in the number of binding sites in the platelets of depressives (29). The combined association of imipramine binding with 5-HT function, as well as the significant reduction in binding density in depressives, suggested the possibility of alterations in imipramine binding in suicide victims. To test this hypothesis, Stanley et al. (30) determined imipramine binding in the brains of suicide victims and controls. Because of the problems previous research groups had encountered conducting post mortem studies, we took particular care in selecting cases for this study. Thus, there were no significant differences between the two groups with respect to age, sex and post mortem interval. The suicide victims chosen for this study had died in a determined man-

ner (e.g., gunshot wound, hanging, jumped from height) and, as is the general practice of these researchers, the control group was chosen to match for sudden and violent deaths.

The findings indicated a significant reduction in the number of imipramine binding sites in frontal cortex (suicides $^{B}max = 330 \pm 39$ fmole/mg/protein; controls $^{B}max = 587 \pm 75$ fmole/mg/protein) with no difference in binding affinity (Kd) (Fig. 1). The results of this experiment seem to be consistent with the accumulating evidence suggesting the involvement of 5-HT in suicide. Specifically, reduced imipramine binding (associated with presynaptic terminals) may indicate reduced 5-HT release and agree with reports of reduced post mortem levels of 5-HT and 5-HIAA in suicides as well as lower levels of 5-HIAA in the CSF of suicide attempters.

Since the completion of this study, there have been four other studies that have measured imipramine binding either in suicide victims or in depressive persons who died from natural causes.

Paul and coworkers (31) measured imipramine binding in hypothalamic membranes from suicides and controls. Both groups were matched for age, gender, and post mortem interval. Imipramine binding was significantly lower in the brains of the suicide victims compared with controls. This group also measured desipramine binding in the same samples and noted no significant difference between the suicide and control group. They interpreted this finding as arguing against the possibility that the reductions they had observed in imipramine binding could be attributed to a drug-induced effect. Perry and colleagues (32) measured imipramine binding in the cortex and hippocampus of depressed individuals dying from nonsuicidal causes. They reported a significant reduction in imipramine binding in the depressive group relative to a nondepressed control group that had been matched for age, sex, and post mortem interval. Crow et al. (20) also reported a significant decrease in imipramine binding in the cortex of suicide victims compared with controls. In contrast to the findings cited above, one study has reported an increase in imipramine binding in the brains of suicides compared with control (33). Possible explanations offered to address this discrepant finding include single point analysis instead of saturation isotherms and inadequate matching of factors such as age, gender and post mortem interval. In summary, five published post mortem studies have measured imipramine binding. Thus far, four of the five studies reported a decrease in imipramine binding and one study found an increase. And, as was the case in those post mortem studies that measured levels of 5-HT and 5-HIAA, none of the aforementioned studies had youth suicide as their focus (2).

In addition to assessing of post mortem presynaptic function of the 5-HT system in suicide, Stanley and Mann also measured post-synaptic 5-HT binding sites using ^{3}H-spiroperidol (5-HT2) (34). 5-HT2 binding in animals has been shown to change in response to chronic antidepressant treatment and lesioning of 5-HT nuclei (26,34).

In this study, suicide victims were compared with controls, and, as in previous studies, both groups were matched for age, sex, post mortem interval, and suddenness of death. Also, care was taken to select subjects who had died by nonpharmacologic means.

The study found significant increase in the number of 5-HT2 binding sites in the frontal cortex of suicide victims with no change in binding affinity (Fig. 2).

Because many of the brains had also been used in the previous report on imipramine binding by Stanley et al. (30), the researchers were interested in assessing the degree to which these measures of receptor function correlated. They found that the number of binding site (^{B}max) for 5-HT2 and imipramine was negatively correlated. This finding is of interest because it closely parallels the experimental observations noted in animal studies. Brunello et al. (26) lesioned

the Raphe nucleus of rats using the 5-HT selective neurotoxin 5,7-dihydroxytryptamine. Two weeks following such lesions, 5-HT levels were significantly reduced. The same researchers found significant reductions in imipramine binding (associated with presynaptic serotonergic terminals) with significant increases in 5-HT2 binding (postsynaptic). They suggested that the increase in 5-HT2 binding might reflect a compensating increase in postsynaptic binding sites secondary to a loss of presynaptic input. Extrapolating to human data in suicide victims where Stanley et al. observed an increase in postsynaptic binding sites as well as a decrease in presynaptic binding sites, it may be that the functional consequences of this receptor arrangement could result in an overall hypofunction of this system. Thus, reduced levels of 5-HIAA in the CSF of suicide attempters as well as reduced levels of 5-HT and 5-HIAA in the brains of suicide victims would be a logical consequence of a hypofunctioning serotonergic systems.

Subsequent to the study done by Stanley et al. (34), there have been two additional reports of 5-HT2 binding in suicides. Owens et al. (19) reported an increase in 5-HT2 binding in nonmedicated suicide victims. Crow and colleagues (20) found no change in 5-HT2 binding between suicides and controls (2).

In addition to examining serotonergic binding sites in suicide victims, muscarinic binding in this group was also measured (35). The rationale for this assessment was based in part on the several lines of cholinergic sensitivity with affective disorders and the high incidence of individuals diagnosed as having an affective disorder who subsequently commit suicide.

In this study, muscarinic binding was estimated using the reversible antagonist 3-quinuclindyl benzilate (QNB). Samples of frontal cortex from 22 suicide and 22 controls matched for age, gender, post mortem interval and suddeness of death were used in this study. As previously, care was taken to chose a majority of cases where the cause of death was nonpharmacological (3).

Scatchard analysis of the binding data indicated that there were no significant differences in the mean number of binding site (Bmax) between the two groups (suicide victims, 493 fmole/mg protein, and control subjects, 492 fmole/mg protein) (Kd) between the means of the two groups (suicide victims, 14 pM, and control subjects, 13.68 pM) (Figs. 3 and 4).

Correlations between ^{B}max or Kd and either the suicide victims or control subjects were not significantly related to factors such as age and interval between death and autopsy. However, when both groups were combined, Bmax was significantly correlated with time between death and autopsy ($r = .35, p < .02$).

Comparisons between ^{B}max values of suicide victims who died by violent means (gunshot wounds, hangings, or jumping from height) and of controls who had died either by violent or nonviolent methods revealed no significant differences. Variations in muscarinic cholinergic binding as a function of the time of day that individuals died have been reported (36). The Bmax values for the combined samples (suicide victims and control subjects) were examined at eight, separate 3-hour intervals by one-way analysis of variance; none of the intervals significantly differed from each other.

Two other studies have estimated QNB binding in suicides and controls. Kaufman et al. (37) determined QNB binding in three brain regions (including frontal cortex) in suicide victims and found no differences between the groups for any of the regions studied. In contrast to our findings and those of Kaufman's, Meyerson and colleagues (33) reported a significant increase in QNB binding in the frontal cortex of a small group of suicides not adequately matched for factors such as age, sex and post mortem interval (2).

More recently Mann et al. (38) have measured beta adrenergic receptors in suicide victims in the hope that such studies might indicate the functional status of central catecholamine neurons in suicidal behavior.

It has been suggested that down-regulation of beta adrenergic receptors may be linked with the therapeutic effect of antidepressants and that changes in these receptors may also relate to the neurochemical substrate of suicide and depression.

The researchers measured beta adrenergic receptor binding in the frontal cortex of suicide victims and controls using dihydroalphrenolol (DHA). There was a 73 percent increase in beta adrenergic receptor binding in suicide victims compared with controls.

In addition to this study, Zanko and Beigon (39) reported an increased number of binding sites (^{B}max) with no change in Kd in a small series of six suicide victims and matched controls. In contrast with the above studies, Meyerson et al. (33) reported no alteration in DHA binding in suicide victims. Thus, two of three studies measuring beta adrenergic receptors report an increase in binding in suicide victims. It should be noted that ante mortem use of antidepressants would not explain the receptor alterations we observed. Data from animal studies indicates that chronic antidepressant treatment causes a down-regulation of beta adrenergic receptors. Findings in suicide victims studied by Stanley et al. indicate alterations in receptor binding in the opposite direction from that which would be expected if drug effects had been present.

Having set forth the principal neurochemical findings in suicide research, it is important also to examine some factors that may exert an influence on some of the measures previously described in this review.

A preliminary analysis of 50 cases with an age range of 16 to 79 years revealed no significant relationship between age and 5-HT or 5-HIAA (2). However, imipramine was positively correlated with age. Severson et al. (40) recently published data on age effects and 5-HT and 5-HIAA levels as well as imipramine binding in human post mortem samples. They too noted that age did not appear to influence 5-HT or 5-HIAA levels. They also found that the ratio of 5-HIAA/5-HT, an estimate of serotonin turnover, was uninfluenced by age. Severson did note a significant positive correlation between imipramine binding and age (range 17-100 years). Severson's and Stanley's findings of a positive correlation between these variables is of interest because the findings are in the opposite direction of those reported by Langer and coworkers (23) for imipramine binding in the platelet. Langer (23) reported that platelet imipramine binding decreases as a function of age. These discrepant findings are of interest because imipramine binding in the platelet and the brain were thought to be identical. Thus, findings such as these raise questions about the validity of peripheral measures as indices of central systems. A significant age-related decrease in 5-HT2 binding sites in frontal cortex ($r = -0.42$, $N = 34$, $p < .01$) was observed in the study of Mann and colleagues (38). A statistically significant increase in cortical DHA binding with age was seen in our study ($r = 0.60$, $N = 19$, $p < .01$) (38).

Another area that also represents a potential problem in post mortem research is that of post mortem interval (PMI) that time between death and the time the brain tissue is removed and frozen. The human post mortem studies conducted by Stanley et al. (41) assessed the influence of post mortem interval on 5-HT and 5-HIAA levels. Their post mortem interval was approximately 15 hours with a range of 6 hours to 45 hours. They found that there was a significant positive correlation between frontal cortex 5-HT levels and PMI. No significant findings were noted for 5-HIAA levels with PMI.

Severson and colleagues (40) also found that PMI was related to significant changes in 5-HT levels. However, their findings were in the opposite direction from that which Stanley and colleagues (41) observed-- namely, they reported a significant decline in 5-HT with increasing PMI. One possible explanation for this discrepancy may be the difference in the length of PMI between the two studies. In Stanley's study, the PMI was ap-

proximately 15 hours, while in Severson's study PMI averaged 36 hours (in some cases >72 hours). It may well be that while 5-HT levels appear to rise initially with a shorter PMI they subsequently fall with a more extensive delay (>1-1/2 days). In any case, previous research has shown that amines, such as DA and 5-HT, are more sensitive to PMI than are their acidic metabolites. Wilk and Stanley et al. (42) had previously published a study that assessed the influence of PMI and DA, DOPAC and HVA levels. They found that DA levels—not DOPAC or HVA—were more likely to be influenced by delay. Also, those same researchers published a similar study on the influence of PMI on 5-HT and 5-HIAA levels. Again, in general, they found a significant change in 5-HT, but not 5-HIAA, levels.

In contrast to variations in the concentrations of biogenic amines, it has been observed that most of the binding sites are uninfluenced by post mortem interval (30). Thus, with the exception of QNB, which displayed a modest decrease in binding density with increased post mortem delay, imipramine, 5-HT_2, and beta adrenergic binding were not affected.

Another area of post mortem research that can result both in variations within and between studies, is nonspecific or "regional" dissections. In our animal studies (43), it had been our practice, and that of others, to analyze samples taken from general areas, e.g., frontal cortex. It occurred to us that our lack of precision in dissection might account for some of the variability we had observed from time to time.

In an attempt to investigate possible regional differences of 5-HT and 5-HIAA concentrations within the cortex, we dissected homogenous samples corresponding to frontal, temporal, and occipital cortex. In this experiment, the frontal cortex showed significantly higher concentrations of 5-HT and 5-HIAA compared with temporal or occipital samples. In a second experiment, three progressive 1 mm slices of the frontal cortex were examined in a rostral to caudal fashion for regional concentration differences of 5-HT and 5-HIAA levels (43). Additional significant variation was noted within the frontal cortex with a rostral to caudal increase in 5-HIAA levels; 5-HT levels were consistent. Therefore, differences are found not only among the general areas of the cortex, i.e., frontal, temporal, and occipital, but significant differences can also be found within each area.

One of the potential criticisms of post mortem studies is that their findings lack a proven clinical utility, as no means of monitoring the alterations reported is provided. Thus, the clinical significance of post mortem findings must be inferred. (Both the ease and correctness with which these inferences are drawn remains largely untested.) Therefore, it would be useful to develop a method with clinical application that could be used in post mortem studies.

In ante mortem studies, biogenic amine metabolites in CSF are generally regarded as the best indicator of neuronal function in the brain. One way of testing the strength of this relationship is by simultaneously assessing the CSF and brain levels of the same metabolite in the same individual.

Stanley et al. (41) measured the acidic metabolites 5-HIAA and HVA, the principal metabolites of serotonin and dopamine, respectively, in the lumbar CSF and brains of the same individuals at autopsy. The post mortem lumbar punctures and samples of frontal cortex corresponding to Brodmann's Area 8-9 were obtained from 48 individuals (37 men and 11 women). The average age was 37 ($\pm$2.6, S.E.) years with a range of 16 to 78 years. The causes of death among the individuals in this study were generally sudden in nature, e.g., homicides, auto accidents, etc. The post mortem interval between death and tissue collection for the individuals in this study ranged from 285 to 1,815 minutes and averaged 891 $\pm$ 58 (S.E.) minutes.

Lumbar CSF samples were obtained. At autopsy, once the organs were removed from

the chest and abdominal cavities, an 18 gauge spinal needle was inserted in the L-3, L-4 inter space. A 10 cc syringe with a leur-lock stop cock was attached to the needle and used to withdraw samples of CSF. (Figure 5)

The results of this study indicate the presence of a significant correlation between CSF and brain levels of 5-HIAA and HVA, $r = 0.78$, $p < .001$; $r = 0.35$, $p < .02$, respectively (Figs. 6 and 7).

In addition to the principal aim of the project presented above (i.e., the assessment of the relationship between metabolite levels in CSF and brain), Stanley et al. (41) were also interested in determining the degree to which post mortem CSF measures agreed with the CSF findings of ante mortem studies. In this regard, some of the findings that point out similarities between these results and those obtained from living individuals are: (1) a significant gradient in metabolite concentration in serial samples of CSF (Figs. 8 and 9); (2) the mean CSF concentrations of 5-HIAA (34.4 ng/ml) and HVA (71.6 ng/ml); (3) a significant correlation between the post mortem CSF concentrations of 5-HIAA and HVA ($r = 0.69$, $p < .001$) (Fig. 10); and (4) an inverse correlation between body height and CSF levels of 5-HIAA.

Thus, the relationship between metabolite levels in the brain and CSF provides direct evidence for the validity of using these CSF measures as an index of brain metabolism in the living. Further, this methodology could be used to examine the interrelationship between a biogenic amine or its metabolite and the status of the various receptors associated with the same neuronal system and to provide a means for applying post mortem finding to the clinical setting.

In summary, there are several lines of evidence suggesting that there may be a neurochemical component associated with the act of suicide. Thus far, the post mortem biochemical evidence tends to support the hypothesis that in individuals who commit suicide, there is some form of serotonergic dysfunction. With regard to youth suicide, it should be emphasized that no post mortem biochemical studies have been conducted on this age group. We are, therefore, left to speculate whether the alterations reported in adult suicide studies will also be found when appropriate youth suicide studies are conducted. As has been previously noted, some of the relevant neurochemical measures are known to be influenced by age, e.g., imipramine binding increases with age. Therefore, it will probably be necessary to conduct normative studies for many of these measures, either separately or in parallel with comparative studies of suicide victims.

One of the frequent criticisms of biochemical post mortem studies is that they fail to obtain diagnostic information. This information is critical if we hope to relate biochemical findings either directly to suicide behavior itself or to specific diagnostic groups.

It should be noted that this term "suicidal behavior" encompasses a complex array of symptoms. Previous studies describing a link between suicidal behavior and serotonin have also reported an association between this neurotransmitter and other behaviors. Specifically, Brown and colleagues (44) have reported a significant inverse correlation between individuals' history of aggressive behavior and their CSF levels of 5-HIAA. Linnoila et al. (45) found lower levels of CSF 5-HIAA in individuals who had engaged in violent and impulsive acts. To the extent that impulsivity and aggression can be regarded as risk factors that have an identifiable biochemical substrate, it will be important for future studies of suicide in youth to assess the degree to which these behaviors are present in this age group. Thus, it may be possible to systematically construct a behavioral and biochemical profile to aid the clinician in identifying individuals at high risk of committing suicide.

Recommendations for future studies of youth suicide should include projects that will integrate biochemical and behavioral factors. For post mortem research, this will

necessitate interviewing next of kin to obtain the needed personality descriptors and diagnostic information that can then be assessed in the light of neurochemical findings. The priority for neurochemical studies should initially parallel studies that have already been conducted in adults. In an effort to maintain a link between post mortem findings and the clinical application of such findings, investigators should obtain samples of post mortem CSF where possible. Ante mortem studies should follow the same basic approach as described for post mortem investigations. Thus, normative behavioral/diagnostic and biochemical data should be collected together so investigators can identify behaviors or clusters of behaviors that may correlate with biochemical findings.

Based on the results of the studies proposed above, it may be important to explore the use of various pharmacologic probes in the treatment of suicidal behavior. The biochemical findings in suicide to date seem to relate more to this specific behavior itself, rather than to any particular diagnostic group. Therefore, while it may be necessary to treat the symptoms associated with an individual's psychiatric syndrome, it may also be necessary to separately treat symptoms associated with their suicidal behavior.

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Post Mortem Neurotransmitter and Metabolite Studies in Completed Studies

Shaw et al. (12)	↓ Brainstem 5-HT
Bourne et al. (13)	↓ Brainstem 5-HIAA
Pare et al. (14)	↓ Brainstem 5-HT No change in brainstem 5-HIAA
Lloyd et al. (15)	↓ Brainstem 5-HT No change in brainstem 5-HIAA
Gillin et al. (16)	↓ Hypothalamus 5-HT Nucleus Acumbens 5-HIAA
Korpi et al. (17)	↓ Hypothalamus 5-HT
Beskow et al. (18)	↓ Brain 5-HIAA
Owens et al. (19)	No change in 5-HIAA levels in frontal cortex
Crow et al. (20)	No change in 5-HIAA levels in frontal cortex
Cochrane et al. (21)	No change in brain 5-HT
Stanley et al. (22)	No change in 5-HIAA or 5-HT levels in frontal cortex

Table 1.

Stanley et al. (30)	↓ ^{3}H-imipramine binding in cortex
Paul et al. (31)	↓ ^{3}H-imipramine binding in brain
Perry et al. (32)	↓ ^{3}H-imipramine binding* in cortex
Crow et al. (20)	↓ ^{3}H-imipramine binding in cortex
Meyerson et al. (33)	↑ ^{3}H-imipramine binding in cortex
Stanley and Mann (34)	↑ 5-HT$_2$ binding in cortex
Owen et al. (19)	↑ 5-HT$_2$ binding in cortex**
Crow et al. (20)	No change in 5HT$_2$ binding in cortex
Stanley (35)	No change in muscarinic cholinergic receptor binding in cortex
Kaufman et al. (37)	No change in muscarinic cholinergic receptor binding
Meyerson et al. (33)	↑ in muscarinic cholinergic receptor binding
Zanko and Biegon (39)	↑ in beta receptor binding
Mann and Stanley (6)	↑ in beta receptor binding
Meyerson et al. (33)	No change in beta receptor binding

* Depressed patients dying of natural causes

** Increased but not significantly

Table 2.

Characteristics of Suicide Victims (n=22) and Control Subjects (n=22) Whose Death was by Nonsuicidal Means

Subject	Age (years)	Sex	Cause of Death	Time Between Death and Autopsy (min.)	Number of Binding Sites (B_{max})	Binding A????? (K??)
Suicide Victims						
1	46	M	Hanging	1,440	191	17
2	13	M	Gunshot wound	1,140	197	15
3	15	M	Hanging	555	677	13
4	25	M	Gunshot wound	1,560	387	28
5	33	M	Gunshot wound	1,020	773	15
6	55	M	Jumping from height	1,140	388	16
7	25	M	Hanging	1,365	450	10
8	30	M	Hanging	1,320	640	11
9	34	M	Jumping from height	1,320	454	13
10	22	M	Gunshot wound	555	671	10
11	25	M	Drowning	1,005	498	8
12	80	M	Gunshot wound	1,335	555	24
13	18	M	Gunshot wound	1,055	505	16
14	30	M	Jumping from height	1,260	553	9
15	37	M	Drug overdose	795	605	11
16	64	M	Drug overdose	1,110	574	16
17	43	M	Gunshot wound	460	583	16
18	65	M	Jumping from height	1,110	406	10
19	30	F	Gunshot wound	1,290	621	12
20	72	F	Drug overdose	1,185	339	17
21	79	F	Drug overdose	1,080	543	12
22	18	F	Jumping from height	600	229	9
Control subjects						
1	45	M	Gunshot wound	1,650	232	8
2	21	M	Gunshot wound	1,205	242	17
3	22	M	Cardiovascular disease	750	735	14
4	20	M	Gunshot wound	1,570	411	23
5	31	M	Cardiovascular disease	880	423	11
6	47	M	Cardiovascular disease	1,200	526	13
7	28	M	Auto accident	735	439	8
8	18	M	Gunshot wound	805	649	19
9	39	M	Falling from height	1,245	510	11
10	30	M	Auto accident	460	527	10
11	26	M	Falling from height	1,350	652	12
12	53	M	Cardiovascular disease	860	393	36
13	24	M	Cardiovascular disease	1,305	485	12
14	23	M	Gunshot wound	1,035	563	10
15	39	M	Knife wound	600	597	11
16	40	M	Gunshot wound	735	606	16
17	33	M	Gunshot wound	435	593	13
18	82	M	Falling from height	770	382	8
19	23	F	Gunshot wound	865	640	10
20	45	F	Knife wound	1,020	592	19
21	73	F	Cardiovascular disease	1,440	279	10
22	50	F	Auto accident	630	343	10

Table 3.

Comparison of maximal binding of (3_H) imiprimine in samples of frontal cortex from suicide vicitims and control subjects. Difference in ^{B}max values is statistically significant ($p < .01$)

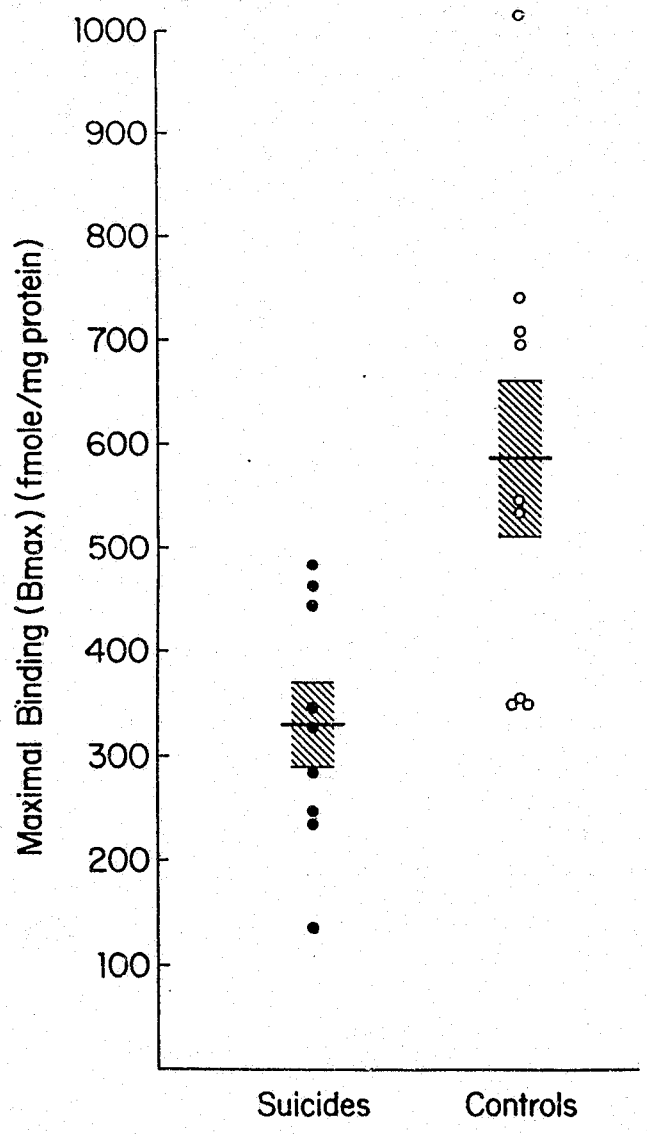


Figure 1.

5-HT$_2$ binding parameters in post mortem frontal cortex from suicide victims and control subjects. ^{B}max and K_d values expressed as means ± S.E. p< 0.01 by Wilcoxon's test (two-tailed) for ^{B}max.

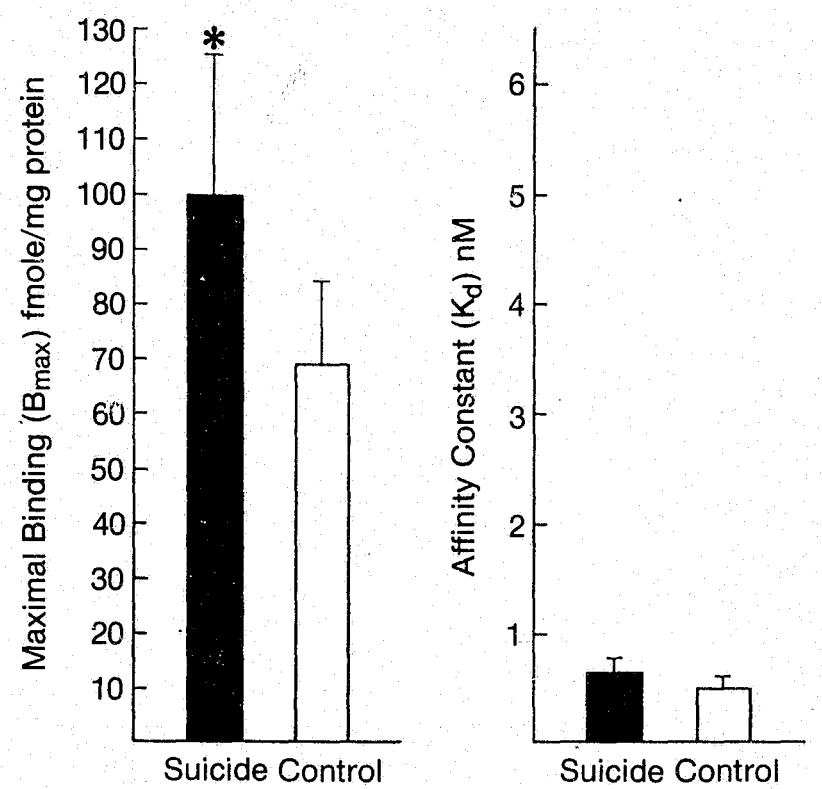


Figure 2.

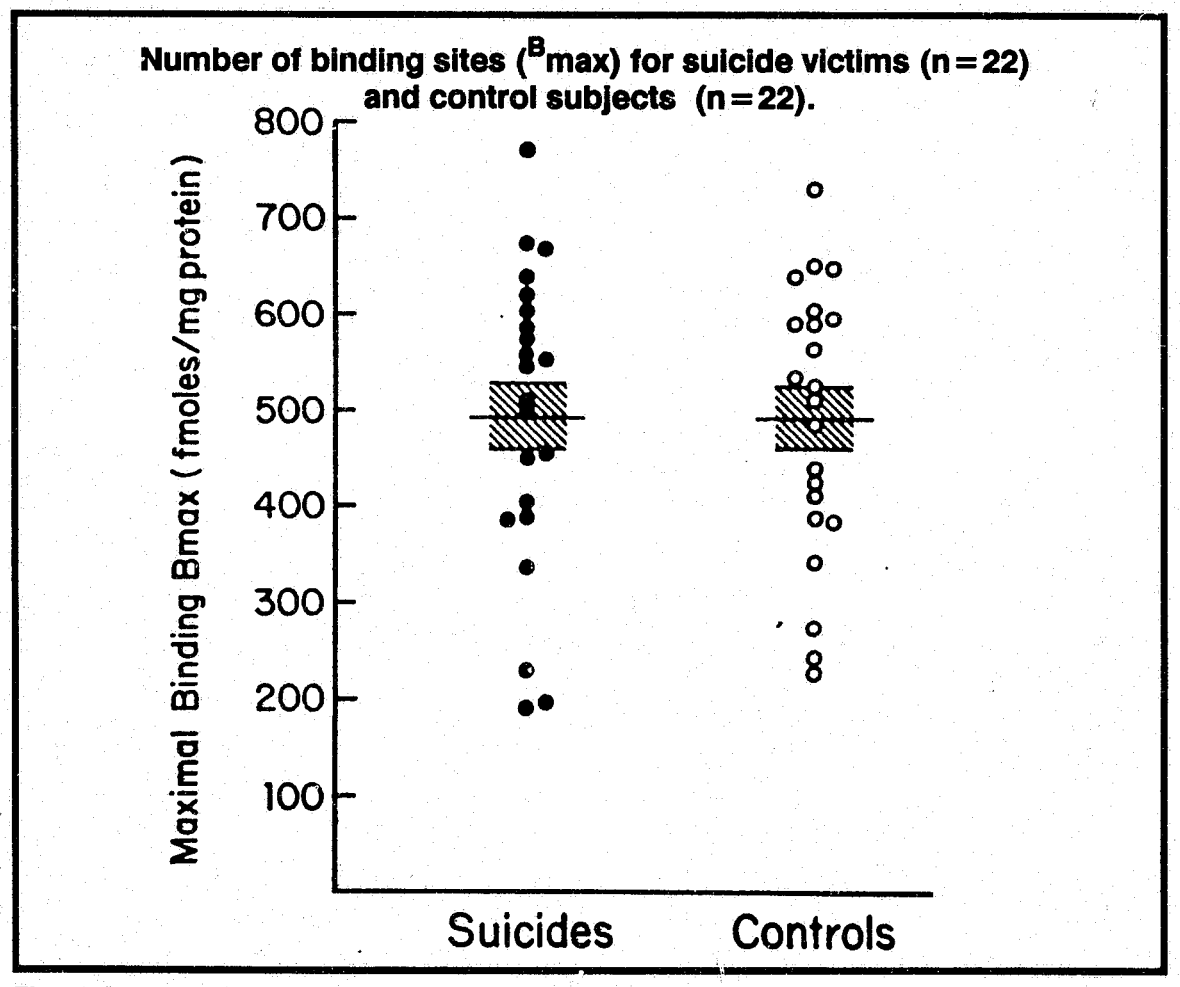

Number of binding sites (^{B}max) for suicide victims (n=22)
and control subjects (n=22).
Maximal Binding Bmax (fmoles/mg protein)
800
700
600
500
400
300
200
100
Suicides
Controls

Figure 3.

Receptor affinities (K_d) for suicide victims (n = 22) and control subjects (n = 22).

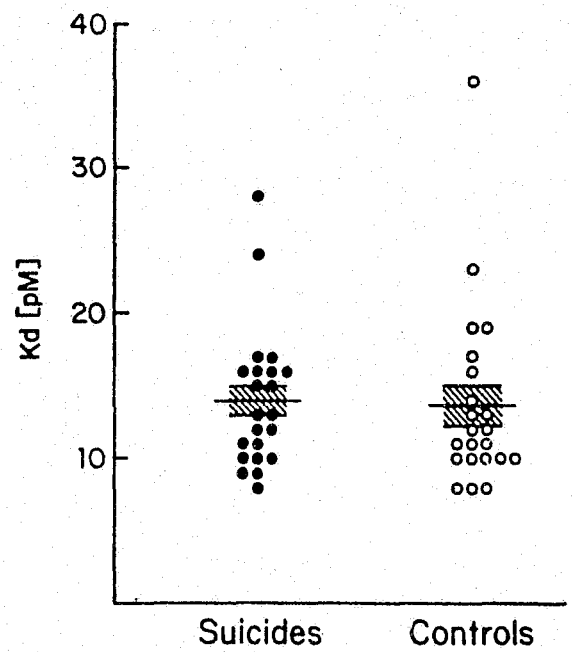


Figure 4.

Diagram of the procedure used to obtain CSF samples.

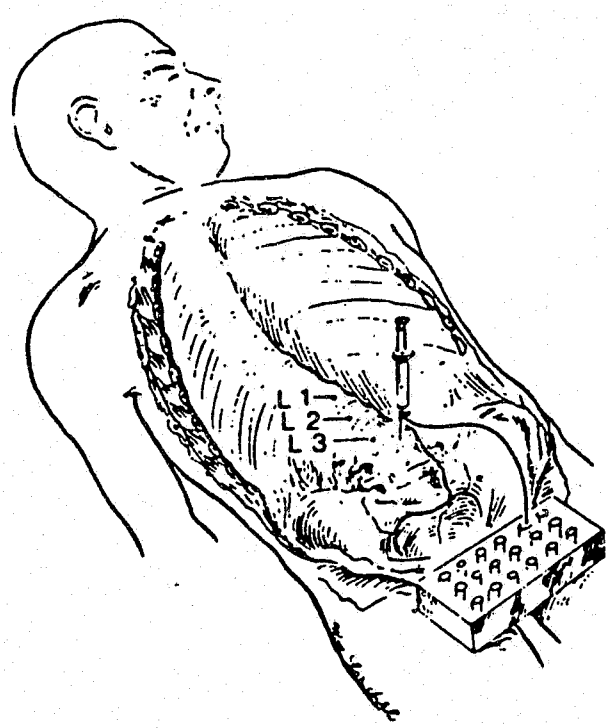
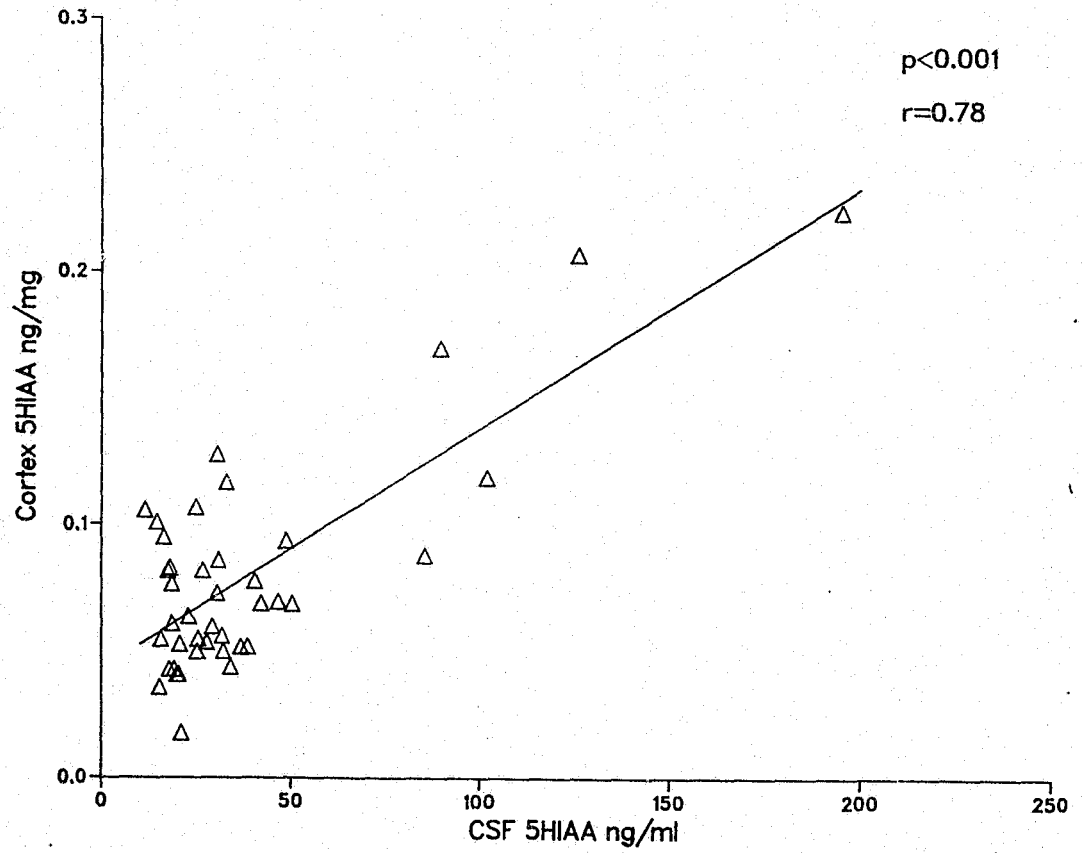
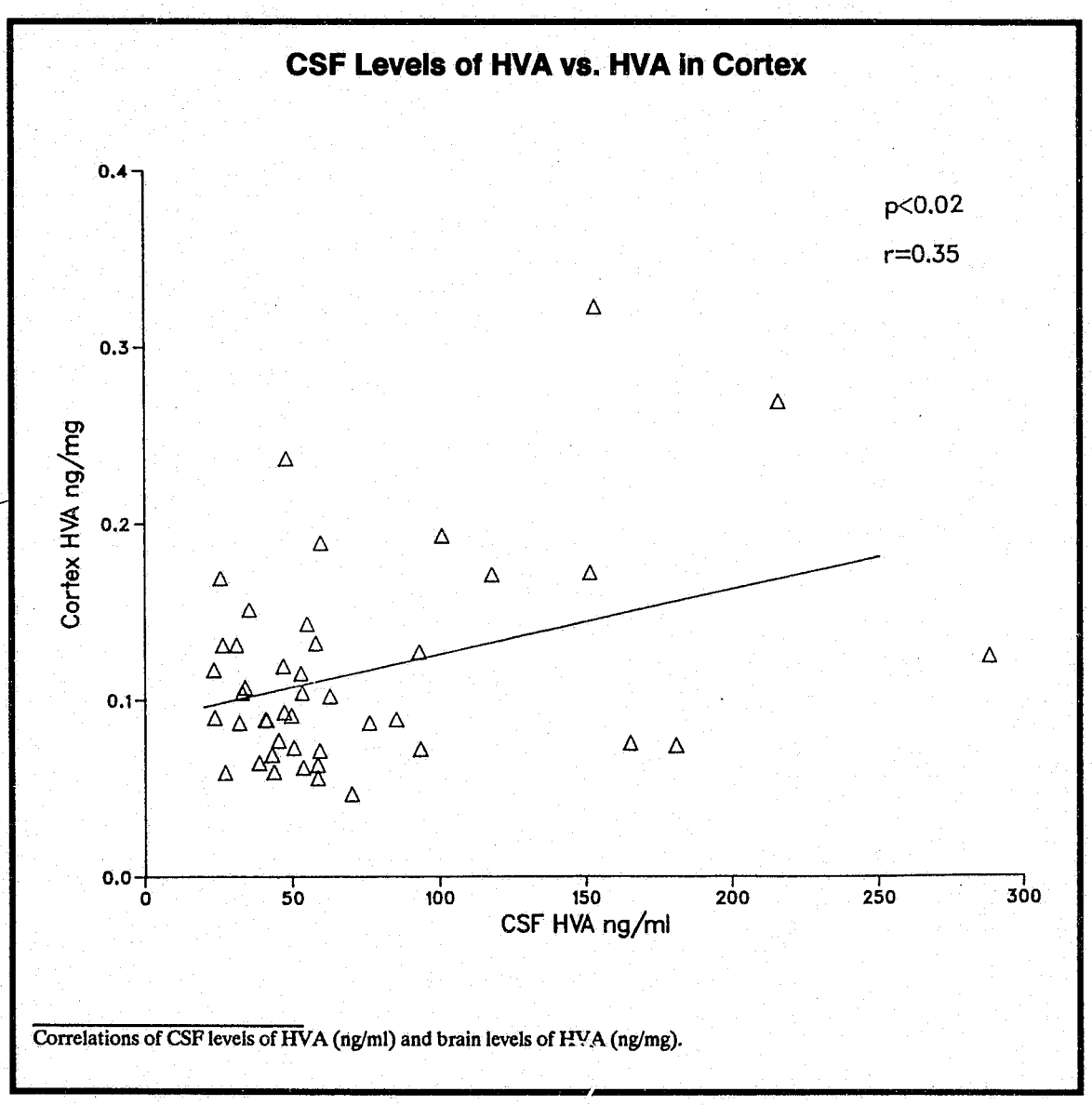


Figure 5.



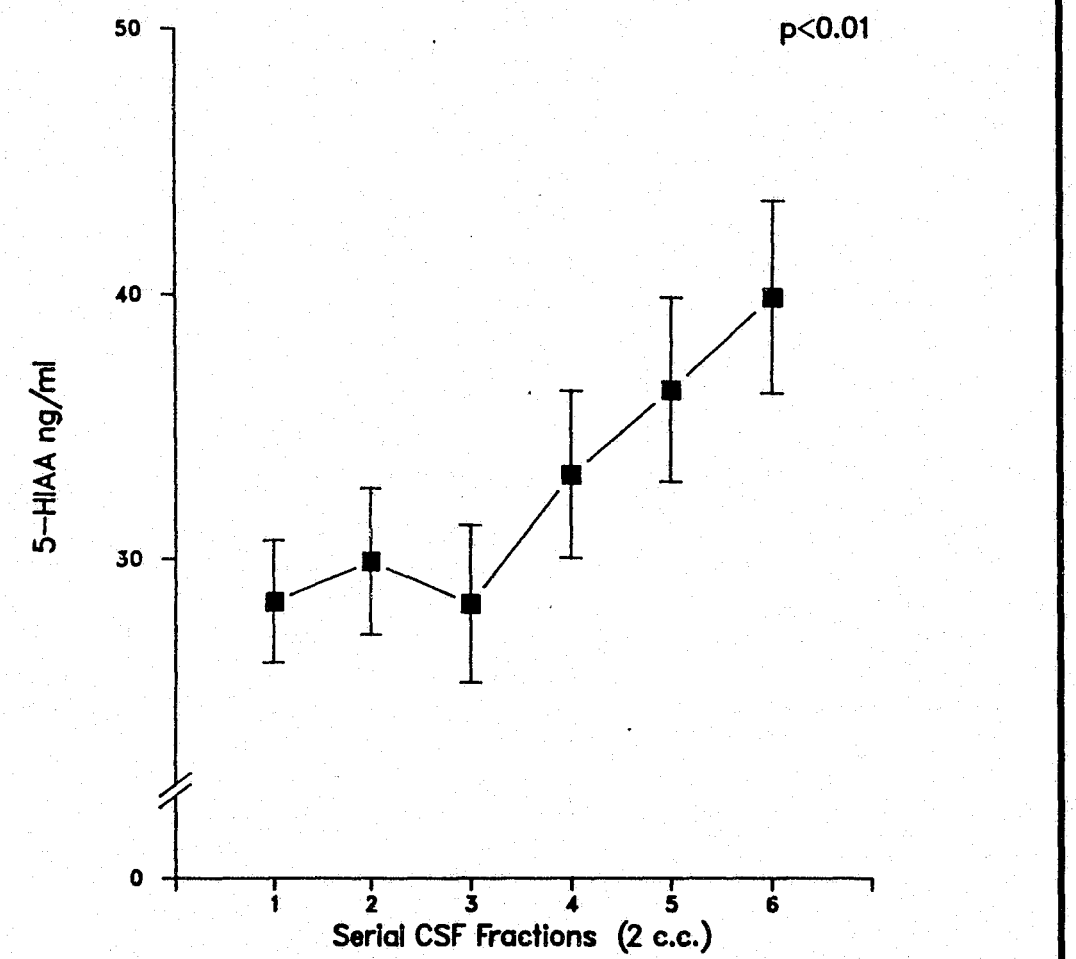
Correlation of the concentration of CSF levels of 5-HIAA (ng/ml) and brain levels of 5-HIAA (ng/mg).

Figure 6.



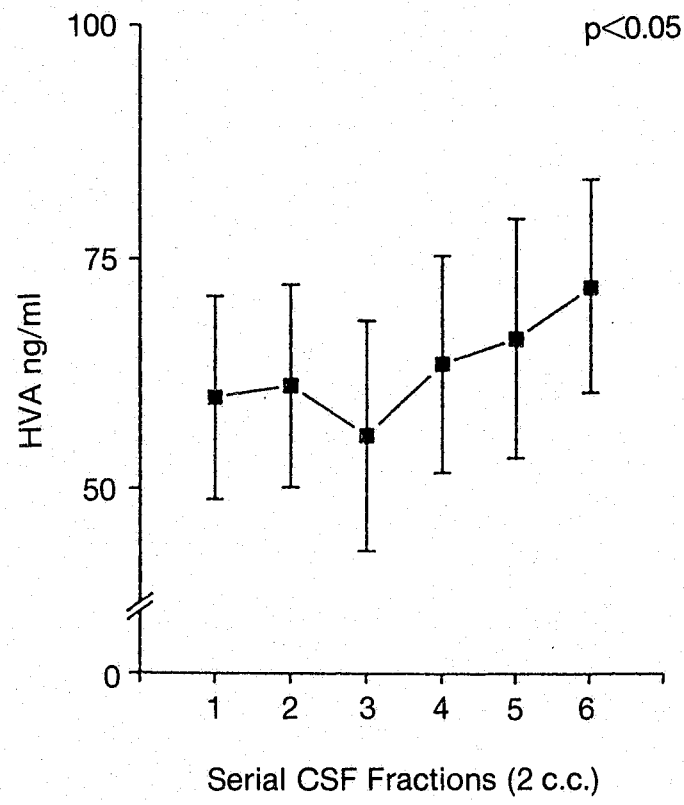
Correlations of CSF levels of HVA (ng/ml) and brain levels of HVA (ng/mg).

Figure 7.



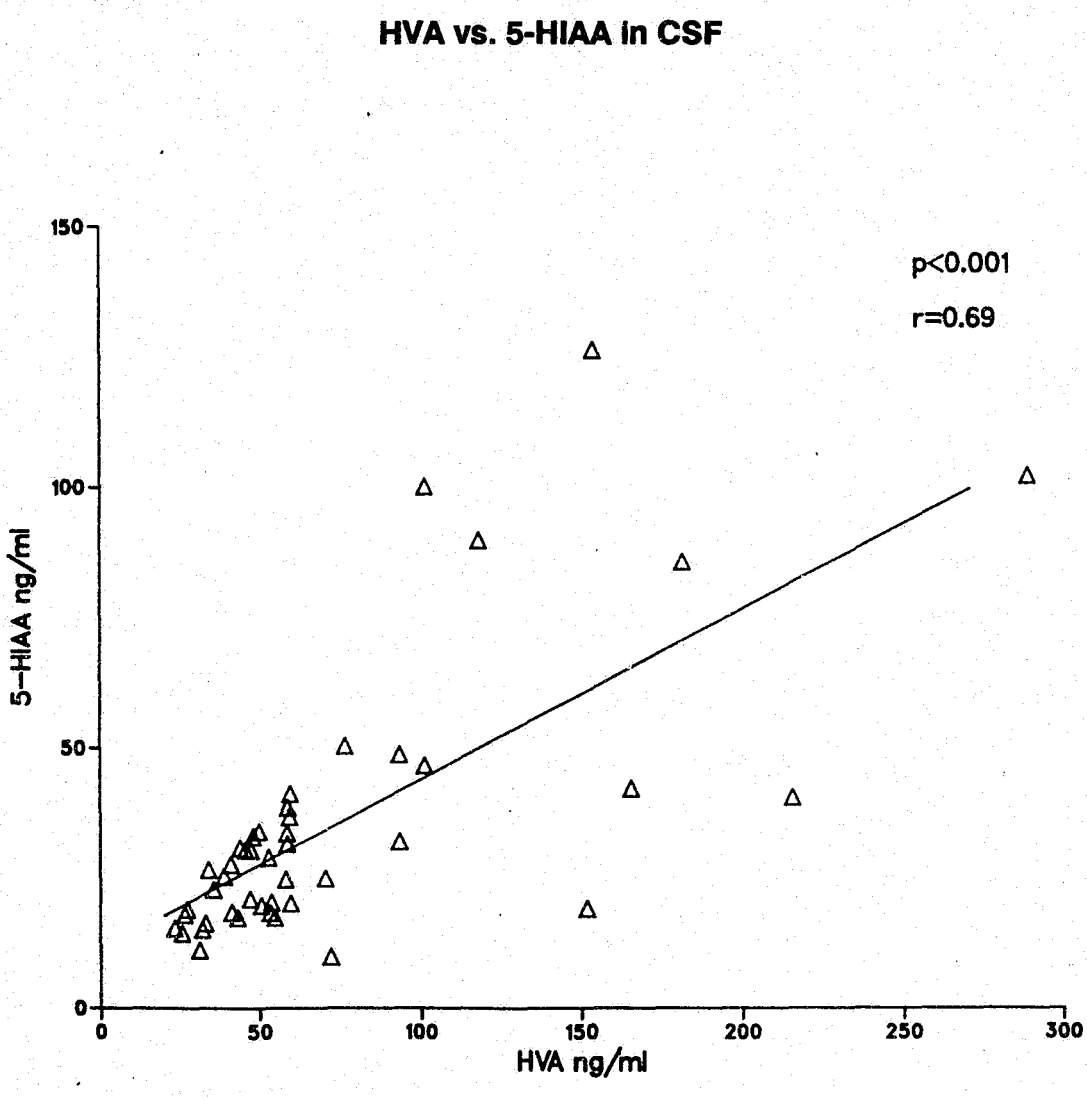
Graph display of progressive concentration gradient for 5-HIAA.

Figure 8.



Graph display of progressive concentration gradient for HVA following serial sampling of CSF fractions (ng/ml).

Figure 9.



Correlations between CSF samples in post mortem samples (ng/ml) of 5-HIAA and HVA.

Figure 10.

THE NEUROENDOCRINE SYSTEM AND SUICIDE

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SUMMARY

Suicide is increased in frequency in Cushing's syndrome which is characterized by increased hypothalamic-pituitary-adrenal axis (HPA) activity. Several types of studies suggest increased HPA axis activity in depression or stress may be related to increased suicidal behavior: increased serum cortisol, increased 24 hour urinary free cortisol and an enhanced 5-hydroxytryptophan-induced increase in serum cortisol. However, these associations are weak and some cortisol measures do not relate to increased suicidal risk. The TRH-induced increase in TSH may be blunted in violent suicide but shows a positive relation to suicidal ideation. There is some evidence linking the HPA abnormalities and the blunted TSH response to serotonin, the neurotransmitter most closely linked to suicide. Suicide in adolescence may occur in the context of a rapidly changing and aroused neuroendocrine system. Hormonal markers of suicide risk and the role of hormones in altering neurotransmitter function appear to be worthy of further study.

INTRODUCTION

The endocrine system is of interest in relation to suicide for a variety of reasons. An increased likelihood of suicide is found in some endocrine disorders, e.g. Cushing's syndrome, and during corticosteroid therapy. As will be reviewed, the thyroid stimulating hormone (TSH) response to thyrotropin-releasing hormone (TRH) and the basal secretion of cortisol correlate with violent suicide or suicidal ideation. Perhaps more importantly, cortisol as well as other hormones can influence the activity of neurotransmitters such as serotonin (5-HT) which may have a more direct causal effect in suicide. Given that no one factor is likely to be the sole determinant of a complex behavior such as suicide, it is important to develop models of the etiology of suicide which integrate a variety of influences such as hormone secretion and neurotransmitter chemistry. We will attempt to do this by considering the hypothalamic- pituitary-adrenal (HPA) axis and the serotonergic system, considering the evidence relating both to suicide, and then the interaction between the two systems. We will also briefly consider other hormones that may contribute to suicide potential and hormone challenge tests that may predict suicide.

There is only minimal data concerning the endocrine status of adolescents who have made suicide attempts or putative biological markers of suicide in adolescents with psychiatric disorders. Therefore, this review will of necessity focus on studies in adult populations. How applicable these results are to adolescents remains to be determined.

In the one instance where data exists for adolescents and adults (the dexamethasone suppression test, DST), the findings are quite comparable. Suicide in both adolescents and adults often occurs as a consequence of major depression or schizophrenia, complicated by alcohol or drug abuse. Both adolescents and adults may suicide impulsively and as a consequence of severe stress. There is no a priori reason to consider any of these factors would act differentially in adolescents, so it is most likely relevant to the task of this symposium on risk factors in adolescent suicide to consider the data concerning suicide in adults. This is not to say that unique biological, especially endocrine, factors are inoperative in adolescents or that they are less important than those common to suicide in both age groups. Rather, it is our belief that future studies on the biology of adolescent suicide may well use findings in older adults as appropriate guidelines for research to determine what are the most important influences on adolescent suicide.

ENDOCRINOPATHIES, CORTICOSTEROIDS AND SUICIDE

There are many aspects of the HPA axis which point toward its importance for understanding the biological contribution to suicide. Six of 35 consecutive patients with Cushing's syndrome, a group of disorders associated with large increases in glucocorticoid output, were reported to have suicidal thoughts and two of these made suicide attempts (Starkman and Schteingart, 1981). In another study, one of 29 cases of Cushing's syndrome made a suicide attempt (Cohen, 1980). Lewis and Smith (1983) reviewed the literature on exogenous corticosteroid-induced psychiatric syndromes and found that 3 percent of the cases for whom outcome was specified committed suicide. This data points towards a role of corticosteroids in increasing vulnerability to suicide. As will be discussed, this might occur because of effects of corticosteroids on neurotransmitter or neuromodulator physiology.

In addition to Cushing's syndrome, other endocrine disorders, various aspects of normal endocrine maturation, function and decline, and hormones other than glucocorticoids, may be associated with profound affective, cognitive and psychomotor disturbances. Hypo- and hyper- thyroidism, hypocortisolism (Addisonian syndrome), hypopituitarism (Simmond's disease), hyperpituitarism, pheochromocytoma, hypo- and hyperparathyroidism, hypo- and hyperglycemia, pancreatitis, pancreatic carcinoma, androgen excess and deficiency and estrogen-progesterone disorders associated with menarche, premenstrual syndrome, oral contraceptives, pregnancy and the postpartum period may produce highly disturbing changes in mental status that could figure in an individual's ability to function adequately, his sense of optimism concerning the future, the desirability of continuing to live, thoughts of suicide and capacity to carry out a suicide attempt. It is beyond the scope of this review to consider these conditions in detail. They are adequately described in textbooks of medicine and clinical endocrinology. Clearly, any adolescent presenting with suicidal ideation or a suicidal attempt should have a thorough medical workup to evaluate the possible presence of an endocrinopathy which might be causing symptoms that directly or indirectly compromise mental status. Conversely, adolescents with serious endocrinopathies such as juvenile diabetes, hypothyroidism or Cushing's syndrome may be at increased risk for suicide and a greater than usual index of suspicion concerning suicide might be advisable in such cases until adequate therapy was instituted.

TRH STIMULATION TEST AND SUICIDE

A blunted TSH response to TRH (<5 uU/ml) has been reported in about 25 percent of depressed patients (Loosen and Prange, 1980). Three studies have reported a relation between a blunted TSH response and violent suicide. Eight depressed patients with past, and three with recent, violent

suicide attempts were found to have a low TSH response compared to patients who had made past (N=7) or current (N=7) nonviolent suicide attempts and 26 depressed patients without any suicide attempts (F=3.46, p< .005) (Linkowski et al., 1983). A two-way ANOVA showed a significant relationship of the TSH response to violence but not for recent vs. past attempts. Seven of 12 patients with an absent TSH response had a previous history of violent suicide attempts compared to four of 39 patients with a maximum TSH response above 1 mU/1 (p <.001). During a five year followup period, three committed suicide by violent means and one by overdose. All had an undetectable TSH response to TRH. Linkowski et al. (1984) subsequently reported similar findings in a slightly expanded sample. In agreement with this, Kjellman et al. (1985) reported that the TSH response to TRH was significantly lower in three depressed patients who made violent suicides than in 27 who had made no attempt or a nonviolent attempt. van Praag and Plutchick (1984) also report an association between violent suicide and a blunted TSH response to TRH.

The possibility that a blunted TSH response to TRH may have long term prognostic significance for suicide is intriguing. This could be mediated by a relationship between the blunted TSH response and specific neurotransmitter abnormalities such as diminished activity in 5-HT pathways. There is some evidence relating the TSH response to TRH to the serotonergic system. Cyproheptadine, a 5-HT antagonist, was found to inhibit the TSH response to TRH in two studies (Ferrari et al., 1976; Egge et al., 1977), but not in another (Goldstein et al., 1979). Cyproheptadine has multiple effects other than 5-HT antagonism and is not a particularly potent 5-HT antagonist. Gold et al. (1977) found a negative relationship between the TSH response and CSF 5-hydroxyindoleacetic acid (5-HIAA), the major metabolite of 5-HT in depressed patients, which suggests that diminished serotonergic activity might be associated with a larger TSH response. Thus, our TSH results indicating a positive relation between the TSH response to TRH and suicidal ideation are consistent with a relation between diminished brain 5-HT and suicidal ideation. Krulich (1979) has reviewed the evidence from rodent studies which suggest that 5-HT may either inhibit or enhance TSH secretion. Krulich et al. (1979) found that quipazine, a 5-HT agonist, did not affect the TRH-induced increase in TSH in the rat but quipazine and 5-HT did inhibit endogenous TSH secretion. The relationship of brain 5-HT, the TSH response to TRH, and suicide requires further study. In light of these findings, we carried out a retrospective analysis of the relationship between suicide ratings and TSH response in a group of newly admitted psychiatric patients to our Mental Health Clinical Research Center who had had a TRH stimulation test (500 ug intravenously). TSH levels over the next 120 minute period was determined by radioimmunoassay. The subjects were drug-free for at least 7 days and consisted of 24 depressed patients (including six schizoaffective depressed, mainly affective), 13 schizophrenic patients (including three schizoaffective depressed, mainly schizophrenic patients), three manic patients and five with miscellaneous diagnoses. Patients were diagnosed according to Research Diagnostic Criteria. Suicidal behavior was assessed during the first week of hospitalization as part of the Schedule for Affective Disorders-Change (SADS-C) interview. Thirteen of the 45 patients admitted to slight or moderate suicidal ideation. Only two patients had made suicide attempts, not considered lethal in intent. There were no violent suicide attempts. We found a significant positive correlation between maximum TSH response to TRH (peak-minus-baseline) and suicide ratings (Spearman rho=0.30, N=45, p=0.044). The mean TSH response to TRH in this group was 9.8 $\pm$ S.D. 5.6 uU/ml. This is very similar to that found in 19 normal controls 8.9 $\pm$ S.D. 7.2 uU/ml. Ten of the 45 patients (22%) had a blunted TSH response (<5uU/ml). Of these, only three had any suicidal ideation, one mild, one slight, one moderate. Further

study is needed to determine if current suicidal ideation is associated with a more robust TSH response but still within the normal limits.

There is conflicting data concerning the linkage between increased HPA axis activity and the blunted TSH response to TRH in depression. Kirkegaard and Carroll (1980), Asnis et al. (1981), Agren and Wide (1982) found no correlation between these two variables. We found no relationship between the TSH and 8 A.M. response to TRH plasma cortisol obtained within the same drug-free evaluation period that included the TRH stimulation test (Spearman rho=0.061, N=38, p=NS). Sixteen of the 45 patients had also undergone other neuroendocrine challenge test within the same three week drug-free period as the TRH test, e.g., the 5-hydroxytryptophan-induced increase in serum cortisol (Meltzer et al., 1984). We also examined the correlation between basal serum cortisol (obtained 60 minutes after catheter placement) and the TSH response in these 16 subjects. We found a highly significant negative correlation between these variables (Spearman rho=-0.65, N=16, p=0.007). This is consistent with the studies of Loosen et al. (1978) who reported a negative correlation between the TSH response to TRH and basal plasma cortisol just before a TRH infusion. The significant correlation between the TSH response to TRH basal and basal serum cortisol levels obtained during the 5-HTP study may be due to lesser influence of stress in the catheter study and the fact that both the TRH and 5-HTP studies were carried out at 10 A.M. Basal cortisol levels obtained at 8 A.M. may reflect the nocturnal surge of cortisol secretion. However, Asnis et al. (1981) did not observe any relationship between the TSH response to TRH and multiple measures of cortisol secretion, including plasma cortisol levels before and throughout the TRH infusion.

HYPOTHALAMIC-PITUITARY-ADRENAL AXIS AND SUICIDE

The presence or absence of a relationship between the TSH response to TRH and basal cortisol is directly relevant to consideration of the importance of TSH as a marker for suicide since there have been a variety of findings which indicate excessive activity of the HPA axis in suicide. Two early National Institute of Mental Health studies reported elevated urinary 24 hour 17-hydroxycorticosteriod (17-OHCS) levels in depressed patients who suicided. The enhanced cortisol secretion preceded the suicide attempts by several weeks (Bunney and Fawcett, 1965; Bunney et al., 1969). These findings were not replicated in subsequent studies of four patients who suicided but who did not evidence elevated 24 hr 17-OHCS prior to suicide with the period of study ranging from a day to eight months prior to suicide (Levy and Hansen, 1969; Fink and Carpenter, 1976). Agren and Wide (1982) found a negative correlation between Medical Lethality of Worst Ever Suicide Attempt and 24 hr urinary free cortisol in 76 patients with major depression. Ostroff et al. (1982), however, did find higher 24 hr urinary cortisol levels (as well as lower urinary norepinephrine-to-epinephrine levels) in three of 22 subjects, two of whom made lethal and one a near lethal suicide attempt.

In addition to urinary cortisol, which is a good measure of adreno-corticoid output, other studies have reported elevated plasma cortisol in suicide. Thus, Krieger (1974) reported that plasma cortisol in 13 patients who suicided during a two-year followup period (21.1 $\pm$ 5.6 ug/dl) was significantly higher than in 39 who did not (16.5 $\pm$ 2.4 ug/dl). However, single plasma samples, especially those obtained by venepuncture, may not be an accurate measure of cortisol output. Venepuncture may induce stress-related cortisol secretion. The results of Kreiger (1974) could indicate that individuals who are vulnerable to suicide may be particularly prone to stress-induced cortisol secretion.

We have recently examined plasma cortisol concentrations in relation to recent suicidal history (Meltzer et al., in preparation). Basal

serum cortisol levels from unmedicated patients with major depression, mania or schizophrenia and normal controls who were part of a study of the cortisol response to 5-hydroxytryptophan (5-HTP) (Meltzer et al., 1984) were analyzed. In this study, subjects were fasted overnight and an indwelling venous catheter was inserted at 9 A.M. Thirty minutes later the first basal sample was withdrawn. Other samples were drawn 15 and 30 minutes later. The 10 A.M. sample (T_0) was related to the Hamilton Depression Rating scale (HDRS) suicide item (0-4) and the SADS-C suicide item (0-6). Serum cortisol (T_0) was significantly but weakly correlated with the HDRS suicide item for all subjects (Spearman rho=0.20, N=107, p=0.04). This included 61 depressives, 16 manics and 30 schizophrenics. The HDRS suicide rating was also correlated with T_0 cortisol in the combined group of affective disorders (rho=0.23, N=77, p=0.05) but not in the depressed patients alone (rho=0.18, N=61, p=0.16). SADS-C suicide ratings and To cortisol were not significantly correlated in the affective disorder patients. The magnitude of the correlation between the HDRS suicide item and serum cortisol indicates only a small portion of the variance in suicide ratings can be attributed to elevated 10 A.M. cortisol levels. However, it is possible that this relationship is stronger at other times of the day. It would be of interest to examine the relationship between serum cortisol between 1 P.M. - 4 P.M. and suicide ratings, since cortisol secretion during this period appears to best reflect 24 hour cortisol output (Halbreich et al., 1982). In the 61 depressed patients, T_0 cortisol was significantly correlated with the Hamilton scale ratings of helplessness (rho=0.38, p=.003), depressed mood (rho=0.29, p=0.02), hopelessness (rho=0.27, p=0.03), paranoid symptoms (rho=-0.26, p=0.06) and work and activities (rho=0.25, p=0.06). These relationships are consistent with the conclusion that increased HPA axis activity is a state marker for severity of depression and as such could be an indicator of suicidality. This may be of some clinical value in patients who falsely deny suicidal ideation and intent.

We have also examined the relationship between basal cortisol levels and suicide attempts, both violent and nonviolent, together and separately, in these patients. As can be seen in Table 1, the 10 A.M. serum cortisol was not significantly different in any of these groups although the highest levels were found in the violent attempters, next in the nonviolent attempters and the lowest in the normal controls. No significant differences in basal serum cortisol were found when the two types of attempters were combined and compared to nonattempters and normal controls (data not presented). The trends evident in Table 1 for all psychiatric patients were more prominent in just the affective disorders (Table 2) but these differences were not significant either.

Basal Serum Cortisol in All Psychiatric Patients in Relation to Suicide Attempts

Group	N	Basal Serum Cortisol (ug/dl)
Normals	21	11.5 ± 5.0*
No Attempts	73	12.0 ±5.1
Nonviolent	11	12.7 ± 7.7
Violent	12	13.6 ± 6.1

* X ± S.D.

Table 1.

Basal Serum Cortisol in Affective Disorders in Relation to Suicide Attempts

Group	N	Basal Serum Cortisol (ug/dl)
Normals	21	11.5 ± 5.0*
No Attempts	55	11.7 ± 4.8
Nonviolent	9	13.5 ± 8.4
Violent	9	15.1 ± 6.4

* X ± S.D.

Table 2.

We did find a trend for serum cortisol in the depressed and manic patients who had made an attempt (14.3 ± 7.3 ug/dl, N=18) to be higher than that of the nonattempters (11.6 ± 4.8 ug/dl, N=76, p=0.08). We examined whether serum cortisol levels above 20.0 ug/dl might have some value as a means of identifying suicide attempters but found no indication that was the case. Nevertheless, the trend in this data, considered in the context of the evidence for an association between excessive HPA axis activity and suicide, suggests that it would be of interest to carry out a prospective study in which serum cortisol was monitored in adolescents at high risk for suicide, e.g., those adolescents presenting at a clinical setting because of the suspicion of being suicidal or adolescent patients placed on suicide precautions in clinical or perhaps forensic settings.

In addition to plasma cortisol studies, there has been one study which related cerebrospinal fluid (CSF) cortisol to suicide. Traskman et al. (1980) reported no differences in CSF cortisol levels in five suicidal patients and 14 nonsuicidal depressives. There was also no relationship between a history of ever making a suicide attempt and high CSF cortisol. CSF cortisol was significantly correlated with urinary free cortisol (r=0.67, N=14, p<.01) which provides further evidence against a relationship between elevated urinary free cortisol and suicide. Nevertheless, further studies of CSF cortisol and suicide, especially violent suicide, would be of interest.

There have been eight published studies of the relationship between dexamethasone suppression test (DST) status at admission to hospital in psychiatric patients and prior suicidal activity. These are summarized in Table 3. Five of the eight found a significant relationship between suicidal activity and nonsuppression. Coryell and Schlesser (1981) found that all four patients who suicided out of a group of 205 unipolar depressions had been nonsuppressors. Carroll et al. (1981) reported that all five melancholic suicide completers were nonsuppressors whereas three completers with diagnoses other than major depression were suppressors.

They also noted eleven other suicide attempters who were nonsuppressors but failed to report how many other nonsuppressors were not suicidal. They proposed that the relationship between suicide and nonsuppression was restricted to melancholics. Banki and Arato (1983) and Targum et al. (1983) also found evidence that nonsuppression predicted suicidal activity. Robbins and Alessi (1985) studied 45 newly hospitalized adolescents, with various psychiatric disorders 23 of whom had attempted to commit suicide. Of the 39 suppressors, 17 (43.6%) made suicide attempts, none considered to have a lethal intent. However, all six nonsuppressors had made suicide attempts; of these, four were medically dangerous or lethal attempts. The two adolescents who had made nonmedically serious attempts and who were nonsuppressors subsequently made medically serious attempts, one of which was fatal. Thus, this study strongly supports a highly significant association of DST nonsuppression with lethal or potentially lethal suicidal behavior in adolescents.

Zimmerman et al. (1986) recently reported no relation between suicidal ideation, serious suicide attempts and nonsuppression in 187 major depressives. Brown et al. (1986) found no differences in the incidence of nonsuppression in 10 recent suicide attempters, 10 past attempters and 37 nonattempters. Moreover, nonserious suicide attempts were more common in suppressors than nonsuppressors. Meltzer et al. (in preparation) have recently reported no relation between violent, nonviolent and no suicide attempts and nonsuppression in 55 patients with major affective disorder. However, there was a trend for suicide attempters to be nonsuppressors (10/16, 62.5%) more commonly than nonattempters (16/39, 41%) (Fisher exact test, p=0.085). We also found that Hamilton Depression Scale suicide ratings were significantly higher in nonsuppressors (all diagnoses) than suppressors and that

nonsuppressors had suicidal ideation significantly more frequently than suppressors. Differences in the number of days between the suicide attempt and the DST could account for some of the discrepencies between studies. However, Brown et al. (1986) found no such correlation in recent attempters. It is possible that the association between nonsuppression and suicide may be confined to patients with endogenous depression as proposed by Carroll et al. (1981).

In addition to these studies of the relationship between suicidal ideation or acts and DST status, there are several other relevant reports. Two studies describe five patients who made suicide attempts within a few days of receiving dexamethasone as part of the DST (Beck- Freis et al., 1981; Asberg et al., 1981). Other investigators did not confirm this finding (Coryell, 1982; Kronfol et al., 1982). Yerevanian et al. (1983) reported an association between failure of the DST to normalize and subsequent suicide. Greden et al. (1980) also noted one such case.

Although there appears to be some evidence supporting a relationship between the DST and suicide, it is important that these results be interpreted cautiously because of the evidence that nonsuppression with the oral 1 mg test may be related to differences in dexamethasone pharmacokinetics. There are now several studies reporting lower dexamethasone levels in nonsuppressors than suppressors (Arana et al., 1984; Berger et al., 1984; Holsboer et al., 1986; Johnson et al., 1985; Lowy et al., in press). Differences in dexamethasone levels might produce both false positives and false negatives. Thus, there could be an association between low plasma dexamethasone levels and suicide rather than nonsuppression and suicide. In any event, it would appear prudent to assess DST status, including measurement of dexamethasone levels, in relation to suicidal activity. Such studies should include post-treatment repeat DST testing and long term followup to assess whether nonsuppression does have prognostic value for suicidal risk.

Suicide and the Dexamethasone Suppression Test

Authors	Patient Population	Suicide/ Attempt Suppression	Suicide/ Attempt NonSuppression	p	Comment
Coryell and Schlesser(1981)	UP Dep	0/109	4/96	0.06	1 suicidal neurotic NS.
Carroll et al (1981)	MDD21 Mixed 3	0/0	16/19		5/8 NS completers.
Banki and Arato(1983)	Mixed	2/20	12/37	<.10	
Targum et al (1983)	UP Dep	3/26	14/23	0.01	5 NS vs 0 S made subsequent attempt.
Robbins and Alessi(1985)	Adolescent. inpatients	17/22	6/6	0.01	4 NS made near lethal attempts. 5 made no serious attempts.
Zimmerman et al (1986)	MDD	12/127* 31/127+	2/60 5/60	NS 0.01	Nonserious more common in S.
Brown et al (1986)	MDD	18/37	9/20	NS	
Meltzer et al (in preparation)	Mixed	6/29	10/26	NS	

NS = nonsuppressor
S = suppressor
* serious suicide attempt
+ nonserious suicide attempt
UP Dep = Unipolar depression
MDD = major depressive disorder.

Table 3.

It appears unlikely that nonsuppression at admission has noteworthy significance for suicide but it is possible that failure to normalize during treatment might. We have demonstrated that depression and nonsuppression may be related to glucocorticoid receptor subsensitivity (Gormley et al., 1985). These results have recently been replicated (Whalley et al., 1986). These studies involved measurement of glucocorticoid receptor concentration in lymphocytes. They could reflect similar changes in the HPA axis. Glucocorticoid influences on serotonergic neurons might mediate the relation between suicide and DST status. This will be discussed subsequently.

In addition to abnormalities in glucocorticoid output, we have raised the possibility that abnormalities in glucocorticoid response may be a factor in major depression and other psychiatric disorders (Lowy et al., 1984). Failure to suppress cortisol after dexamethasone may be a special instance of glucocorticoid receptor (GCCR) resistance. The lack of stigmata of Cushing's syndrome in psychiatric patients with excessive glucocorticoid output suggests some GCCR subsensitivity. Glucocorticoid receptor number or affinity may change in response to changes in the availability of glucocorticoids, e.g., administration of dexamethasone (1-24 mg) produces a decreased number of GCCR in lymphocytes from normal volunteers which can be detected as little as 12 hours after first administration (Bloomfield et al., 1981; Schlechte et al., 1982). GCCR down regulation following glucocorticoid administration can also occur in a selective manner within the brain (Meany and Aitken, 1985; Tornello et al., 1982). Alterations in the level of endogenous glucocorticoids can also modify GCCR number e.g., stress results in the decreased number of GCCR in both brain and liver (Loeb and Rosner, 1979; Sapolsky et al., 1984). Chrousos et al. (1983) has reported a familial glucocorticoid resistance in man characterized by a marked increase in serum cortisol levels, abnormal DST and no physical stigmata of glucocorticoid excess. A decreased number or affinity of the GCCR in lymphocytes was observed.

We have found decreased *in vivo* inhibition of the lymphocyte proliferative response to the mitogens conconavalin A (ConA) and phytohemaglutinin (PHA) following 1 mg dexamethasone in depressed patients who are nonsuppressors (Lowy et al., 1984). Depressed patients, especially nonsuppressors, also had lower binding of 3H-triamcinalone (Gormley et al., 1985). The failure to suppress serum cortisol following dexamethasone was associated with a smaller decrease in GCCR content. We measured serum dexamethasone levels and found significant negative correlations between the change in the PHA response, but not in the ConA response (Meltzer et al., 1984). We have also observed a subsensitivity of the lymphocytes of patients who were nonsuppressors to the inhibitory effect of 10-9 and 10-10M dexamethasone on the lymphoproliferative response to ConA (Lowy et al., in press). These concentrations of dexamethasone correspond to those present at 8 A.M. after a 1 mg dose. The difference between suppressors and nonsuppressors was observed only with ConA, not PHA.

Because of this, we thought it would be important to examine the relationship between suicide and subsensitivity to glucocorticoids as indicated by the *in vivo* responses to ConA and GCCR content. The presence of GCCR subsensitivity might counteract the effect of increased glucocorticoid output. The combination of the two factors might turn out to be a better predictor of suicide than measures of glucocorticoid output such as basal plasma cortisol or urinary free cortisol alone. We correlated Hamilton Depression Scale suicide ratings with these measures in unmedicated patients, the majority of whom met RDC for major depression. The results are preliminary because the number of subjects for whom data is available is small. We found no significant correlations between the change in the ConA and GCCR content following dexamethasone or basal GCCR concentration and the suicide rating. Since the group included only two subjects who had

made a severe suicide attempt, further study is needed to rule out a relationship between GCCR resistance and suicide.

We have reported that the 5-HTP-induced increase in serum cortisol showed a significant positive correlation with HDRS suicide ratings at admission in 24 depressed and manic patients and that seven patients who made violent attempts had a larger cortisol response to 5-HTP than 33 who had not (Meltzer et al., 1984). We have continued this investigation using the same methodology with the exception that L-5-HTP 100 mg has been substituted for D,L-5-HTP, 200 mg. We have now examined our data in relation to suicidal attempts at any time in life, with information from the patient and informants. As can be seen in Table 4, patients with affective disorders who made violent attempts had the highest cortisol response, followed by those who made no attempt, a nonviolent attempt, and normal controls. The violent attempters had a significantly greater cortisol response than the nonviolent attempters ($p=0.003$) and the normal controls ($p=0.0008$) but just failed to differ from the nonattempters ($p=0.08$).

Glucocorticoids modulate the biosynthesis and functional activity of many neurotransmitters and neuromodulators. Thus, abnormalities in the GCCR could contribute to some of the known biochemical changes associated with depression. 5-HT, in particular, interacts with glucocorticoids in a variety of ways. 5-HT has a well known stimulatory effect on the adrenocortical system (Meltzer et al., 1984). Glucocorticoids, in turn, have been shown to have a facilitory effect on 5-HT biosynthesis and turnover (Rastogi and Signhal, 1978; deKloet et al., 1982). Glucocorticoids also modify 5-HT receptors (Bigeon et al., 1985) and various serotonergic drugs modify GCCR (Angelucci et al., 1982; Patacchioli et al., 1984). A decrease in glucocorticoid-mediated 5-HT synthesis due to a GCCR dysfunction could contribute to the postulated decreased level of 5-HT which occurs in some depressed patients. Recently, an association between the DST and platelet 5-HT uptake in depressed patients has been reported (Meltzer et al., 1983). In addition, dexamethasone has been shown to directly modify cerebrospinal fluid levels of the 5-HT metabolite, 5-hydroxyindoleacetic acid, in psychiatric patients (Banki et al, 1983).

Cortisol Response to 5-Hydroxytryptophan in Patients with Major Affective Disorders

Group	N	Cortisol Response (AUC)
Normal Controls	22	1624 ± 540
No Attempt	55	2112 ± 713
NonViolent Attempt	9	1776 ± 1046
Violent Attempt	9	2772 ± 846

$F = 6.10$, $df = 3,89$, $p = 0.0008$

Table 4.

Adrenalectomy increases 5-HT1 receptor binding in some regions of the hippocampus (Bigeon et al., 1985). Adrenalectomy also counteracted the stimulatory effect of vasoactive intestinal peptide (VIP) on 5-HT1 binding sites in the dorsal subiculum of the hippocampus, but not the inhibitory effect of VIP on the 5-HT1 binding sites in the suprachiasmatic nucleus. Other complex interactions between VIP and adrenal steroids on 5-HT1 binding were also reported (Rostene et al., 1985). Adrenalectomy also increases brain ^{3}H-imipramine binding (Arora and Meltzer, in press). Chronic corticosteroid administration appears to have mixed effects on 5-HT function (Dickson et al., 1985; Nausieda et al., 1982).

As discussed elsewhere in this symposium, 5-HT is thought to play an integral role in the biology of suicide, especially violent suicide, impulsivity or violence per se. In view of the above mentioned interactions between 5-HT and glucocorticoids, it will be important to obtain biological measures of both serotonin and glucocorticoid activity or function in individuals who have made suicide attempts or are considered high risks. Further basic re-

search on the interaction of these two systems is strongly indicated.

CONCLUSION

There is a possibility of neuroendocrine trait markers for violent or lethal suicide. A blunted TSH response, abnormal DST or increased UFC appears to be associated to past, current or future violent suicides. Similarly, the 5-HTP-induced increase in serum cortisol may be largest in patients who have made a violent suicide attempt anytime in life. Some, all or none of these neuroendocrine abnormalities may relate to decreased brain serotonergic activity. If they are related to decreased serotonergic activity, then the results would be consistent with a broad range of other biochemical studies summarized elsewhere in this report. Together the neuroendocrine studies suggest a concerted effort should be made to identify the abnormalities of 5-HT and the endocrine system in anyone who has made a violent suicide attempt and survived. The blunted TRH response may be related to increased HPA activity. More sophisticated ways of assessing increased HPA activity are now available to be applied to suicide research. A DST with measures of dexamethasone levels and a measure of glucocorticoid receptor sensitivity might prove a more sensitive index of suicidal activity. The 1-4 P.M. cortisol output, ACTH and CRF stimulation tests, measures of serum cortisol binding globulin and circadian rhythm disturbances are among the measures that might be evaluated. The aim of these studies would be to identify possible biological markers and to further develop an integrated neuroendocrine-neurotransmitter hypothesis of the etiology of suicide. For some biological factors that predispose to suicide, suicidal ideation, nonviolent, nonlethal intent attempts may represent a continuum. For other factors there may be a unique association with each level of suicidal intent or in relation to violence. A uniform way of collecting and presenting data in this regard might be useful. Methods for quantifying duration and intensity of ideation might help.

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GENETICS AND SUICIDAL BEHAVIOR

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There are five lines of evidence about genetic factors in suicide. This paper will review the clinical, twin, Iowa-500, Amish, and Copenhagen adoption studies, all of which provide evidence about genetic factors in suicide. Most of these are studies of suicidal behavior among adults but it is likely that genetic factors for suicide are similar in both adolescents and adults.

CLINICAL STUDIES

A family history of suicide has been noted to be associated with suicidal behavior at all stages of the life cycle. There are five such studies among adolescents. In 1974 Shaffer (1) reported a comprehensive survey of all 31 suicides among children aged 14 years or younger in England and Wales during the seven years from 1962 to 1968. Suicidal behavior in a first degree relative had occurred in seven of these 31 youth suicides (22.6 percent). In four relatives this suicidal behavior had occurred before the child's suicide, but in three other cases a first degree relative attempted suicide after the child had committed suicide. There was also a high incidence of depression among the first degree relatives (20 percent).

In 1981 Tishler et al. (2) found that 22 percent of a series of 108 adolescents seen at a children's hospital emergency room after attempting suicide had a history that "at least one family member had exhibited suicidal behavior in the past."

In 1982 Garfinkel et al. (3) reported a review of the hospital charts of 505 children and adolescents who appeared at the emergency room of the Hospital for Sick Children in Toronto between January 1, 1970, and January 30, 1977, and had "deliberately inflicted self-injury with a documented conscious desire to die from the injury." A control group was derived by examining the charts of individuals of the same sex and of a similar age who did not have a history of attempting suicide but who had been admitted at about the same time to the same emergency room. The researchers found that significantly more of the youthful suicidal attempters, than their controls, had a family history of suicidal behavior (8.3 percent vs 1.1 percent) (Table 1).

Garfinkel et al. also used Weisman and Worden's Risk/Rescue Rating Scale (4) to obtain ratings of severity for the adolescent's suicide attempts. Interestingly, they found that significantly more of those who had made serious suicide attempts had a family history of suicide (Table 2).

As found in Shaffer's London study, the suicide attempters in Garfinkel et al.'s study also had a significant excess of relatives with mental illness and they concluded: "A strong genetic loading for affective disorder in families of individuals who attempt suicide is supported by our findings of an eight times higher rate of suicide attempts or suicide in the families of the index group and an absence of completed suicide in the families of the controls." They also noted: "Attempted suicide is on a continuum with completed

suicide, as demonstrated by the finding that there was no family history of completed suicide in the control group and that the followup mortality rate from suicide in the index group surpassed the death rate for the controls."

In 1985 Shafii et al. (5) reported data derived from psychological autopsies carried out after lengthy home visits with the families of 20 children and adolescents who had committed suicide in Jefferson County, Louisville, between January 1980 and June 1983. Friends and significant others were also contacted and three extensive questionnaires were completed. Shafii et al. were able to match 17 of the suicide victims with controls drawn from among the suicide victim's closest friends. These controls, and their families, were interviewed using the same methodology as was used with the families of the suicide victims. Shafii et al. also found that significantly more of the youth suicide victims, than controls, had a family history of suicide (Table 3). Again, there was a significant difference between the families of suicide victims and controls for emotional problems in the family. These workers concluded that "exposure to suicide or suicidal behavior of relatives and friends appears to be a significant factor in influencing a vulnerable young person to commit suicide."

In an ongoing study, Shaffer et al. (6) are performing extensive psychological autopsies on a consecutive series of youthful suicides under 19 years of age occurring in New York City. In a preliminary report of the first 52 suicide victims studied, they noted that a substantial number (20, 38 percent) had a rela-

Family History Differences Between Children and Adolescents Who Attempted Suicide and Controls

	Suicide Attempters			Controls					
	Available	With Charact.		Available	With Charact.		Signif		
Characteristic	N	N	%	N	N	%	x^2	df	P
Family History of mental illness	442	228	51.6	452	74	16.4	122.3	1	.01
History of suicide	443	37	8.3	442	5	1.1	23.95	2	.01
Suicide attempts		26	5.9		5	1.1			
Completed suicide		11	2.5		0				

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Table 1.

Variables Discriminating the Severity of 604 Suicide Attempts by Children and Adolescents.

	Percent of Attempts					
	Low Danger	Moderate Danger	Severe Danger	Significance		
Variable	(N=385)	(N=149)	(N=70)	x^2	df	P
Family history of suicide	4.6	12.7	16.1			
No family history of suicide	95.4	87.3	83.9	13.09	4	.01

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Table 2.

tive who had either committed or attempted suicide. Although cautioning that the family data are complex and are not yet fully explored, Shaffer et al. (7) consider that this aspect of these youthful suicides may represent an environmental rather than a genetic phenomenon; they may be imitative acts similar to the recently well publicized clustering of teenage suicides.

Among adults who exhibit suicidal behavior, there are also surprisingly few studies about the presence or absence of a family history of suicide. In an early study Farberow and Simon (15) reported that among 100 suicide victims in Vienna and Los Angeles, six had a parent who had killed himself, a rate more than 88 times the expected rate. Robins et al. (8) found that 11 percent of 109 suicide attempters had a family history of suicidal behavior. Murphy et al. (9) reported that one third of 55 callers to a suicide prevention center had a family history of suicidal behavior and that this was significantly more likely to be the case if the caller had himself attempted suicide. Flinn and Leonard (10) noted that among 480 young nonpsychiatric subjects, those reporting their own suicidal behavior also reported more knowledge about suicidal behavior in others.

More recently, Murphy and Wetzel (11) systematically interviewed a random sample of all persons seen and admitted during a one-year period at the St. Louis County Hospital following a suicide attempt. Of the 127 patients in the study, 14 percent gave a family history of suicide, 24 percent a family history of attempted suicide, and 6 percent a family history of suicide threats. One or more of these family suicidal behaviors was reported by 36 percent of the suicide attempters. Among suicide attempters with a primary diagnosis of primary affective disorder, 17 percent had a family history of suicide and 17 percent a family history of suicide attempt (Table 4). As individuals with affective disorders comprise a larger proportion of suicides than individuals with personality disorders, Murphy and Wetzel predicted that

Significant Differences Between Children and Adolescents Aged 12-19 Who Committed Suicide and Matched-Pair Control Subjects.

	Suicide Victims N=20		Control Subjects N=17		McNemar Test	
Variable	**N**	**%**	**N**	**%**	**(df=1)**	**P**
Family and environmental variables						
Exposure to suicide	13	65	3	18	6.12	<.008
Sibling's or friend's (attempted or completed suicide)	12	61	2	12	6.12	<.008
Parent's or adult relative's (suicidal ideation, threats, or attempts of completed suicide)	6	30	2	12	2.25	n.s[a]
Parent's emotional problems	12	60	4	24	5.14	<.02

[a] $x2=3.3$, df=1, P<.04

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Table 3.

more of their patients with affective disorder could be expected to present a significant suicide risk in the future. Therefore, they concluded that a "systematic family history of such behavior coupled with modern clinical diagnosis should prove useful in identifying those attempters at increased risk for suicide."

The first study providing data about how commonly a family history of suicide is found among psychiatric patients was that of Pitts and Winokur (12). They found that among 748 consecutive patients admitted to a hospital, 37 reported a possible or definite suicide in a first degree relative (4.9 percent). In 25 (68 percent) of these 37 cases the diagnosis was an affective disorder, and these investigators noted that the statistical probability of this distribution occurring by chance was less than 0.02. When the probable diagnoses in the cases of the first degree relatives who suicided were considered, in 24 of the 37 patient-relative pairings, both members had affective disorders. Pitts and Winokur estimated that 79 percent of the suicides of the first degree relatives were associated with probable affective disorder.

In 1983, Roy (13) reported a study of all the 5,845 psychiatric patients admitted to the Clark Institute of Psychiatry in Toronto between January 1974 and June 1981. There were 243 inpatients with a family history of suicide (4.2 percent), a percentage very similar to the 4.9 percent reported by Pitts and Winokur nineteen years earlier. The patients with a family history of suicide were compared with the 5,602 inpatients without such a history. A family history of suicide was found to significantly increase the risk for an attempt at suicide in a wide variety of diagnostic groups (Table 5). Almost half (48.6 percent) of the patients with a family history of suicide had themselves attempted suicide. More than half (56.4 percent) of all the patients with a family history of suicide had a primary diagnosis of an affective disorder and more than a third (34.6 percent) had a recurrent unipolar or bipolar affective disorder.

Recently Linkowski et al. (14) investigated past suicidal behavior and family history of suicide among a consecutive series of 713 patients with affective disorder admitted over several years to the psychiatric department of the University of Brussels. They found that 123 of the depressed patients (17 percent) had a first or second degree relative who had committed suicide. They also found that a family history of suicide significantly increased the probability of a suicide attempt among the depressed women, especially the risk for a violent suicide attempt. Among the male depressives, a family history of suicide significantly increased the risk only for a violent suicide attempt (Tables 6 and 7). Linkowski et al. concluded that "a positive family history for violent suicide should be considered as a strong predictor of active suicidal attempting behavior in major depressive illness."

A family history of suicide has also been found significantly more among psychiatric patients who commit suicide (16). As manic-

Family History of Suicidal Behavior by Broad Diagnostic Groups

Diagnostic Group	F	% with Family History of Suicide	Attempt	Any[a]
Personality disorders	56	20	34	46
Primary affective disorder	29	17	17	38
Other diagnoses and none	42	5	17	21
All patients	127	14	24	36

[a]Any suicidal behavior includes suicide and attempted and threatened suicide.
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Table 4.

depression is the psychiatric diagnosis most commonly found among suicide victims, it is not surprising to find that, across the various published series, approximately 10 percent of manic depressive patients have a family history of suicide (17-20).

A family history of suicide has also been noted to be associated with suicidal behavior among individuals in the last stages of the life cycle. Batchelor and Napier (21) found that among 40 consecutive cases of attempted suicide admitted to a general hospital, aged 60 years or over, a family history of suicide was present in 7 (17 percent) of the cases.

A consecutive series of 5845 inpatients admitted to the Clarke Institute of Psychiatry between January 1974 and June 1981. Patients, by diagnostic group, who attempted suicide comparing those with a family history of suicide with those without such a history.

	Second- or first-degree relative suicided			No family history of suicide		
Diagnostic Group	No. Attempted	(%)	No. of Attempts	No. Attempted	(%)	P
Schizophrenia	15/33	(45.4)	28	150/1114	(13.5)	<.0001
Unipolar	13/32	(41.6)	24	50/373	(13.4)	<.0001
Bipolar	22/58	(37.9)	48	56/405	(13.9)	<.0001
Depressive neurosis	26/47	(55.3)	45	221/715	(30.9)	<.0001
Personality disorder	33/48	(68.8)	89	328/1048	(31.3)	<.0001
Alcohol	3/7	(42.9)	3	42/147	(28.5)	NS
Others	6/18	(33.3)	16	378/1801	(21.0)	NS
Total	118/243	(48.6)	252	1225/5602	(21.8)	<.0001

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Table 5.

Clinical characteristics of the major depressive (MD) patients

	MD with past violent suicidal attempt		MD with past non-violent suicidal attempt		MD with no suicidal attempt	
	Males	Females	Males	Females	Males	Females
BP FH+*	3	6	0	7	14	14
FH−	10	11	9	19	72	79
UP FH+	4	12	1	19	16	27
FH−	16	15	23	84	92	160
Total	33	44	33	129	194	280

* FH+ patients with familial history of suicide
BP = bipolar; UP = unipolar
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Table 6.

THE IOWA-500 STUDY

The Iowa-500 study is a followup study of just over 500 psychiatric patients consecutively admitted to the University of Iowa Psychiatric Hospital between 1934 and 1944. The 525 patients in the study were chosen because they met certain research criteria. They consisted of 200 schizophrenic, 100 manic, and 225 depressed patients. They were compared with a control group of 160 psychiatrically normal individuals admitted to the University of Iowa Hospital during the same period for appendectomy or herniography. Followup studies between 1972 and 1976 revealed that 30 of these 685 subjects subsequently committed suicide; 29 of the suicides were found among the 525 psychiatric patients and only 1 among the 160 normal controls (5.5 percent vs 0.6 percent) (30). This finding is impressive evidence for the close association of suicide with psychiatric disorder.

The Iowa-500 study has yielded other informative data (31) and Tsuang has recently reported the development of this study in another important direction. He and his associates not only followed up the psychiatric patients and controls but also their first degree relatives (32). The first degree relatives were interviewed, and Tsuang was interested in the answers to four questions which are relevant to the possible role of genetic factors in suicide. These questions were:

1. Are relatives of patients with schizophrenia and affective disorders subject to higher risk of suicide than relatives

Significances and relative odds ratios for the comparisons tested in subgroups of depressive attempters and non-attempters

	Comparison*					
	A		B		C	
	M	F	M	F	M	F
Significance of main effect**						
Polarity	n.s.	0.045	n.s.	n.s.	n.s.	0.021
Family history (FH+)	n.s.	0.004	n.s.	0.0003	0.010	0.010
Age	n.s.	n.s.	n.s.	n.s.	0.050	n.s.
Relative odds ratio***						
Polarity (BP vs UP)	0.65					2.43
Family history (FH+ vs FH-)		2.02		3.53	14.96	2.68
Age, years						
31-45 vs 15-30					0.32	
46-60 vs 31-45					4.92	
>60 vs 46-60					2.19	
>60 vs 15-30					3.46	
No. of patients	260	453	260	453	66	173

*A) Presence versus absence of any suicidal attempts; B) violent versus non-violent attempt plus no suicidal attempt; C) violent versus non-violent attempts.
M = males; F = females
**All interactions between main effects (polarity x FH+, polarity x Age, and FH+ x Age) non-significant.
***Given only for statistically significant main effects.
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Table 7.

of nonpsychiatric control patients?

2. Are relatives of patients with schizophrenia and affective disorders who committed suicide subject to higher risks of suicide than relatives of patients who did not commit suicide?
3. Is the risk of suicide among relatives of schizophrenics different from that for relatives of manics and depressives?
4. Are the suicide risks different for male and female relatives of patients from different diagnostic categories?

The first degree relatives of the psychiatric patients were found to have a risk of suicide almost eight times greater than the risk in the relatives of the normal controls. When only deceased relatives were considered, the relatives of psychiatric patients were found to have a risk of suicide almost six times greater than the risk among the deceased relatives of the controls (Table 8).

Among the first degree relatives of the psychiatric patients, those who were the relative of one of the 29 patients in the Iowa-500 study who committed suicide themselves had a four times greater risk of committing suicide compared with the relatives of the patients who did not commit suicide. Among the deceased relatives, the suicide risk was three times greater (Table 9).

Next, the individual psychiatric diagnoses were examined. The risk of suicide was sig-

Risk of Suicide among Relatives of Patients and Controls

		Relatives[a]				
		Suicides				
Subjects	N	N	%		BZ	MR(%) ± SE
Patients (N=510)						
All relatives	3941	55	1.4		2348	2.3 ± 0.3[b]
Deceased relatives	2294	55	2.4		1338	4.1 ± 0.5[b]
Controls (N=153)						
All relatives	1403	2	0.1		672	0.3 ± 0.2
Deceased relatives	589	2	0.3		305	0.7 ± 0.5

a. BZ = Bezugsziffer (age-adjusted size of the sample), MR = Morbidity risk.
b. P<.01 (comparison of patients with controls).
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Table 8.

Risk of Suicide Among Relatives of Patients with and without Suicide

		Relatives[a]				
		Suicides				
Subjects	N	N	%		BZ	MR(%) ± SE
Suicide (N=29)						
All relatives	193	9	4.7		114	7.9 ± 2.5[a]
Deceased relatives	136	9	6.6		78	11.5 ± 3.6[a]
No suicide (N=481)						
All relatives	3754	46	1.2		2234	2.1 ± 0.3
Deceased relatives	2158	46	2.1		1259	3./ ± 0.5

a. P<.05 (comparisons of suicide with no suicide).
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Table 9.

nificantly greater among the first degree relatives of depressed patients than it was among the relatives of either schizophrenic or manic patients. When the relatives of patients who committed suicide were compared, the suicide risk was even higher, but it was equally high among the relatives of both depressed and manic patients (Table 10).

The suicide risk was also examined separately for the male and female relatives of the psychiatric patients. In general, the suicide risk was higher for male first degree relatives than it was for females (Table 11).

Thus, this followup of the first degree relatives of the subjects in the Iowa-500 study is

Risk of Suicide Among Living and Dead Relatives of Schizophrenics, Manics, and Depressives with Suicide and without Suicide.

Patients	Suicides N	Suicides N	Suicides %	Relatives BZ	Relatives MR(%) ± SE
Schizophrenia (S)					
Suicide (N=8)	41	0	0.0	23	0.0 ± 0.0
No Suicide (N=187)	1159	9	0.8	723	1.2 ± 0.4
Total (N=195)	1200	9	0.8	746	1.2 ± 0.4
Mania (M)					
Suicide (N=6)	53	3	5.7	32	9.4 ± 5.2
No Suicide (N=86)	748	4	0.5	426	0.9 ± 0.5
Total (N=92)	801	7	0.9	458	1.5 ± 0.6
Depression (D)					
Suicide (N=15)	99	6	6.1	59	10.2 ± 3.9
No Suicide (N=208)	1847	33	1.8	1085	3.0 ± 0.5
Total (N=223)	1946	39	2.0	1144	3.4 ± 0.5

Significant comparisons are as follows: Suicide, S vs M ($P<.10$), S vs D ($P<.01$); no suicide, S vs D ($P<.01$), M vs D ($P<.01$); and Total S vs D ($P<.01$), M vs D ($P<.05$).
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Table 10.

Risk of Suicide Among Relatives of Schizophrenics, Manics, and Depressives by Sex

Diagnostic Group	Suicides N	Suicides N	Suicides %	Relatives BZ	Relatives MR(%) ± SE
Schizophrenia					
Male relatives	601	9	1.5	359	2.5 ± 0.8[a]
Female relatives	590	0	0.0	394	0.0 ± 0.0
Mania					
Male relatives	395	5	1.3	221	2.3 ± 1.0
Female relatives	390	2	0.5	238	0.8 ± 0.6
Depression					
Male relatives	994	30	3.0	587	5.1 ± 0.9[a]
Female relatives	921	9	1.0	568	1.6 ± 0.5

a. $P<.01$ (comparison of males and females).
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Table 11.

an important study and demonstrates that there are genetic factors in suicide. The main findings are summarized in Table 12.

TWIN STUDIES

Compelling evidence for the genetic transmission of manic-depression and schizophrenia is that the concordance rate for these psychiatric disorders is substantially higher among identical twins, who share the same genes, than it is among fraternal twins who share only 50 percent of their genes (22). Thus, if the propensity to commit suicide was genetically transmitted, concordance for suicide should be found more frequently among identical than fraternal twins. This was well stated by Kallman (23); "If hereditary factors play a decisive role we should find a concordant tendency to suicide more frequently in one-egg than in two-egg pairs regardless of ordinary differences in environment. If the main emphasis is placed on certain constellations of nongenetic factors, concordance should be expected in some twin pairs of either type, who shared the same environment and responded to a similar degree of distress with the same type of psychosis."

Kallman had collected 2,500 twin index cases from mental institutions, TB hospitals, old age homes, and other parts of the population of New York State. In 1947, he reported that among this clinical material, there were 11 twin pairs where one twin was known to have committed suicide. Three of these 11 twin pairs were monozygotic and 8 dizygotic. In none of these 11 twin pairs had the other twin committed suicide (24). This negative finding led him to conclude that "there is no statistical evidence for the popular notion that the tendency to commit suicide recurs in certain families as the result of a special hereditary trait or of a particular type of genetically determined personality deviation."

However, 20 years later in 1967, Haberlant (25,26) pooled the accumulated data from twin studies from different countries. By then, 149 sets of twins had been reported in which one twin was known to have committed suicide. Among these twin pairs there were nine sets of twins where both twins had committed suicide. All of these nine twin pairs were identical twins; there was no set of fraternal twins concordant for suicide (Table 13).

Four of these nine monozygotic twin sets concordant for suicide came from the Danish Psychiatric Twin Register and their case histories revealed that in three of them the twins were also concordant for manic-depressive disorder (27). In another of these nine monozygotic twin sets, the twins were also concordant for schizophrenia. Since Haberlandt's review, Zair (28) has reported a tenth pair of identical twins who both com-

Summary of Morbidity Risks of Suicide in Patients and Relatives

	Patients			Relatives			Relatives of Suicides		
Diagnostic Group	N	BZ	MR%	N	BZ	MR%	N	BZ	MR%
Schizophrenia	8	125	6.4	9	746	1.2	0	23	0.0
Mania	6	62	9.7	7	458	1.5	3	32	9.4
Depression	15	173	8.7	39	1144	3.4	6	59	10.2
Control	1	97	1.0	2	672	0.3	0	7	0.0

BZ = Benzugsziffer (age-adjusted size of the sample)
MR = Morbidity risk
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Table 12.

mitted suicide. Again there was an association with affective disorder as both twins had killed themselves during a depressive episode and both their parents and a grandmother had also been treated for depression.

Approximately 1 in 250 live births is an identical twin and between 0.5 and 1 percent of all deaths among the general population are due to suicide. Thus, it is somewhat surprising that only 10 pairs of monozygotic twins concordant for suicide have been reported in the 173 years since the first report of suicide in twins (29). Also, in 5 of these 10 twin pairs, the twins were also concordant for either depression or schizophrenia. Thus, although twin data provide evidence for the genetic transmission of suicide, this evidence may be partly confounded by the issue of the genetic transmission of psychiatric disorders themselves.

Suicide in Twins

Type of twins	Number of twin pairs	Number of twin pairs where both twins committed suicide (%)
Identical	51	9* (17.7%)
Fraternal	98	0 (0%)

P <0.0001
* Four of these 9 sets of twins have been reported twice. They are included in Haberlant's 1967 review(26) and have also been reported in detail in 1970 by Juel-Nielsen and Videbech.(27)
Reproduced with permission of Diseases of the Nervous System(22)

Table 13.

THE AMISH STUDY

In 1985 Egeland and Sussex (33) made their first report on the suicide data obtained from the study of affective disorders among the Old Order Amish community of Lancaster County in southeastern Pennsylvania. This is a continuing study into the genetics and course of illness of the affective disorders among this population (34). Suicide research among the Amish is of great interest for several reasons. They are an Anabaptist, nonviolent, pacifist society where there are no violent crimes and where there has been no known murder. Alcohol is prohibited and there is no alcoholism. Also, the Amish are a wealthy farming community among whom there is no unemployment. Their strong religious beliefs foster a tightly knit community, and three generations commonly live together under the same roof. Family life is valued and divorce precluded. Social isolation is rare and the cohesive nature of their community offers social support for individuals who encounter stress or adverse life events. Thus, several of the important social risk factors for suicide among individuals in the general population such as unemployment, divorced or separated marital status, social isolation, and alcoholism are risk factors not commonly found among these Amish (35-38). This means that genetic factors for suicide may play a larger part in suicides occurring among the Amish.

Not surprisingly, suicide is a relatively rare event among this group of Amish. In fact Egeland and Sussex were only able to find 26 suicides over the 100 years from 1880 to 1980. Over these 100 years the suicide rates among these Amish have consistently been substantially lower than the rates for the rest of the United States.

Egeland and Sussex's team used the Schedule for Affective Disorders and Schizophrenia-Lifetime Version (SADS-L). They conducted an average of six interviews, with various family members, for each of the 26 suicide victims. A five-member psychiatric board used the Research Diagnostic Criteria (RDC) to make psychiatric diagnoses based on these interviews and supplemented by information from other sources. The first important finding of the study was that 24 of the 26 suicide victims met RDC criteria for a major affective disorder. Eight had bipolar I, four bipolar II, and 12 unipolar affective disorder. A further case met the diagnostic criteria for a minor depression. Furthermore, most of the suicide victims had a heavy family loading for affective disorders.

For example, among the eight bipolar I suicide victims the morbidity risk for affective disorders among their 110 first degree relatives was 29 percent compared with the 1 to 4 percent found among the general population.

The second finding of the study was that almost three quarters of the 26 suicide victims were found to cluster in four family pedigrees, each of which contained a heavy loading for affective disorders and suicide. Figure 1 shows a very heavy loading for affective disorders in one family where there have been seven suicides. All seven suicide victims were found among individuals with definite affective disorder. Figure 2 shows a second pedigree, also with a heavy loading for affective disorders, where there have been six suicides, five of which were found among individuals with definite affective disorder.

Interestingly, the converse was not true as there were other family pedigrees with heavy loadings for affective disorder but without suicides. It is also of note that the morbidity risk for affective disorders among 170 first degree relatives in other bipolar I pedigrees without suicide was, similar to that found in bipolar pedigrees with suicide, also in the 20 percent range. Thus, in this study, a familial loading for affective disorders was not in itself a predictor for suicide.

The third finding of the study was that only six of the 26 suicide victims (23 percent) had received any psychiatric treatment despite the fact that 24 of them had severe affective disorders whose natural history is usually that of recurrent episodes. The other 20 suicide victims had either never received any medi-

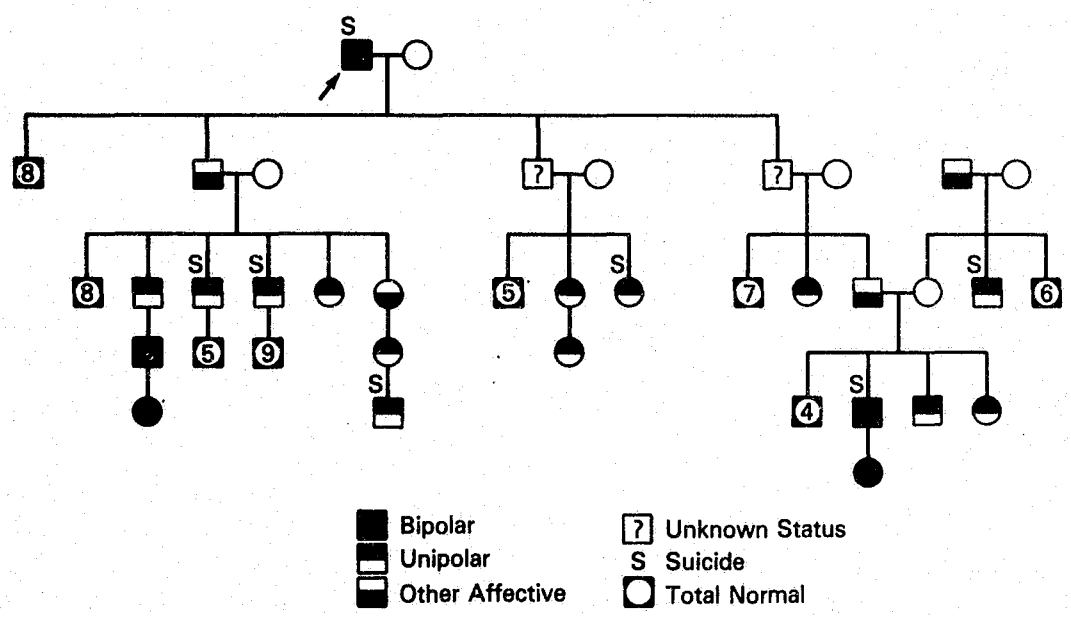

Figure 1.

cal treatment for their psychiatric disorder, or they were seeing a family doctor at the time they committed suicide, or they were planning to seek help for themselves.

Egeland and Sussex concluded: "Our study replicates findings that indicate an increased suicidal risk for patients with a diagnosis of major affective disorder and a strong family history of suicide." They also noted: "Bipolar and unipolar illness conveying a high risk as a diagnostic pattern in pedigrees. The number not receiving adequate treatment for manic-depressive illness (among the suicides) supports the common belief that intervention for these patients at risk is recommended. It appears most warranted in those families in which there is a family history of suicide. The clustering of suicides in Amish pedigrees follows the distribution of affective illness in the kinship and suggests the role of inheritance."

DANISH-AMERICAN ADOPTION STUDIES

The strongest evidence that we have for the presence of genetic factors in suicide comes from the adoption studies carried out in Denmark by Schulsinger, Kety, Wender, and Rosenthal (39-41). The strength of the adoption strategy is that it is one of the best ways to tease apart "nature" from "nurture" issues. This is because individuals separated at birth, or shortly afterwards, share their genes, but no subsequent environmental experiences, with their biological relatives. In contrast, adoptees share their environmental experiences through childhood and adolescence with their adopting relatives but they

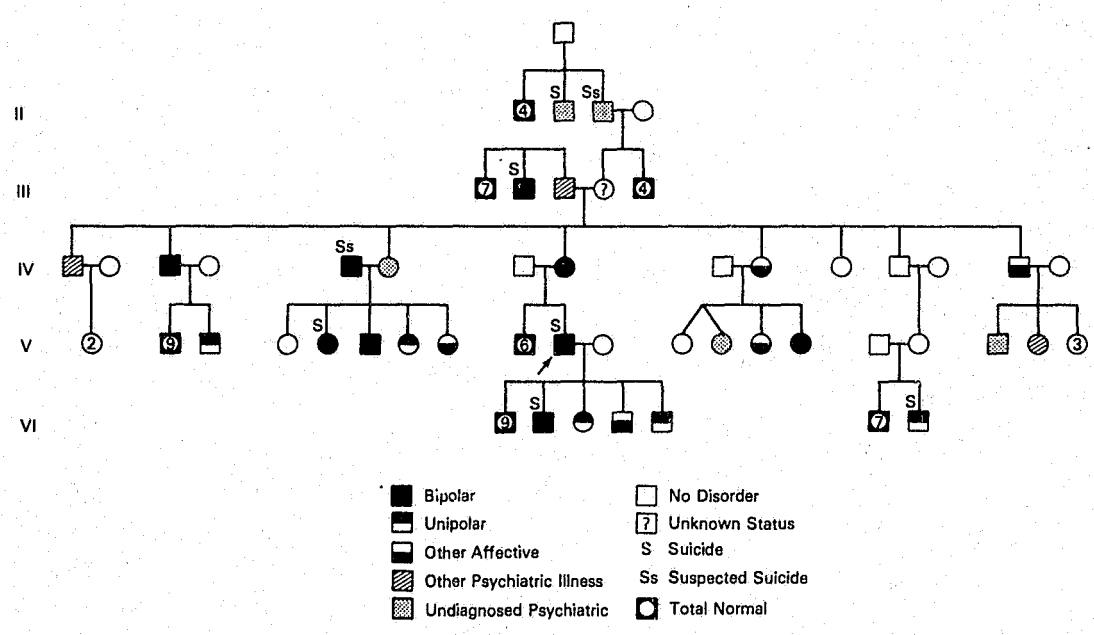

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Figure 2.

share no genes with them.

The Psykologisk Institut has a register of the 5,483 adoptions that occurred in greater Copenhagen between 1924 and 1947. A screening of the registers of causes of death revealed that 57 of these adoptees eventually committed suicide. They were matched with adopted controls for sex, age, social class of the adopting parents, and time spent both with their biological relatives and in institutions before being adopted. Searches of the causes of death revealed that 12 of the 269 biological relatives of these 57 adopted suicides had themselves committed suicide compared with only 2 of the 269 biological relatives of the 57 adopted controls. This is a highly significant difference for suicide between the two groups of relatives (Table 14). None of the adopting relatives of either the suicide or control group had committed suicide.

Also, these striking results are of additional interest because the suicides were largely independent of the presence of psychiatric disorder. Schulsinger and coworkers also investigated whether or not the names of the 12 biological relatives who committed suicide appeared on the psychiatric case registers. They found that 6 of these biological suicide relatives had had no contact with the psychiatric services and thus presumably did not suffer from one of the major psychiatric disorders commonly found among suicide victims--manic-depression, schizophrenia, or alcoholism--as these are chronic disorders with frequent relapses usually requiring psychiatric hospitalization. Schulsinger et al. (39) therefore proposed that there may be a genetic predisposition for suicide independent of, or additive to, the major psychiatric disorders associated with suicide.

Wender et al. (41,42) went on to study another group of the Danish adoptees. These were the 71 adoptees identified by the psychiatric case register as having suffered from an affective disorder. They were matched with 71 control adoptees without affective disorder. The results of this study showed that significantly more of these adoptees with affective disorder, than their controls, had committed suicide. Thus this study, too, demonstrates that there is a genetic component to suicide (Table 15).

Of further interest in this study was the examination of the adoptee suicide victims and their biological relatives by the type of affective disorder suffered by the suicide victim. It was particularly adoptee suicide victims with the diagnosis of "affect reaction" who had significantly more biological relatives who had committed suicide than controls. The diagnosis of "affect reaction" is used in Denmark to describe an individual who has affective symptoms accompanying a situational crisis--often an impulsive suicide attempt (Table 16). These findings led Kety (42) to suggest that a genetic factor in suicide may be an inability to control impulsive behavior which

Incidence of Suicide in the Relatives of Adoptees Who Committed Suicide and Their Controls

Adoptees	Biological Relatives		Adoptive Relatives	
57 adoptees died by suicide	12/269	(4.5%)	0/148	(0%)
57 matched control adoptees	2/269	(0.7%)	0/150	(0%)

P<0.01
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Table 14.

Incidence of Suicide in the Relatives of Adoptees Who Have Suffered a Depressive Illness and Their Controls

Adoptees	Biological Relatives		Adoptive Relatives	
71 adoptees with depression	15/407	(3./%)	1/187	(0.5%)
71 matched control adoptees	1/360	(0.3%)	2/171	(0%)

P<0.01
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Table 15.

has its effect independently of, or additively to, psychiatric disorder. Psychiatric disorder, or environmental stress, may serve "as potentiating mechanisms which foster or trigger the impulsive behavior, directing it toward a suicidal outcome (42)."

Kety (42) also noted that there has been much recent work on the biology of impulsivity and that disturbances in central serotonin systems have been described in relation to suicidal behavior in personality disordered individuals and in patients with various other psychiatric disorders (reviewed in this volume by Asberg). In this regard it is noteworthy that Buchsbaum et al. (44) found that significantly more college students with low levels of the enzyme monoamine oxidase (MAO) in their blood platelets had a family history of suicidal behavior compared with students with high platelet MAO levels. This enzyme is involved with the metabolism of serotonin. Furthermore, as there is some evidence that lithium may be useful in impulsive and aggressive individuals (43), Kety (42) also suggested that controlled trials of drugs acting on central serotonin system might be informative among patients who exhibit suicidal behaviors.

SUMMARY

Suicide, like so much else in psychiatry, tends to run in families. The question is what is being transmitted. No doubt in some youthful suicide victims what is transmitted is not a genetic factor but a psychological factor. The family member who has committed suicide may serve as a role model to identify with, and the option of committing suicide becomes one possible "solution" to intolerable psychological pain. However, the family, twin, and adoption studies reviewed here show that there are genetic factors in suicide. In many suicide victims, these will be genetic factors involved in the genetic transmission of manic depression, schizophrenia, and alcoholism--the psychiatric disorders most commonly associated with suicide. However, the Copenhagen adoption studies strongly suggest there may be a genetic factor for suicide independent of, or additive to, the genetic transmission of psychiatric disorder. Interestingly, support for this possibility comes from the recent Amish studies, which showed that suicide was much more likely to occur when an individual had genetic vulnerabilities to both suicide and to affective

Incidence of suicide in the biological relatives of depressive and control adoptees

Diagnosis in Adoptee	Incidence of suicide in biological relatives		Significance
Affective reaction	5/66	(7.6%)	P <0.0004*
Neurotic depression	3/127	(2.4%)	P <0.056
Bipolar depression	4/75	(5.3%)	P <0.0036
Unipolar depression	3/139	(2.2%)	P <0.06/
No mental illness	1/360	(0.3%)	

* compared with biological relatives of control adoptees with no known history of mental illness

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Table 16.

illness.

There is a possible practical implication for the prevention of youth suicide arising from this review. It is that an adolescent who develops a depressive episode, or who exhibits suicidal behavior, and who has a family history of suicide might be considered to be at risk of committing suicide. Such an individual might, therefore, be more closely assessed and followed, particularly with a view to determining whether he is developing a recurrent affective disorder for which psychopharmacological intervention might be appropriate.

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SUMMARY AND OVERVIEW OF RISK FACTORS IN SUICIDE

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INTRODUCTION

This conference brings together two independent traditions in the study of suicide--the psychosocial and the psychiatric-biomedical. Although we focus here primarily on potential biological risk factors, we also highlight opportunities for interdisciplinary cooperation that could enhance scientific understanding and lead to improvements in treatment and prevention. The educational efforts that we hope will grow from this conference should, wherever possible, be based on firmly established knowledge, rather than simply belief systems--however compelling they may seem. Much of the apparent disparity among the different schools of thought represented at this conference might be due to the fact that different approaches focus on different populations. By and large, psychosocial studies have focused on individuals with suicidal ideation who contact suicide prevention programs, whereas the psychiatric-biomedical studies have focused on actual suicides or major suicide attempts, largely among individuals with a major psychiatric diagnosis.

Biological investigations of suicidal behavior have been most active in the following areas of study: brain chemistry as measured through cerebrospinal fluid (CSF); postmortem analyses of tissues from individuals who have committed suicide; neuroendocrine correlates; and genetics. Each of these subjects has been well reviewed by the previous authors, Asberg (1), Stanley (2), Meltzer (3), and Roy and Kety (4). Rather than covering the same ground again, we will briefly summarize these excellent reviews and then add some comments of our own.

CSF BIOCHEMICAL STUDIES

Asberg reports that several studies have found an increased rate of suicide attempts in psychiatric patients with low CSF concentrations of the serotonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA). Many of the study populations were depressed patients, but similar studies involving populations with other psychiatric diagnoses, such as personality disorders (5,6) and schizophrenia (7,8), suggest that the association between low levels of CSF 5-HIAA and suicide is not confined to depression. The association may not, however, be present in manic-depressive patients.

Asberg notes that evidence to date also suggests that low concentrations of CSF homovanillic acid (HVA), a metabolite of dopamine, are associated with suicide attempts in depressed patients. This associa-

tion has not been found in other psychiatric populations.

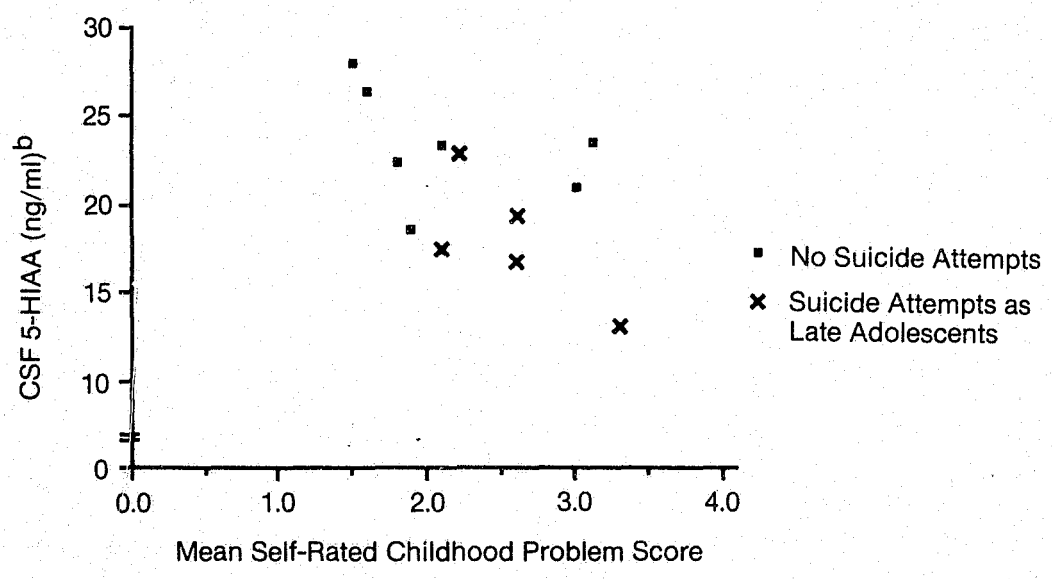
Asberg points out that CSF metabolites are only indirect measures of amine turnover in the brain. She notes some confounding influences on such measures--age, sex, body height, concentration gradient, circadian and seasonal rhythms, drug effects, medical diseases, diet, and physical activity. Methodological problems include lumbar-puncture location and subject position, amount of CSF drawn, handling and storage, assay methods, and within-subject stability of CSF 5-HIAA. Despite these problems, the biochemical methodology is elegant compared to measures of suicidal behavior. Among problematic methodological factors Asberg notes, is the lack of clear definitions of **suicide attempt** in most studies and the assumption made in "life history" measurements of behavior that biological systems remain stable over time.

Asberg characterizes low CSF 5-HIAA as an indicator of vulnerability rather than as a marker of the **state** of depression. She cites longitudinal CSF studies as well as genetic evidence in support of this conclusion.

The mechanisms by which serotonin function influences suicidal behavior are unknown, but Asberg points out that some evidence links impulsivity and difficulties in handling aggression to suicide attempts. Formulations of such a link come from animal studies, classical psychoanalytic observations, and behavioral and biochemical studies in clinical populations.

Asberg suggests that including lumbar punctures to obtain CSF is a reasonable part of the clinical assessment in some psychiatric patients. In conclusion, she proposes a

Self-Rated Childhood Problems and CSF 5-Hydroxy Indoleacetic Acid (5-HIAA) Levels of 12 Male Patients with Borderline Personality Disorder[a]



[a] The self-rated scores were negatively correlated with CSF 5-HIAA ($r=-0.63$, $p<0.03$)

[b] Measured by gas chromotography — mass spectrometry

Figure 1.

model of interaction between biological vulnerability and psychiatric symptoms (e.g., depression), psychological factors, adverse environmental occurrences, and childhood history.

Of most interest to us is the factor that implies a **trait**, a relatively stable characteristic that changes little, if at all, with clinical condition, in contrast to the factor that changes with clinical **state**. Our data (5,6,9) show that young adults with a history of aggressive and impulsive behavior (including a childhood history) have low levels of CSF 5-HIAA. Such evidence suggests that these behaviors reflect, in part, certain trait characteristics, which may be relatively independent of changing environments and personal relationships. More ambiguous are data linking CSF 5-HIAA levels to Asberg's categories of nonviolent and violent suicide, the latter usually associated with the lowest levels of CSF 5-HIAA. Is the violent behavior a reflection of an isolated **state** or is it one episode in a long-time history of similar behavior, not all of which may have been self-destructive or suicidal?

Some studies indicate that young children have higher levels of CSF 5-HIAA than do adults. It is unclear whether this difference relates to the observations that serious suicidal behaviors are more common in adults and adolescents than in young children. In our replication study, young adults and late adolescents with the lowest levels of CSF 5-HIAA had childhood histories that included many affective-impulsive symptoms, but no reported incidence of childhood suicidal attempts. (Figure 1)

POSTMORTEM STUDIES

Stanley reviews postmortem studies of biogenic amines, their metabolites and enzymes, and receptor binding. He points out that available information indicates that suicide victims are diagnostically heterogenous, so that differences in neurochemistry found at autopsy may be more related to suicidal behavior than to depression per se. He also cautions that none of the postmortem studies he reviews focus on youth.

Postmortem enzyme studies of suicide reveal no consistent patterns. Stanley's own group found no differences between suicidal subjects and controls in either the A or B forms of monoamine oxidase (MAO). Previous findings of lowered brain MAO activity among suicide victims may have been related to alcoholism.

Earlier studies of serotonin and its metabolite 5-HIAA generally found decreased levels in subcortical nuclei, including the hypothalamus and parts of the brain stem. Some of the variability in these studies is undoubtedly due to confounding variables, such as manner of death (e.g., drug overdose), and the extent of delay between death and autopsy ("postmortem interval").

Receptor-binding studies may be less influenced by these variables. Stanley's group controlled for age, sex, and postmortem interval, as well as the manner of death, which in each case was sudden and violent. They found significantly fewer imipramine-binding sites in the frontal cortex of suicide victims, a finding consistent with the association between suicide and low central serotonin function since imipramine binding is a marker for presynaptic serotonin nerve terminals. Of the four other imipramine-binding studies published, three have replicated the findings of Stanley and his colleagues. However, generalizing from these results in adults to suicide in the young is risky because some relevant neurochemical measures, such as imipramine binding, are known to be influenced by age. Thus, Stanley's call for studies of young people, both normal controls and suicide victims, is well taken. He points to the need for better diagnostic information and greater specificity in reporting related aggressive, violent, and impulsive behavior. He closes by suggesting a behavioral-biochemical profile to help clinicians identify patients at high risk for suicide.

Issues that seem important to us include the fact that subjects in most postmortem studies of serotonin (5-HT) and its metabolite (5-HIAA) are predominantly depressed patients. None of the reports indicate any attempt to determine a history of aggressive behaviors. This absence of data on aggressive-impulsive behavior in completed suicides seems especially to highlight the importance of collecting careful psychological autopsy data in conjunction with the biological assessments in postmortem studies.

A curious discrepancy is apparent in this literature. The lowered 5-HT functioning in the frontal cortex suggested by receptor studies has not been subjected to postmortem analysis, which is so aptly suited to anatomical localization. Older studies have, however, shown lower levels of 5-HT and/or 5-HIAA in the midbrain-brainstem area, the nucleus acumbens, and hypothalamic area, the latter of which has also been shown to have increased 5-HT presynaptic receptor changes (10,11,12). These apparent inconsistencies may be clarified as postmortem and receptor studies move beyond the preliminary stage. Catecholamine neurotransmitter-metabolite studies are not consistent and relevant receptor data are lacking; the same can be said for the cholinergic systems.

NEUROENDOCRINE STUDIES

A link between suicide and hormonal functioning is strongly suggested by the suicidal behavior of individuals with endocrinopathies, particularly Cushing's syndrome. In his review of endocrine abnormalities in suicide, Meltzer suggests that they may serve as weak markers for suicide, but further research is more likely to show their role in influencing neurotransmission, which in turn may be more directly associated with causal factors.

Although urinary corticosteroids were the original biological variable associated specifically with suicidal behavior (13), plasma and CSF studies are still too few to warrant any conclusion. An association between dexamethasone suppression test (DST) nonsuppression and suicidal behavior seemed to be positive in earlier studies, but more recent studies bring this association into question. Some earlier indications that the administration of the test dose of dexamethasone might increase the risk of suicidal behavior seem not to be borne out in the more recent analyses.

Meltzer discusses new work on glucocorticoid-receptor-resistance (GCCR) studies. In an earlier report, he indicated that the plasma 5-hydroxytryptophan (5-HTP)-induced cortisol response was negatively correlated with CSF 5-HIAA; such a correlation might link the urinary and plasma cortisol findings with CSF 5-HIAA in suicidal patients. In ongoing studies of patients with major affective disorders, the elevated cortisol response to 5-HTP seems particularly linked to a history of violent suicide attempts.

Early studies in patients with histories of violent suicidal attempts showed a blunted thyroid-stimulated-hormone (TSH) response to thyrotropin-releasing hormone (TRH); more recent work, including some of Meltzer's, does not always confirm the early reports, however. Evidence that the TSH response is negatively related to CSF 5-HIAA is consistent with a relationship between low levels of brain serotonin and suicidal ideation, which had been shown to be positively related to the TSH response.

It seems particularly important to us that continued efforts be made to integrate the neuroendocrine and the 5-HT data. Animal studies indicate that increased plasma cortisol decreases 5-HT synthesis in the CNS via activation of liver tryptophan hydroxylase, which shifts peripheral tryptophan to the kynurenine pathway from its availability to the CNS for 5-HT synthesis (14). Humans with carcinoid syndrome (5-HT-secreting tumors in the small intestine) are often depressed, insomniac, and irritable, if not overtly aggressive; they may have a decreased 5-HT synthesis in the CNS secondary to decreased availability of the precursor, tryptophan. If so, the treatment of these patients

with para-chlorophenylalanine (PCPA), a 5-HT synthesis inhibitor that crosses the blood-brain barrier (12), might be expected to worsen their CNS symptoms, as has been reported (15,16).

GENETIC STUDIES

Roy and Kety point out that suicidal behavior and depression are common in first-degree relatives of children and adolescents who commit suicide--both before and after the suicide. A significantly higher rate of psychiatric illness has also been found. In his ongoing study, Shaffer has found that 38 percent of suicidal adolescents have a family history of suicide. Increased incidence of suicidal behavior has also been shown in relatives of suicidal adults; a recent, controlled study found that among 127 patients admitted to a hospital following suicide attempts, 24 percent gave a family history of suicide attempts. Psychiatric diagnoses commonly associated with a family history of suicide are personality disorders and affective illness, especially manic-depressive illness.

The familial association with suicidal behavior is clear enough, but it begs the question of its source--in psychosocial or biomedical-genetic factors or some combination of them. First one must know what is transmitted: is it suicide per se, a vulnerable personality (i.e., aggressive/impulsive), or an illness (i.e., affective disorder)? Secondly, one must know whether proneness to suicide is transmitted genetically or environmentally through learning.

Twin and adoption studies address both of these questions. Evidence from all the twin studies together appears to show a genetic vulnerability both toward suicidal behavior and severe mental illness.

The Danish adoption study provides especially strong evidence for a genetic factor in suicide, and further, the data indicate that this genetic vulnerability to suicide can be inherited independently of overt psychiatric illness. Among the adoptees who committed suicide, half had a major psychiatric illness among their biological first-degree relatives; the remainder had family histories of suicide without a major psychiatric diagnosis but often with a history of aggressive/impulsive symptoms. Psychiatric and/or suicidal histories were virtually absent among the adoptive families or their relatives. The Amish study has shown that a heavy loading for affective disorder and for suicide can be somewhat independent of each other.

It seems to us particularly important to pursue the identification or clarification or possible biological differences within special families or populations with known, epidemiologically characterized behavioral vulnerabilities. An example of such work is the ongoing attempt to clarify how chromosome 11 may be related to the occurrence of affective disorders (and possibly to suicidal behavior) in the Amish population, and whether this finding can be characterized in other populations. Clearly, genetic factors are involved in suicidal behavior, but that is not to say that environmental (learning) factors are not operating.

RESEARCH STRATEGIES

Before proposing research strategies, we will briefly summarize the five categories of risk factors that ought to be considered.

Behavior

Longitudinal history from childhood to the present. As noted above, not only does a history of aggressive and impulsive behavior seem to be associated with vulnerability to suicide, but affective or impulsive symptoms in childhood are related to low levels of CSF 5-HIAA in adolescence, which in turn is associated with increased suicidal behavior. In addition, differences in drug states may be relevant to behavioral predispositions. The natural history of an illness should also be taken into account; for example, manic-depressive illness--a condition with a high risk for suicide--has been hypothesized to begin when a genetic vulnerability interacts

with an environmental stressor, and once such an interaction begins, it takes on a life of its own, eventually requiring little environmental stress to produce recurrences.

Aggression history. The single best predictor for aggressive behavior is a history of such behavior, just as the best single predictor for suicidal behavior is a history of it (17,18).

Family History

The data reviewed here make a strong case for the importance of assessing family history of both suicidal and aggressive-impulsive-violent behaviors as well as of psychiatric illnesses.

Psychiatric History and Diagnoses

The evidence further argues for determining whether a psychiatric illness is present in individuals who are prone to self-destructive behavior. Indeed, the number of individuals who actually kill themselves in the absence of a psychiatric illness would appear quite low. As noted earlier, the psychosocial focus of the suicide prevention movement has primarily derived its experience from working with people who threaten or attempt suicide, while the clinical-medical focus on suicide as an integral part of major psychiatric illness has primarily derived its experience from working with patients with completed or nearly completed suicide. Although the domains of attempters and completers do overlap somewhat, by and large they represent different populations (19). The major affective illnesses, particularly manic-depressive illness, alcoholism, schizophrenia, and other psychoses all have substantially higher associations with suicidal behavior than one would expect for a normal population. Individuals suffering from these major psychiatric disturbances make up the majority of completed suicides. To this we can now add that the risk is increased when one of these disorders occurs in an individual with aggressive/impulsive "personality" traits. On a practical level, a proper diagnosis can lead to appropriate treatment for the specific disorder, and indeed we believe that this will turn out to be the single best approach to preventing actual suicides.

Medical History

The presence of a major medical illness is a risk factor for suicide. In addition, some specific medical disorders have been associated with a higher incidence of suicidal or aggressive behavior. Most are associated with disturbances in corticosteroid or serotonin metabolism. They include:

- Endocrinopathies, particularly Cushing's syndrome (corticosteroids).
- Metabolic disorders, i.e., carcinoid syndrome (serotonin), Lesch-Nyhan syndrome (serotonin alteration and aggressive behavior (20), incidence of suicide is unknown).
- Neurological disorders, i.e., Parkinson's disease (21,22) and epilepsy (low CSF 5-HIAA) (23,24) and Gilles de la Tourette syndrome (sometimes associated with low CSF 5-HIAA and, often, aggressive behavior (25), but incidence of suicide in unknown).

Biological Parameters

In the future, we should do studies to clarify the seasonality of suicide (26), receptor studies *in vivo*, controlled pharmacological studies of suicidal and aggressive behaviors, and seriously consider doing lumbar punctures as part of the psychiatric assessment in some patients. Very few of such studies are being done now. The development of a clinical-risk profile for suicidal behavior might be very useful to clinicians. An important and unanswered clinical-scientific question related to the biological factors that may contribute to the high incidence of suicide in manic-depressive illness, given the fact that the association between low levels of the serotonin metabolite and a history of suicide, consistent across a wide variety of disorders, does not hold for manic-depressive patients. Nevertheless, the tripartite relationship between suicide, aggression, and affective ill-

ness remains an important cornerstone on which to build further understanding. (Figure 2)

One of our stated goals in the introduction was to promote and foster interdisciplinary collaboration and mutual cooperation in the pursuit of scientific knowledge in the service of public health. Some of the areas of research most likely to support such a goal include:

- Genetic research, especially of special populations (e.g., Amish, Indians, Greenlanders, Hungarians), offers opportunities for further dissection of genetic and environmental factors.
- Much could be gained from pursuing psychological-autopsy data with the same methodological vigor that has been applied to the biological postmortem studies. In such studies we need to assign as much importance to measures of "personality" dimensions as we do to formal psychiatric diagnoses. In this regard, we should evaluate the relationship between formal psychiatric profiles--e.g., sensation-seeking (27)--and relevant biological measures.
- Longitudinal studies are particularly important if we are to tease apart whether some behaviors are strongly dependent upon an environmental stimulus or whether some individuals tend to repeat the same kinds of behaviors independent of a particular environment. The state vs. trait issues cannot be confidently elaborated without such studies.
- Powerful statistical methods should follow well thoughtout hypotheses rather than blindly applied in the hope of uncovering significant associations among large samples. When such findings do occur, they must be replicated with a fresh sample.

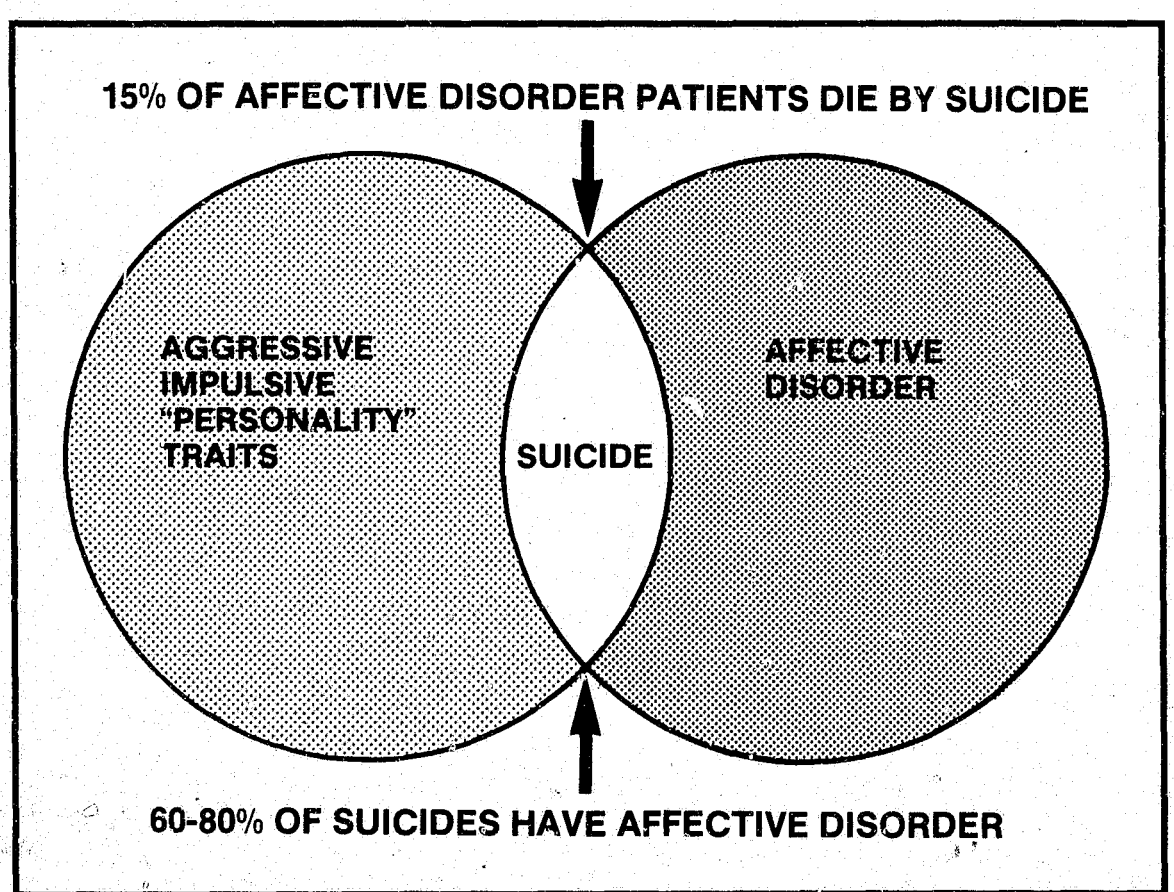


Figure 2.

- Few studies have examined the importance of drug states as predispositions to suicidal behavior.

SUMMARY

Certain principles should underlie our attempts to make a significant and meaningful difference in dealing with the major public health problem of suicidal behavior, particularly in youth. Recommendations receiving the highest priority should be based on sound, scientific data. Second priority should be assigned to activities that will promote the development of needed data (e.g., well-controlled epidemiological studies). For services, the highest priority should go to programs that provide direct treatment to high-risk individuals--those with a psychiatric or medical disorder known to be associated with a high rate of completed suicide (as distinct from suicidal ideation), those who have made previous suicidal attempts, and those with a strong family history of suicidal behavior. Obviously, preference must be given to treatments for which efficacy is based on actual data, rather than impressions or hopes.

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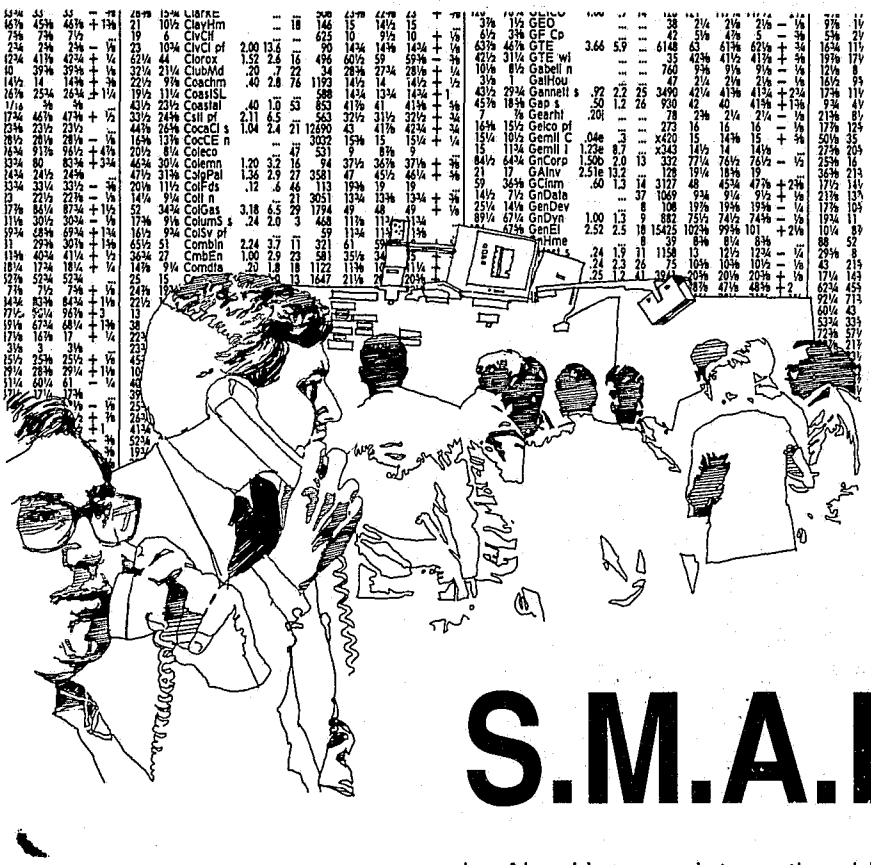

S.M.A.R.T.

by Alan Harman, International Editor

To help in detecting stock market fraud, the Royal Canadian Mounted Police (RCMP) has developed a computer program called Stock Market Analysis for Reconstructing Trades (SMART). The system eliminates much of the work in looking for market manipulations.

Sergeant George Gunn, a member of the Mounties' commercial unit in Toronto, believes SMART is unique to the RCMP, but said it will be made available to regulators and police officers both inside and outside Canada.

SMART analyzes thousands of stock market trades faster and more efficiently that any human investigator, Gunn said. He said investigating commercial crime and stock-related fraud in particular is difficult and often unrewarding because offenders use the interconnected high-tech wizardry of the international financial markets to cover their tracks. Investigators, trying to follow paper trails, have lagged behind.

SMART is designed to close that gap. "It will make life a lot easier," Gunn said. "Quite literally, it will revolutionize our investigations in this area."

SMART was developed by four RCMP computer programmers in Ottawa using principles supplied by Gunn after he spent 18 months analyzing trades in a mutual fund fraud case. Gunn said SMART would have taken a week to do the same research.

"This revolutionized what we've done in the past. It's a way of using what information is at our disposal to get more investigations done," he said.

Before SMART, the RCMP opened a stock investigation by seizing the records of brokers, especially the trading tickets, the broker's record of customer orders, when such paper records had not "disappeared." The documents were then examined for manipulated opening and closing prices, trading by or between related companies, people or trusts, and multiple accounts at one or a number of brokerages. It was a time-consuming operation.

However, this information is also kept by many brokers on IBM computer tape—and this is where SMART comes into play. The program searches through the brokers' tapes looking for anything—from a particular name or account, to finding who opened or closed a particular stock. Because some Canadian brokers do not use IBM record-keeping, the Mounties have asked Canadian regulators for assistance in requiring brokers to have their computer records compatible with SMART.

But before evidence generated by SMART is used widely in the courts it will have to proven. Presently there is a question whether the courts will accept computer-generated evidence. The RCMP hopes the courts will accept information generated by SMART without insisting on seeing the actual paper order tickets. It is expected it will be three years before there is a final ruling.

Even if the courts reject the SMART-generated evidence, the program will still show investigators where to look in the paper records for the evidence they need.

Gunn said one problem for investigators is that many victims of stock fraud never realize that crime was the reason they lost money. "When you're an investor on a speculative market, you know you're investing in speculative issues that are based on a hope and a dream," he said. "So when a share price falls, many investors don't suspect manipulation. They think, 'there was no gold in them thar hills,' and don't realize they were suckered."

The basic modus operandi of a stock manipulator is to gain control of a company, and then manipulate trading of its shares to make unsuspecting investors believe the share price will continue its climb. Usually, this is done by using many trading accounts at a number of brokerages to manipulate opening and closing prices as well as daily high and low prices and trading volumes.

"A good manipulation will not send the stock straight through the roof," Gunn said. "There will be peaks and valleys arranged to escape notice of the stock exchanges,

which have parameters for tracing stock activity."

In the "blow-off" stage of the manipulation, the manipulator dumps his stock as the shares peak in price, takes his profit and disappears. Gunn said he had spoken to investors who, even after a case had gone to court, didn't realize they had been taken. "That makes the job of investigating stock-related crime difficult because, without an obvious victim, it's hard to spot a crime, let alone catch the criminal."

Then there's the problem of the victim who knows he's been taken, but refuses to complain—people who invest through a Swiss account, for example, that has money not declared to tax authorities. Gunn said the internationalization of business can be a problem for investigators, but jurisdictions that shelter transactions are often unattractive to the manipulator because they are unstable.

For those who think stock manipulation is a victimless crime, Gunn said its long-term effect is to scare away small investors and hurt the ability of companies to attract new capital. "Manipulation results in damage to the integrity of the marketplace, to the public confidence and to the market's effectiveness in allocating financial resources," he said.

"It is a predatory crime, often not known to the victim. Fraud all too often masquerades as high risk venture capital with the victim totally unaware he was suckered."

Gunn believes there's plenty of stock fraud for SMART to detect. When he was on the drug squad it was estimated 10% of dealers were prosecuted. "I don't see any reason to change my position from drugs to stock fraud," he said. L&O

"Looks like somebody finally figured out what that coffee machine has been making."

Books And Videos

Police Officer's Guide

by Bill Clede
Stackpole Books, 1990
$19.95/$26.95 in Canada; 240 pp.

From the origins of police and principles of the criminal justice system, to the personal and professional skills, and weapons one uses, Clede provides an inside look at law enforcement that's valuable for rookie and veteran alike. Virtually all subjects covered in recruit academy, and many that aren't, are included in this book.

Tim Dees of the Reno, NV, police said, "It's a fine overview of police work generally, and gives some much-deserved attention to the lesser-known aspects of law enforcement, such as railroad police, conservation officers, and canine operations."

Police Officer's Guide is divided into five sections: Background, Principles, Skills, On the Street, and Weapons. Appendices give information on federal agencies, helpful agencies, and associations of interest to police officers.

Its purpose is to present an understanding of the profession, skills needed to succeed, and options one might use to fulfill the responsibilities of the job. It also gives you an understanding of concerns usually not covered in recruit academy, such as other police services, family problems, and career concerns. It explains the judicial and penal systems, then provides an overview of everything you need to know to advance, and survive, in the police profession.

If you are considering a law enforcement career, or if it has been a while since you completed the academy, this book will introduce you to concepts you never knew or long since forgot. Larry Welch, associate director of the Kansas Law Enforcement Training Center, calls it, "the easiest-to-read, most complete law enforcement guide I've seen in years."

Police Officer's Guide is available through local bookstores. It may be ordered direct from the publisher by calling 1-800-READ-NOW, or by calling Police Bookshelf 1-800-624-9049.

Tactical Shotgun Techniques

Video Productions, Inc., 2437 Albany Ave., West Hartford, CT 06117
$44.50; 43 minutes
Reviewed by Bill Clede

The shotgun is now a patrol, rather than special purpose, weapon. Shotgun training is improving and new techniques developed by training counselors are trying to reach instructors, but too few have learned them. You can see these new techniques explained and demonstrated in a new 43-minute video featuring the famous Jeff Cooper. It was shot at his American Pistol Institute in Paulden, AZ.

Right up front, the video makes a point of the versatility of the shotgun, identifies the parts of the gun, and hammers home the safety rules. The stance and how to mount the gun are explained. Then the video shows the ready positions, high and low. It emphasizes cycling the action immediately after you've shot it, and to combat load as many shells as you fired.

But marksmanship and gun handling are only two points in the triad of combat shooting. The third is "mind set," what Cooper calls being ready for a confrontation, being able to react when you must. The video explains two different sling carries. It covers the half-step. Then all of the elements covered previously are employed in tactical scenarios.

What would normally be a dry lecture is condensed and effectively presented. Students could go straight to the range after viewing this interesting video and better understand what is being taught. No video can replace hands-on practice, but this video can help improve comprehension.