Book Chapter for: "The Hidden Epidemic: The Impact of Early Life Trauma on Health and Disease" R. Lanius & E. Vermetten editors. Cambridge University Press, 2009

FINAL 2-07-2009

Chapter title:

The Relationship of Adverse Childhood Experiences to Adult Medical Disease, Psychiatric Disorders, and Sexual Behavior: Implications for Healthcare

Vincent J. Felitti, MD (<u>VJFMDSDCA@mac.com</u>) Co-Principal Investigator, Adverse Childhood Experiences (ACE) Study Kaiser Permanente Medical Care Program, San Diego, CA. USA Robert F. Anda, MD, MS (robanda@bellsouth.net) Co-Principal Investigator, Adverse Childhood Experiences (ACE) Study Atlanta, GA. USA

The Relationship of Adverse Childhood Experiences to Adult Medical Disease, Psychiatric Disorders, and Sexual Behavior: Implications for Healthcare

"In my beginning is my end." T.S. Eliot, Four Quartets¹

Introduction:

Biomedical researchers increasingly recognize that childhood events, specifically abuse and trauma, have profound and enduring effects on the neuroregulatory systems mediating medical illness as well as on behavior from childhood into adult life. Our understanding of the connection between trauma in childhood and the pathways to in adulthood is still being formed pathology as neuroscientists begin to describe the changes that take place on the molecular level as a result of events that occurred decades earlier.

The turning point in modern understanding of the role of trauma in medical and psychiatric pathology is commonly credited to Freud, who studied patients of the French neurologist, Charcot, attributing their unusual behavior to histories of trauma rather than to underlying biomedical pathology.² Subsequently, the writings of Freud and Breuer well as represented a departure Janet from as the traditional view that mental illness and unexplained medical disease were the result of divine retribution or demonic possession, instead revealing that they were strongly associated with a history of childhood abuse.³

The focus of this chapter will be an examination of the relationship between traumatic stress in childhood and the leading causes of morbidity, mortality, and disability in the United States: cardiovascular disease, chronic lung disease, chronic liver disease, depression and other forms of mental illness, obesity, smoking, and alcohol and drug abuse. To do this, we will draw on our experience with the Adverse Childhood Experiences (ACE) Study, a major American epidemiological study providing retrospective and prospective analysis in over 17,000 individuals of the effect of traumatic experiences during the first eighteen vears of life on adolescent and adult medical and psychiatric disease, sexual behavior, healthcare costs, and life expectancy.⁴

The ACE Study is an outgrowth of repeated counterintuitive observations made while operating a major weight loss program that uses the technique of supplemented fasting, which allows non-surgical weight reduction of approximately three hundred pounds (135 Kg) per vear. Unexpectedly, our Weight Program had a high dropout rate, limited almost exclusively to patients successfully losing weight. Exploring the reasons underlying the high prevalence of patients inexplicably fleeing their own success in the Weight Program ultimately led us to recognize that weight loss is often sexually or physically threatening and that certain of the more intractable public health problems like obesity were *also* unconscious, or occasionally conscious, compensatory behaviors which were put in place as solutions to problems dating back to the earliest years, but hidden by time, by shame, by secrecy, and by social taboos against exploring certain areas of life experience. It became evident that traumatic life experiences during childhood and adolescence were far more common than generally recognized, were complexly interrelated, and were associated decades later in a strong and proportionate manner to outcomes important to medical practice, public health, and the social fabric of the nation. In the context of everyday medical practice, we came to recognize that the earliest years of infancy and childhood are not lost but, like a child's footprints in wet cement, are often life-long.

The findings from the ACE Study provide a remarkable insight into how we become what we are as individuals and as a nation. They are important medically, socially, and economically. Indeed, they have given us reason to reconsider the very structure of medical, public health, and social services practices in America.

Outline of the ACE Study and its setting:

The Adverse Childhood Experiences (ACE) Study was carried out in Kaiser Permanente's Department of Preventive Medicine in San Diego, in collaboration with the US Centers for Disease Control and Prevention (CDC). This particular Department of Preventive Medicine provided an ideal setting for such collaboration because for many years we have carried out detailed biomedical, psychological, and social (biopsychosocial) evaluations of over 50,000 adult Kaiser Health Plan members a year. The CDC contributed the essential skill sets for study design and massive data

management required for meaningful interpretation of clinical observations.

Kaiser Health Plan patients are middle-class Americans; all have high quality health insurance. In any 4-year period, 81% of adult Plan members in San Diego choose to come in for comprehensive medical evaluation. We 26,000 consecutive adults coming through asked the Department if they would help us understand how childhood events might affect adult health status. The majority agreed and, after certain exclusions for incomplete data and duplicate participation, the ACE Study cohort had over 17,000 individuals. The Study was carried out in two waves, to allow mid-point correction.

The participants were 80% white including Hispanic, 10% black, and 10% Asian; 74% had attended college; their average age was 57. Almost exactly half were men, half women. This is a solidly middle-class group from the 7th largest city in the United States; it is not a group that can be dismissed as atypical, aberrant, or 'not in my practice'. Disturbingly, it is us - a point not to be overlooked when considering the problems of translating this information into action.

Eight categories of adverse childhood experiences (ACEs) were studied in the first wave; two categories of neglect were added in the second wave. We empirically selected these categories because of their discovered high prevalence in the Weight Program. Their prevalence in a general, middle-class population was also unexpectedly high. We created for each individual an ACE Score, a count of the number of *categories* of adverse childhood experience that had occurred during the first eighteen years of life. ACE Score does not tally incidents within a category. The scoring system is simple: the occurrence during childhood or adolescence of any one category of adverse experience is scored as one point. There is no further scoring for multiple events within a category; thus, an alcoholic and a drug user within a household score the same as one alcoholic; multiple sexual molestations by multiple individuals are totaled as one point. If anything, this tends to understate our findings. The ACE Score therefore can range from 0 to 8 or 10, depending on the data being from Wave 1 or Wave 2. Specifics of the questions underlying each category are detailed in our original article.4

Only one third of this middle-class population had an ACE Score of 0. If any one category was experienced, there was 87% likelihood that at least one more category was present. One in six individuals had an ACE Score of 4 or more, and one in nine had an ACE Score of 5 or more. Thus, every physician sees several high ACE Score patients each Typically, they are the most difficult patients of day. the day. Women were 50% more likely than men to have experienced five or more categories of adverse childhood We **believe** that here is a key to what, in experience. epidemiology, appears as mainstream women's natural proneness to ill-defined health problems like fibromyalgia, chronic fatigue syndrome, obesity, irritable bowel syndrome, and chronic non-malignant pain syndromes. We now see these as medical constructs, artifacts resulting from medical blindness to social realities and ignorance of the impact of gender.

Somewhat surprisingly, the ACE categories turned out to be approximately equal in impact; an ACE Score of 4 thus consists of *any* four of the categories. The categories do not occur randomly; the number of individuals with high ACE Scores is distinctly higher than if the categories exist independently of each other.⁵ The ten reference categories experienced during childhood or adolescence are as below, with their prevalence in parentheses:

- Abuse
- 1. emotional recurrent threats, humiliation (11%)
- 2. physical beating, not spanking (28%)
- 3. contact sexual abuse (28% women, 16% men; 22% overall)
- Household dysfunction
- 1. mother treated violently (13%)
- 2. household member was alcoholic or drug user (27%)
- 3. household member was imprisoned (6%)
- 4. household member was chronically depressed, suicidal, mentally ill, or in psychiatric hospital (17%)
- 5. not raised by both biological parents (23%)
- Neglect
- 1. physical (10%)
- 2. emotional (15%)

The essence of the ACE Study has been to match retrospectively, approximately a half century after the

fact, an individual's current state of health and wellbeing against adverse events in childhood (the ACE Score), and then to follow the cohort forward to match ACE Score prospectively against doctor office visits, ER visits, hospitalization, pharmacy costs, and death. We recently have passed the fourteen-year mark in the prospective arm of the Study.

Findings:

We will illustrate with a sampling from our findings in the ACE Study the long-lasting, strongly proportionate, and often profound relationship between adverse childhood experiences and important categories of emotional state, health risks, disease burden, sexual behavior, disability, and healthcare costs - decades later.

Psychiatric Disorders:

The relationship between ACE Score and selfacknowledged chronic depression is illustrated in Fig. 1A.⁶ Should one not be confident of the reliability of selfacknowledged chronic depression, there is a similar but stronger relationship between ACE Score and later suicide attempts as shown in Fig. 1B.⁷ The p value of all graphic depictions herein is .001 or better.

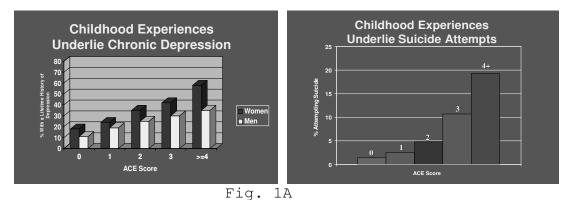


Fig. 1B

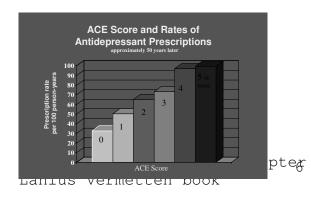


Fig. 1C

One continues to see a proportionate relationship between ACE Score and depression by analysis of prescription rates for antidepressant medications after a ten-year prospective follow-up, now approximately fifty to sixty years after the ACEs occurred. (Fig. 1C).⁸ It would appear that depression, often unrecognized in medical practice, is in fact common and has deep roots, commonly going back to the developmental years of life.

An analysis of population attributable risk (that portion of a problem in the overall population whose prevalence can be attributed to specific risk factors) shows that 54% of current depression and 58% of suicide attempts in women can be attributed to adverse childhood experiences. Whatever later factors might trigger suicide, childhood experiences cannot be left out of the equation. Seeman, McEwen, et al⁹ have described this general concept of background burden as allostatic load.

A similar relationship exists between ACE Score and later hallucinations, shown in Fig. 1D. Lest one reasonably suspect that, at ACE Score 7 or higher, people will likely be using street drugs or alcohol to modulate their feelings, and that *these* might be the cause of hallucinations, we have corrected for alcohol and drug use and find the same relationship exists.¹⁰

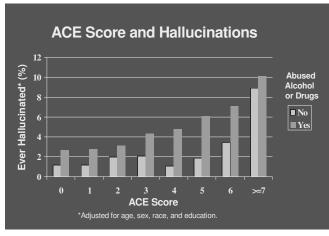


Fig. 1D

Clinicians treating somatization and disorders with no clear medical etiology, as well as those dreading such patients, will find Fig. 1E of special interest. Indeed, this figure exemplifies our observation in the Weight Program that what one sees, the presenting problem, is often only the marker for the real problem, which lies buried in time, concealed by patient shame, secrecy, and sometimes amnesia - and frequent clinician discomfort. usually considered a theatrical Amnesia, device of Hollywood movies of the 1940s, is in fact alive and well, though unrecognized, in everyday medical practice. In our Weight Program, we found 12% of the participants were partially or sometimes totally amnestic for a period of their lives, typically the few years before weight gain In the ACE Study, we found that there was a began. distinct relationship of ACE Score to impaired memory of childhood, and understand this phenomenon to be reflective of dissociative responses to emotional trauma. (Fig. 1F)¹¹

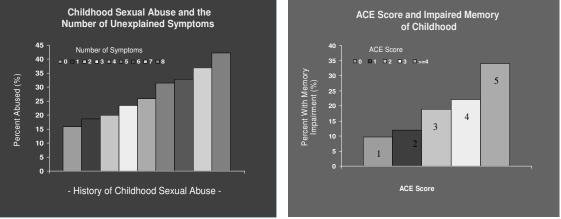


Fig. 1E



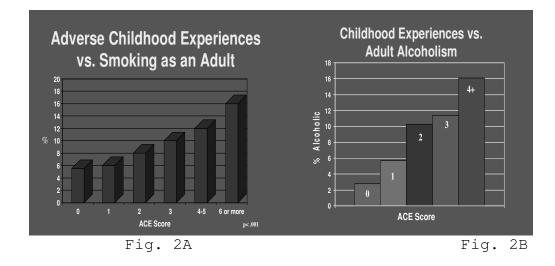
All told, it is clear that adverse childhood experiences have a profound, proportionate, and longlasting effect on emotional state, whether measured by depression or suicide attempts, by protective unconscious devices like somatization and dissociation, or by self-help attempts that are misguidedly addressed solely as long-term health risks -- perhaps because we physicians are less than comfortable acknowledging the manifest short-term benefits these "health risks" offer to the patient dealing with hidden trauma.

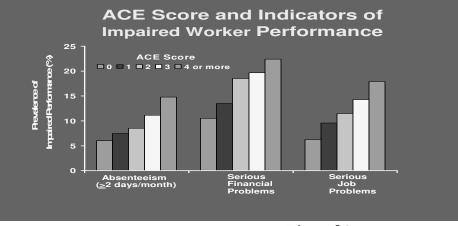
Health risks:

The most common contemporary health risks are smoking, alcoholism, illicit drug use, obesity, and high-level

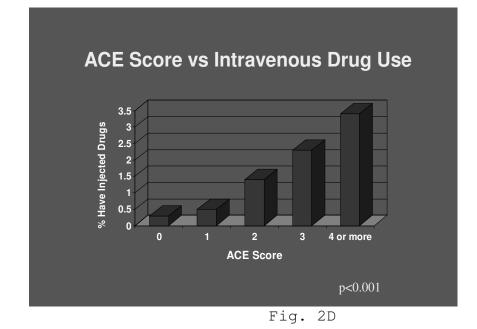
promiscuity. Though widely understood to be harmful to health, each is notably difficult to give up. Conventional logic is not particularly useful in understanding this apparent paradox. As though opposing forces are not known in biological exist commonly systems, little to consideration is given to the possibility that many longterm health risks might also be personally beneficial in the short term. For instance, American Indians understood the psychoactive benefits of nicotine for centuries with their peace pipe, before its risks were recognized. We repeatedly hear from patients of the benefits of these "health risks." Indeed, relevant insights are even built into our language: "Have a smoke, relax." "Sit down and have something to eat. You'll feel better." Or, needing 'a fix', referring to IV drug use. Conversely, the popular reference to "drug abuse" serves to conceal the short-term It is perhaps not functionality of such behavior. . meaningless that the demonized street drug, crystal meth, is the very compound that was introduced in pure form and reliable dosage in 1940 as one of the first prescription antidepressants in the United States: methamphetamine.

the ACE Study, we found strong, proportionate In relationships between the number of categories of adverse childhood experience (ACE Score) and the use of various psychoactive materials or behaviors. The saying, "It's hard to get enough of something that almost works." Three common categories of what are provides insight. usually termed addictions (the unconscious compulsive use of psychoactive agents) are illustrated in this section. Self-acknowledged current smoking (Fig. 2A)^{12, 13}, self-defined alcoholism (Fig. 2B)^{4, 6, 14}, and self-acknowledged injection drug use (Fig. 2C)¹⁵ are strongly related in a proportionate manner to our several specific categories of adverse experiences during childhood. Additionally, we found that poor self-rated job performance correlates with ACE Score.¹⁶ (FIG 2C).









The relationship of ACE Score to IV drug use is particularly striking, given that male children with ACE Score 6 or more have a 4,600% increased likelihood of later becoming an injection drug user, as contrasted with an ACE Score 0 male child; this moves the probability from an arithmetic to an exponential progression. Relationships of this magnitude are exceptionally rare in epidemiology. This, coupled with related information, suggests that the basic cause of addiction is predominantly experiencedependent during childhood and not substance-dependent. This challenge to the usual concept of the cause of addictions has significant implications for medical practice and for treatment programs.¹⁷

Sexual Behavior:

Using teen pregnancy and promiscuity as measures of sexual behavior, we found that ACE Score has a proportionate relationship to these outcomes. (Fig. 3A, 3B.) So too does miscarriage of pregnancy, indicating the complexity of the relationship of early life psychosocial experience to what are usually considered purely biomedical outcomes.¹⁸

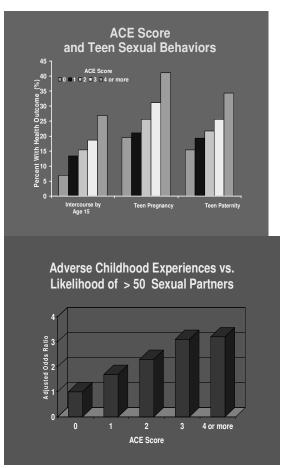


Fig. 3A

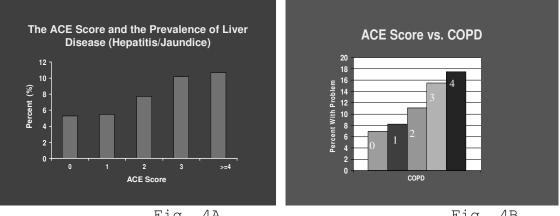
Fig. 3B

Medical disease

We found in the ACE Study that biomedical disease in adults has a significant relationship to adverse life experiences in childhood. The implication of this observation that life experience can transmute into organic disease over time is a profound change from an earlier era when infectious diseases like rheumatic fever or polio, or nutritional deficiency like pellagra, would come to mind as the main medical link between childhood events and adult disease. In spite of this change in the etiology of medical outcomes, we find no evidence that there has been a change in the frequency of overall adverse childhood experiences in various age cohorts spanning the twentieth century.¹⁹

Three examples of the links between childhood experience and adult biomedical disease are the relationship of ACE Score to liver disease²⁰ (Fig. 4A), chronic obstructive pulmonary disease or COPD²¹ (Fig. 4B), coronary artery disease or CAD²² (Fig. 4C), and autoimmune

disease.²³ The data for CAD show the effect of ACE Score after correcting for, or in the absence of, the conventional risk factors for coronary disease like hyperlipidemia, smoking, etc.







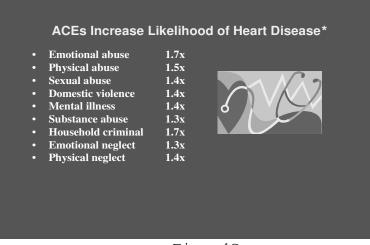


Fig. 4C

Certain of these relationships of childhood experience to later biomedical disease might initially be thought to be straightforward, for instance assuming that COPD or CAD are merely the obvious outcomes of cigarette smoking. In this case, one might reasonably assume that the total relationship of adverse childhood experience to later biomedical disease lies in the observation that stressful early life experience leads to a coping behavior like smoking, which becomes the mechanism of biomedical damage. While this hypothesis is true, it is incomplete; the actual situation is more complex. For instance, in our analysis published in *Circulation*²², we found that there was a strong relationship of ACE Score to coronary disease, after

correcting for all the conventional risk factors like smoking, cholesterol, etc. This illustrates that adverse experiences in childhood are related to adult disease by two basic etiologic mechanisms:

- conventional risk factors that actually are attempts at self-help through the use of agents like nicotine with its documented, multiple psychoactive benefits, in addition to its now well-recognized cardiovascular risks, and
- the effects of chronic stress as mediated through the mechanisms of chronic hypercortisolemia, proinflammatory cytokines, and other stress responses on the developing brain and body systems, dysregulation of the stress response, and pathophysiological mechanisms yet to be discovered.

Public Health Paradox is implicit in А these observations. One sees that certain common public health problems, while indeed that, are often also unconsciously attempted solutions to major life problems harkening back to the developmental years. The idea of the problem being the solution, while understandably disturbing to many, is certainly in keeping with the fact that opposing forces routinely co-exist in biological systems. Understanding that it is hard to give up something that almost works, particularly at the behest of well-intentioned people who have little understanding of what has gone on, provides us a new way of understanding treatment failure in addiction programs where typically the solution rather than the core problem is being addressed.

Healthcare costs:

At the fourteen-year point in the prospective arm of the Study, we have only begun to analyze pharmacy data. Given the average age of our cohort, we are now looking at prescription drug use fifty to sixty years after the fact. Prescription costs are an increasingly significant portion of rapidly rising national healthcare expenditures in the United States. The relationship of ACE Score to antidepressant prescription rates has already been shown in Fig. 1C. Below, in Fig. 5A and 5B, we show the relationship of adverse childhood experiences to the decades-later use of anti-psychotic and anxiolytic medications⁸. Analyses of the relationships of ACE Score to doctor office visits, Emergency Department visits, hospitalization, and death are in progress. The economic effect of Fig. 1E will be intuitively obvious to

practitioners who have observed that multi-volume patients commonly do not have a unifying diagnosis underlying all the medical attention. Rather, they have a multiplicity of symptoms: illness, but not disease. Kirkengen has more fully discussed the nature, origins, and often-unwitting medical creation of this complex phenomenon in her book, *Inscribed Bodies*.²⁴ The 2000 Nobelist in Economics, James Heckman, has grasped the enormity of the economic and social consequences of the long-term effects of adverse childhood experiences and has written perceptively on the subject²⁵.

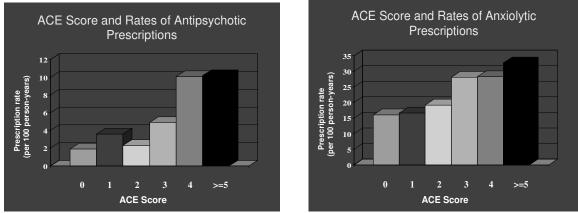


Fig. 5A



Life expectancy

Although we have not yet begun our prospective analysis of adult death rates as they may be related to adverse childhood experiences, a suggestive insight can be provided by use of the null hypothesis. Using the null hypothesis, we might propose that if there is no relationship of ACE Score to ultimate mortality, then we ought to be able to predict certain expected findings and consequently test for them. Thus, if there is no relationship of ACE Score to adult mortality, the age distribution of Kaiser Health Plan members choosing to come for comprehensive medical evaluation ought in to be independent of ACE Score. In Fig. 6A, we see that the age distribution for ACE Score 0 individuals is what one would likely to come expect: old people are more in for comprehensive medical evaluation than are young people, and intermediate age quantiles have the expected relative proportionality. However, at ACE Score 2, what had been

the most common age quantile has become the least common, and what had been the least common has become the most common. At ACE Score 4, the initially most common age quantile has almost disappeared. We anticipate that, when our prospective analysis of death rates is completed, it will illustrate convincingly that there is an increasing death rate as the ACE Score increases. Certainly, this would be the expected continuation of our findings that ACE Score is strongly related first to health risks, then to disease, then to one outcome of disease: death.

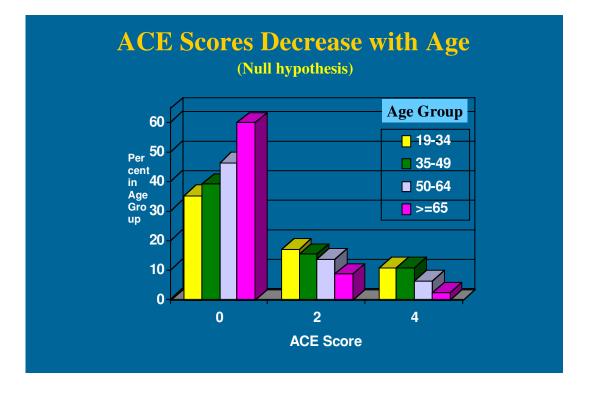


Fig. 6A

Reasonably, one might challenge this interpretation of selective attrition by hypothesizing that our patients are progressively so humiliated by exposure of their increasing ACE Scores that they are subsequently avoiding necessary Such an hypothesis is not supported by our medical care. Some years ago we had on site for six months a findings. psychoanalytically-trained psychiatrist who saw selected patients immediately hiqh ACE Score after their comprehensive medical evaluation, rather than after psychiatry. An anonymous referral to questionnaire, returned by 81% of the patients he saw, showed that his hour-long interview was interpreted by patients as highly desirable and appreciated. Talking about the worst secret

Felitti/Anda ACE Study chapte_{f6} Lanius Vermetten book of one's life with an experienced person, being understood, and coming away feeling still accepted as a human being, seems to be remarkably important and beneficial, perhaps not unlike the rite of confession in the Roman Catholic Church. Indeed, seeking understanding and acceptance is a deep and human need, hearkening back to the Biblical enjoinder, "With all thy getting, get understanding."

Implications for healthcare:

We have made a limited but instructive attempt to integrate the ACE Study findings into clinical practice. At Kaiser Permanente's high-volume Department of Preventive Medicine in San Diego, we have used what we learned to expand radically the nature of our Review of Systems (ROS) and Past History questionnaire. We have now asked routinely of over 440,000 adult individuals undergoing comprehensive medical evaluation a number of questions of newly discovered relevance, the following of which are a sample:

- Have you ever been a combat soldier?
- Have you ever lived in a war zone?
- Have you been physically abused as a child?
- Have you been sexually molested as a child or adolescent?
- Have you ever been raped?
- Who in your family has been murdered?
- Who in your family has had a nervous breakdown?
- Who in your family has been a suicide?
- Who in your family has been alcoholic or a drug user?

Such questions have been accepted by patients in the context of a well-devised medical questionnaire that is filled out at home. Examiners have learned that the most productive response to a Yes answer is, "I see that you have - - - -. Tell me how that has affected you later in your life." While not a simple transition for staff, and one requiring an organized training effort, the transition has been effective and with measured benefits. An independent organization carried out a neural network artificial intelligence analysis – an approach to mathematical modeling and data mining - of the data from 120,000 patient evaluations (2 years' work) using this new

approach: a truly biopsychosocial approach to comprehensive medical evaluation. Surprisingly, a 35% reduction in doctor office visits (DOVs) was found in the vear subsequent to evaluation, compared to the year before. Additionally, analysis showed an 11% reduction in Emergency (ED) visits Department and a 38 reduction in hospitalizations. This change was dramatically and unexpectedly different from a much smaller, 700-patient evaluation carried out 20 years earlier when we worked in the more usual medical mode. That earlier approach provided a net 11% reduction in DOVs compared to the antecedent year, in spite of a 14% referral rate. No evaluation was made then of ED visits or hospitalization. Finally, we found that the unexpectedly notable reductions in DOVs and ED visits totally disappeared in the second year after comprehensive evaluation, when there was a reversion to prior baseline. While the underlying information was present in charts with laser-printed clarity, it was almost never integrated into subsequent Interpreting the basis of this major medical visits. reduction in doctor office visits was not within the purview of the ACE Study design, but the impression of the clinicians seeing these patients is that it represents the benefit of having, through a comprehensive medical history, the worst secrets of one's life understood by another, and still being accepted as a human being. The Swiss psychologist, Alice Miller,²⁶ describes this as the role of 'the enlightened witness', again reminiscent of Confession in the Catholic Church, a technique whose persistence over two millennia suggests it has functional benefit to those involved in its use.

If these first year results are replicable, and we believe they should be, the implications for primary medical care are those of a paradigm shift. While offering tremendous opportunity, paradigm shifts are resisted. The philosopher, Eric Hoffer, has discussed this problem in his book, *The Ordeal of Change*²⁷. Jeffrey Masson, in *Assault on Truth*²⁸ describes the enormous social pressures on Freud to recant his interpretation of his findings of traumatic sexual experiences in childhood as being valid. Louise De Salvo points out in *Virginia Woolf*²⁹ how literary commentators almost uniformly avoid discussing the themes of incest in Woolf's work in favor of erudite discussions of her style and literary techniques.

If the treatment implications of what we found in the ACE Study are far-reaching, the problems of integrating this information into clinical practice are absolutely daunting. Simply put, it is easier for all of us to deal with the presenting symptom of the moment than to attempt to understand it in the full context of the patient, particularly when that full context involves thematic material of child abuse and household dysfunction that are usually protected by social taboos against exploring these areas of human experience. Though the proposed approach demonstrably would save time and money in the long run, most of us operate in the short run, and respond to valid forces that are both external and internal.

The very nature of the material in the ACE Study is such as to make most of us uncomfortable. Why would a physician or leader of any major health agency want to leave the familiarity of traditional biomedical disease and enter this area of threatening uncertainty that none of us have been trained to deal with? As physicians, we typically focus our attention on tertiary consequences, far downstream, while the primary causes are well protected by time, social convention, and taboo. We have often limited ourselves to the smallest part of the problem, that part in which we are erudite and comfortable as mere prescribers of medication or users of impressive technologies. Thus, although the ACE Study and its fifty-some publications have generated significant intellectual interest in North America and Europe during the past dozen years, its only beginning to be translated into findings are significant clinical or social action. The reasons for this are important to consider if this information is to be converted into meaningful social and medical opportunity.

Conclusion:

The influence of childhood experience, including often-unrecognized traumatic events, is as powerful as Freud and his colleagues originally described it to be. These influences are long-lasting, and neuroscientists are now describing the intermediary mechanisms that develop as a result of these stressors. Unfortunately, and in spite of these findings, the biopsychosocial model and the medical model of psychiatry remain at odds rather than taking advantage of the new discoveries to reinforce each other.

Many of our most intractable public health problems are the result of compensatory behaviors like smoking,

overeating, and alcohol and drug use which provide immediate partial relief from the emotional problems caused by traumatic childhood experiences. The chronic life stress of these developmental experiences is generally unrecognized and hence unappreciated as a second etiologic mechanism. These experiences are lost in time and concealed by shame, secrecy, and social taboo against the exploration of certain topics of human experience.

findings of the Adverse Childhood Experiences The (ACE) Study provide a credible basis for a new paradigm of medical, public health, and social service practice that would start with comprehensive biopsychosocial evaluation of all patients at the outset of ongoing medical care. We have demonstrated that this approach is acceptable to patients, affordable, and beneficial in multiple ways. The potential gain is huge. So too is the likelihood of clinician and institutional resistance to this change. Actualizing the benefits of this paradigm shift will depend on first identifying and resolving the various bases for resistance to it. In reality, this will require far more planning than would be needed to introduce a purely intellectual or technical advance. However, our experience suggests that it can be done.

References

1. Eliot, TS. *Four Quartets*. Harcourt, Brace, and World. New York, 1943.

- Breuer, J. and Freud, S. "Studies on Hysteria," [1893-95] in Standard Edition, vol. 2, trans. Strachey, J. Hogarth Press. London, 1955.
- 3. Ibid.
- Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS. The relationship of adult health status to childhood abuse and household dysfunction. <u>American Journal of</u> Preventive Medicine. 1998; 14: 245-258.
- 5. Dong M, Anda RF, Felitti, VJ, Dube SR, Williamson DF, Thompson TJ, Loo CM. Giles WH. The interrelatedness of multiple forms of childhood abuse,

neglect, and household dysfunction. Child Abuse and Neglect. 2004; 28: 771-784.

- 6. Anda RF, Whitfield CL, Felitti VJ, Chapman D, Edwards VJ, Dube SR, Williamson DF. Alcohol-impaired parents and adverse childhood experiences: the risk of depression and alcoholism during adulthood. Psychiatric Services. 2002; 53: 1001-1009.
- 7. Dube SR, Anda RF, Felitti VJ, Chapman D, Williamson DF, Giles WH. Childhood abuse, household dysfunction and the risk of attempted suicide throughout the life span: Findings from the Adverse Childhood Experiences Study. Journal of the American Medical Association. 2001; 286: 3089-3096.
- Anda RF, Brown DW, Felitti VJ, Bremner JD, Dube SR, Giles WH. The Relationship of Adverse Childhood Experiences to Rates of Prescribed Psychotropic Medications in Adulthood. <u>American Journal of</u> Preventive Medicine. 2007; 32: 389-94.
- 9. Seeman T, McEwen B, Rowe J, Singer B. Allostatic load as a marker of cumulative biological risk. <u>Proceedings of the National Academy of Sciences</u>. 2001; 98: 4770-4775.
- 10. Whitfield CL, Dube SR, Felitti VJ, Anda RF. Adverse Childhood Experiences and Subsequent Hallucinations. <u>Child Abuse & Neglect.</u> 2005; 29: 797-810.
- 11. Anda RF, Felitti VJ, Walker J, Whitfield CL, Bremner JD, Perry BD, Dube SR, Giles WH. The Enduring Effects of Abuse and Related Adverse Experiences in Childhood: A Convergence of Evidence from Neurobiology and Epidemiology. <u>European Archives of Psychiatry and</u> Clinical Neurosciences, 2006; 256: 174-186.

12. Anda RF, Croft JB, Felitti VJ, Nordenberg D, Giles WH, Williamson DF, Giovino GA. Adverse childhood experiences and smoking during adolescence and adulthood. Journal of the American Medical Association. 1999; 282: 1652- 1658

13. Edwards VJ, Anda RF, Gu D, Dube SR, Felitti VJ. Adverse childhood experiences and smoking persistence

Felitti/Anda ACE Study chapte₂₁ Lanius Vermetten book in adults with smoking-related symptoms and illness. The Permanente Journal. 2007; 11: 5-13.

14. Dube SR, Miller JW, Brown DW, Giles WH, Felitti VJ, Dong M, Anda RF. Adverse Childhood Experiences and the Association with Ever Using Alcohol and Initiating Alcohol Use During Adolescence. Journal of Adolescent Health. 2006; 38: 444. e1-10.

15. Dube SR, Anda RF, Felitti VJ, Chapman DP, Giles WH. Childhood Abuse, Neglect, and Household Dysfunction and the Risk of Illicit Drug Use: The Adverse Childhood Experiences Study. Pediatrics. 2003; 111: 564-572.

- 16. Anda RF, Fleisher VI, Felitti VJ, Edwards VJ, Whitfield CL, Dube SR, Williamson DF. Childhood Abuse, Household Dysfunction, and Indicators of Impaired Worker Performance in Adulthood. <u>The</u> Permanente Journal. 2004; 8: 30-38.
- 17. Felitti VJ. Ursprünge des Suchtverhaltens Evidenzen aus einer Studie zu belastenden Kindheitserfahrungen. <u>Praxis der Kinderpsychologie und Kinderpsychiatrie</u>. 2003; 52: 547-559.
- 18. Hillis SD, Anda RF, Dube SR, Felitti VJ, Marchbanks PA, Marks JS. The Association Between Adolescent Pregnancy, Long-Term Psychosocial Outcomes, and Fetal Death. Pediatrics. 2004; 113: 320-7.

19. Dube SR, Felitti VJ, Dong M, Giles WH, Anda RF. The Impact of Adverse Childhood Experiences on Health Problems: Evidence from Four Birth Cohorts Dating Back to 1900. Preventive Medicine. 2003; 37: 268-77.

20. Dong M, Dube SR, Felitti VJ, Giles WH, Anda RF. Adverse Childhood Experiences and Self-reported Liver Disease: New Insights into a Causal Pathway. <u>Archives</u> of Internal Medicine, 2003; 163: 1949-1956.

21. Anda RF, Brown DW, Dube SR, Bremner JD, Felitti VJ, Giles WH. The Relationship of Adverse Childhood Experiences to the Prevalence, Incidence of Hospitalization, and Rates of Prescription Drug Use of Obstructive Pulmonary Disease in a Cohort of Adults. (in preparation)

- 22. Dong M, Giles WH, Felitti VJ, Dube, SR, Williams JE, Chapman DP, Anda RF. Insights into causal pathways for ischemic heart disease: Adverse Childhood Experiences Study. <u>Circulation</u>. 2004; 110: 1761– 1766.
- 23. Dube S, Fairweather D, Pearson W, Felitti V, Anda R, Croft J. Cumulative Childhood Stress and Autoimmune Diseases in Adults. <u>Psychosomatic</u> Medicine. 2009. (In press)

24. Kirkengen, AL. *Inscribed Bodies*. Kluwer Academic Publishers. Dordrecht, 2001.

25. Heckman J, Knudsen E, Cameron J, Shonkoff J. Economic, Neurobiological, and Behavioral Perspectives on Building America's Future Workforce. <u>Proceedings of the National Academy of Sciences</u>. 2006; 103:10155-10162.

26 Miller, Alice. *The Body Never Lies*. W. W. Norton. New York, 2006.

27. Hoffer, Eric. The Ordeal of Change. Harper and Row. New York, 1959.

28. Masson JM. Assault on Truth. Farrar, Straus, and Giroux. New York, 1984.

29. De Salvo, Louise. Virginia Woolf: The impact of childhood sexual abuse on her life and work. Beacon Press. Boston, 1989.