For evolutionary psychiatrists, psychologists and others interested In sociophysological integration

ASCAP

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"The more we know about the physiology of the brain, it seems, the more we need to know about the environment and psychosocial domains."

David Kupfer, 1997 [1]

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ASCAP Society Mission Statement:

The ASCAP Society represents a group of people who view forms of psychopathology in the context of evolutionary biology and who wish to mobilize the resources of various disciplines and individuals potentially involved so as to enhance the further investigation and study of the conceptual and research questions involved.

This scientific society is concerned with the basic plans of behavior that have evolved over millions of years and that have resulted in psychopathologi-cally related states. We are interested in the integration of various methods of study ranging from cellular processes to individuals in groups.

ASCAP Newsletter Aims:

- ♦A free exchange of letters, notes, articles, essays or ideas in brief format.
- ♦Elaboration of others' ideas.
- ♦Keeping up with productions, events, and other news.
- ♦Proposals for new initiatives, joint

The ASCAP Newsletter is a function of the ASCAP Society.

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ADDRESSED TO & FROM ...

News from the Psychotherapy Section, World Psychiatric Association

I am pleased to announce that the Executive Committee of the Psychotherapy Section of the World Psychiatric Association has requested our Editor to join the Committee, and that *ASCAP* should become the official newsletter of the Section. I first approached the Secretary of Sections of the WPA with this proposal in November, 1997 and it is now most gratifying to have it unanimously endorsed by the members of our Committee.

The application of evolutionary biology to the study of psycho-pathology and the furtherance of psychotherapy has been all along one of the objectives of *ASCAP,* and this association with the Psychotherapy Section of the WPA comes at a time when *ASCAP* has produced two issues devoted to Psychotherapy, derived from the papers presented in Tucson at the annual meeting last summer. Our former President, Kent Bailey, and our Editor, are both to be warmly congratulated on this symposium.

On the subject of congratulations, it would also be appropriate to congratulate our Editor on producing ten volumes of *ASCAP* over the past ten years. He has done this almost single-handedly, and with a devotion which belies the work it has entailed. He has managed to produce, month after month, a newsletter that is amusing, inspiring, topical and informative. Long may it continue now in association with our Psychotherapy Section. And I hope that *ASCAPs* other interests, in sociophysiology, neuroscience and other a "bottom-up" approaches, will complement the work of those whose main concern is psychotherapy and top-down perspectives.

I hope that readers of *ASCAP* will take the opportunity of joining the Psychotherapy Section of the WPA. Although this is primarily a medical association, non-medical members are welcome. Our next meeting is in Hamburg, August 6-11,1999.

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Involuntary Strategies: A Response to Tim Miller

Many thanks for publishing our letter and article on standby in the July issue. The ASCAP Society meeting in Tucson seems to have gone exceptionally well. We all enjoyed reading the reports.

I could not resist replying to Tim Miller's article Involuntary Strategies published in the August edition. He raises forcibly some of the most common objections to scientific knowledge of humankind, and his ideas are well worth a wider discussion.

As regards to human origins, we certainly live in exciting times. The "Out of Africa" supporters seem to be winning the argument with the proponents of the regional evolution of humankind.

The analysis of Neanderthal mitochondrial DNA (mtDNA) *"implies that the Neanderthal divergence [from humankind] is of considerable antiquity, dating to 555,000 to 690,000 years ago. This is about four times greater than the time back to the common ancestor of modem human mtDNA (120,000 to 150,000years)".* (R.Ward&C. Stringer: *Nature,* 1997; 388:225-226).

Accordingly, on the basis of these results, Neanderthals cannot be ancestral to humankind. Moreover, the African Pleistocene becomes pivotal to understanding human evolution.

The idea of the importance of climatic variability to human evolution continues to gather support. Ian Tattersall, who works in the Department of

Anthropology, American Museum of Natural History, New York, writes that *"One of the trendiest recent exercises in palaeoanthropology has been the publication of books that in one way or another blame the emergence and subsequent evolution of our own dubious hominid lineage on the climatic oscillations of the Pleistocene epoch."* He finds *"it inconceivable that the dramatic worldwide warmings and coolings of the Pleistocene... did not radically affect the course of hominid evolution".* (IanTattersall: *Nature,* 1997;388:638).

Potts' book *Humanity's Descent: The Consequences of Ecological Instability,* which I have just finished reading, is convincing on the role of African climatic oscillations in human evolution. The work, which has now been published in paperback (price US $14.00, Avon Books, ISBN 0 380 71523 6), really is compulsory reading for anyone who uses the concept of the Era of Evolutionary Adaptation. Incidentally, Potts writes *"Perhaps language evolved because of the value of stories in relaying information within the social group",* humankind as the story-telling animal!

Darwin's highly influential speculation was that bipedalism was an adaptation to a savanna lifestyle. An alternative proposed by Potts is that bipedalism was a response to a prolonged variability in forest cover caused by climatic instability. New research favours Potts:" *Yet our evidence suggests that the earliest bipedal hominid known to date lived at least part of the time in wooded areas"* (M. Leakey & A. Walker: Scientific American, June 1997,60-65). In this article, bipedalism is backdated to at least circa 4 million years ago. The earliest bipeds were, seemingly, upright chimpanzees.

Michael Davies

Editor's Note: The article which came with this letter, will be published in the December issue.

Answer to the 10 Commandents

In The 10 (Plus) Commandments of an Evolutionary Forensic Psychiatry by J. Anderson Thomson obviously delights in shocking the bourgeoisie, and he has obvious talent as a writer of lurid headlines. But is this what we want to do with evolutionary psychology?

Not that the principles he labels "commandments" are incorrect. They are just overstated for effect. They are also used to bolster the untenable position that rapists are just like the rest of us.

This point is contradicted in his own list of principles, specifically "Commandment" Ten. In it, he describes the neurological impairment caused by childhood neglect and abuse. Presumably, he is talking about the childhoods of the violent offenders he deals with. If neglect and abuse play such a large role in creating violent criminals, what is the meaning of "commandments" such as "Males are violent by temperament" or "Battering, sexual assault and rape are evolved mechanisms of the male mind"?

Now it is certainly true that males have the potential for violence and that they will rape under some circumstances. But it is also true that most men don't kill or rape except under very specific conditions (war, social upheaval, extreme inequality, etc.).

Violent and sexual offenders are generally not ordinary males; there is something wrong with them. Ordinary males are subject to influences that control and moderate their potential for violence. They will, under most circumstances, choose reproductive strategies that don't involve rape even though rape can be adaptive.

If J. Anderson Thomson wants the world to understand that we too might have offended, but for the accidents of embryology and the grace of parents who didn't abuse and neglect us, that's fine, but he needs to find better ways of doing it.

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Simon Drew - Russell Gardner Interchange - Re: Helping a Graduate Student

SD: Has there been much collaboration between the social competition advocates (i.e. yourself, Price, Gilbert and Sloman) and those working on the connection between serotonin, mood and status (i.e. Raleigh and McGuire etc.)?

RG: The two groups know of each other but haven't really collaborated. McGuire's approach to human ethology has been quite different. I do not know what Raleigh has published more recently.

SD: Also has there been much communication with those working on the connection between social comparisons and affect (i.e. Buunk)? A synthesis of these three bodies of literature to my naive eye would seem to be fruitful.

RG: Sounds like a good thing to do. Don't discount the importance of the fresh approach your naivete provides.

SD: Is the general consensus that clinical depression is an maladaptive exaggeration of an adaptive mechanism? Or is even severe depression seen to have had an adaptive purpose?

RG: Most clinical psychiatrists seem content with the "biochemical abnormality" explanation cited throughout the patient population as well. This general attitude (which seems strange when you think about it) is why I have proposed that psychiatry needs a basic science in several recent publications and why I have convened a blue ribbon committee in the Group for the Advancement of Psychiatry (GAP) to address Psychiatry's need for a basic science.

Any work that you do will be paid close attention to by high-flyers. The committee includes the editor of *Biological Psychiatry* and the former psychiatry chairman and Dean of the Cornell School of Medicine, for instance.

SD: I'm sorry if my questions miss the point of the literature, hopefully as I develop a deeper understanding my questions will become more relevant.

RG: I believe your questions are right on. You should subscribe to *The ASCAP Newsletter and* discuss things with that group as you work things through. I'll send you more material from older volumes as I get time.

SD: Yes, I do know of your paper but am yet to read it.

RG: Check the September issue for Wilson's latest on adaptation in mania. Of course, you probably know my 1982 paper in the *Archives of General Psychiatry.*

SD: Yes, I have since found this article and several others, and am finding them fascinating, particularly the following:

Raleigh, McGuire, Brammer, Pollack, & Yuwiler: Serotonergic mechanisms promote dominance acquisition in adult male vervet monkeys. *Brain Research,* 1991;559:181-190.

I am working on a paper on depression from the evolutionary perspective. I have read a large portion of the literature on the social competition hypothesis, and am going through this year's *ASCAP Newsletters.*

What is in the pipeline as regards this area, and also has anyone been working on any alternatives to the hypothesis? What are the latest articles in the area, particularly those I may have missed in my literature searches?

If you have the time your help would be appreciated. I'm considering perhaps doing a Ph.D. in the area. At the moment I'm completing my honours year, my supervisor is Linda Mealey, and my thesis is about altruism as a means of establishing reputation.

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WORLD PSYCHIATRIC ASSOCIATION (WPA)

http://www.who.ch/programmes/ina/ngo/ngo181.htm

Founded: June 1961, Montreal, at the 3rd World Psychiatric Congress, replacing the International Society for the Organization of World Psychiatric Congresses set up in 1950 in Paris.

Objectives/ Aims/Principles: Advance international cooperation in the field of psychiatry by coordinating on a worldwide basis the activities of its Member Societies and in other ways to promote activities designed to lead to increased knowledge in the field of mental illness and better care for the mentally ill.

Membership: Some 100,000 members grouped into 80 National Member Societies in 80 countries.

WPA organizes World Psychiatric Congresses every 3 years and holds regular regional and interregional scientific meetings. These serve to facilitate exchange of information concerning the problems of mental diseases and help strengthen relations between psychiatrists working in various fields and between societies existing in different countries. Operates educational programmes for psychiatrists and doctors from developing countries.

Publications: WPA Bulletin & E.C. Communique.

Members of the Speciality Sections of the Association serve on World Health Organization (WHO) expert advisory panels, and WHO staff participate in WPA sections, such as that on education in psychiatry, epidemiology and community psychiatry, and on drug dependence.

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Dr. Gilbert's Address

Thank you for advising me that some Italian colleagues of Dr. Liotti were trying to contact me. For those who are trying to contact me, regarding research and other things, please write or E-mail me at:

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Evolutionary Psychology Internet Links?

http://www.behavior.net/column/brody/evpsychlinks.html

Please E-mail any contributions to ascap@utmb.edu, or mail hard copy and 3.5" HD diskette to: Russell Gardner, Jr., c/o Frank Carrel, Department of Psychiatry & Behavioral Sciences, University of Texas Medical Branch, Galveston, Texas 77555-0428, USA. WordPerfect, Microsoft Word or ASCII format preferred. Diskettes will be returned to you.

Thank you.

ARTICLE:

by Russell Gardner, Jr.

Sociophysiology Meets Belief Theory (AKA Control Mastery)

I write this ending a week in San Francisco. This is Suzie's stamping grounds and she long since had planned a vacation here. Thanks indirectly to Paul Gilbert and his networking capacities, Lynn O'Connor (LOC) from San Francisco had come to the Tucson meeting of the ASCAP Society. She, learning of our San Francisco plans, quickly arranged that I speak to the San Francisco Psychotherapy Research Group, and invited me to various other seminars and meetings of this distinguished organization led by Joseph Weiss (JW) and Harold Sampson (HS), psychoanalyst and psychologist, who have done many studies of psychotherapy. I accumulated CME credits, met a number of new people (including one, Bill Meehan, already an ASCAP Society member!), and learned some additional rationale for why I do some of the things I do with patients and how in the future I might do them better with guidelines furnished by these clinician-investigators.

Thus Dr. Weiss's book, *How Psychotherapy Works (HPW)* was sent me preparatory to the trip.[1] In the clearly written work, JW puts forth the theory that has guided the group and he illustrates it with many clinical examples. His book didn't exactly label his system of thinking (at least that I noticed), so I thought of it as Belief Theory because the core idea holds that people show up to see therapists to get help for pathogenic beliefs that guide their actions although there is another planful part of their thinking directing the person to behave less pathologically. People guide their lives according to such plans; they actively use therapy; that is, they can anticipate just what they have to do if there are only a limited number of sessions.

The planful unconscious represents not the disorganized, chaotic caldron of early Freudian thinking, but a highly organized blueprint for one's best welfare. Pathogenic beliefs distorting such plans stem from troubling experiences in childhood with parents and siblings or strongly felt opinions from powerful others that make little sense for the patient's present day but retain power anyway, because if true, the patient or loved ones are endangered. Such beliefs often engender guilt, as when one has seemingly outdone one's siblings and a parent harps on this. The therapist helps the patient overcome the pathogenic beliefs so the patient can implement his/her own plan without conflict. The therapist should responsibly maintain safety for the patient (in sociophysiological language, be an ally). Patients frequently "test" to see if the therapist will help them confirm or disconfirm the beliefs; the special jargon asks if the therapist behaves preplan or antiplan? From what the therapist does or doesn't do, the patient will feel supported in his/her own core wishes; or on the other hand, the pathogenic beliefs will be supported (if the last happens, the therapist would have made an antiplan intervention and the patient will show distress).

As already mentioned, on reading *HPW,* I had thought of this simply as Belief Theory and said so in my title. But in the best of proplan responses to my effrontery, Dr. Weiss, Lynn O'Connor, and organizer of the series of grand rounds-like talks at which I spoke, Marshall Bush, all suggested that it was even better than the official name of the approach, Control Mastery, which, as they reported it, had been rather accidently arrived at. Rather than being put down for my ignorance, I felt supported in my heresy, heard and appreciated. No wonder I had a good time in the beautiful city and liked the approach.

Now let me tell you of specific instances wherein I felt the theory to be implemented. I participated in the following seminars:

(1) In a first meeting of a JW-led group, Marriage, Family and Child Counsellor Peter Schumacher (PS) told of his recent work with a 40 year old male, new to his practice, who had been the youngest of a sibship. His older sisters had had problems with developmental disorders. The patient had learned to be highly responsible but he didn't know exactly how. Now his relatively new girlfriend was depressed. She wept much and the patient felt helpless to do much about it but assumed he was at fault, responsible and guilty anew. Dr. Weiss intervened to say that survivor guilt was likely a major factor. PS said to the patient with reference to the girl-friend, "So it's hard for you to be happy if she is not." The patient agreed and went on to tell how he is unhappy at work as well, unappreciated and distressed. The group saw PS's comment as a preplan one, focused upon the patient's distress. That it was successfully proplan could be discerned by his response; he expanded his range of complaint, feeling PS to have been a responsive audience.

Audience was my term and LOC in conversation over coffee later agreed that being a good audience to one's patient (or child, client, employee or friend) indeed constitutes a worthy aim. I had found myself thinking of belief therapy as a subset of sociophysiological therapy (and this is fundamentally what I spoke about in my own formal remarks summarized below). Concepts from sociophysiol-ogy connected to the new language. Audience communicational state (or psalic) occupies sociophysiological theory. Humans are avid listeners and respondents to the stories of others, whether these are dramatic presentations, formal remarks, or the gossip that Robin Dunbar suggests has replaced grooming as a more efficient way of relating intimately to more conspecifics even though it requires a bigger brain.[2] By the way, PS later came to my formal remarks and gave me his card, expressing interest in sociophysiology and *The ASCAP Newsletter.* We hope that he might contribute to this or other commentary.

(2) Two days later, another research-focused group led not only by JW but by LOC as well examined the transcript of a six-session "phonographically recorded" treatment done in 1941 by Carl Rogers. Rogers, not a physician, led the client-centered movement that gave another name to patients (clients), via which he contributed to non-physicians having a role in the care of troubled people.[3] His influence was great in his time and even without medical credentials, he achieved the distinction of Professor of Psychiatry at the University of Wisconsin. Rogers knew his clients potentially had "unified selves" and he saw his task as fostering their development. The transcript featured an inhibited young man. Debates around the table featured whether the comments made by Rogers were proplan or not (he mostly was, but sometimes slipped). The language seemed at times sexist; even Carl Rogers was of his time. I learned how a meaningful proplan interpretation has clear effects on the patient. LOC proudly told of a study currently underway that monitors heart rate; preliminary results show that after a therapist's proplan statement, the patient's heart rate reduces and the person shows other evidences of a relaxation and acceptance. This work is in the tradition of LOC's father, I. Arthur Mirsky of Pittsburgh. I had worked in my earlier career with figures of psychosomatic medicine and knew of Dr. Mirsky as an important figure often referred to by my teachers, Morton Reiser, Herbert Weiner, and Milton Rosenbaum. I learned that when growing up Lynn had been in and out of the Rosenbaum household as they all spent time together in Cincinnati. Joseph Weiss also originally hailed from that seminal city.

(3) The SF Psychotherapy Research Group has many seminars. Harold Sampson leads one too, also using *HPW* as the text. I attended the third session in a series. He talked briefly at the onset describing a patient who was persistently critical of HS. The patient had himself been criticized when little. The patient turned passive into active, a frequently mentioned tactic described by the group. To be proplan, one doesn't react in kind and points out the tactic as time goes on.

A patient presented by therapist Patsy Wood, Ph.D., (PW) was a 21 year old woman from a

distant state, who had lost her mother to cancer ten years before. Her father stopped his career to take care of her and her younger siblings, but depressed, he was also nonfunctional and had preserved the house exactly as it had been before the death.

Though guilty about leaving her younger siblings, she moved away from there to San Francisco with three other young people from her town, one of them a quasi-significant other (QSO), quasi-because she wished to part from him but he wanted her and she guiltily stayed with him in a sexual relationship. PW said that it was good she left her siblings, thereby making a pro-plan statement. PW and the group formulated that her pathogenic beliefs included guilt over being a survivor (survivor or outdoing guilt is a common finding in Control Mastery research). The three other apartment occupants drank to excess and one often brought bar-buddies home for drunken parties after the bars had closed despite protests from neighbors. The patient, on the other hand, drank little and worked successfully at the best job of the group, getting promoted and basically paying for the flat that she had found on arrival to SF and that they rented together. She was depressed, however, with trouble sleeping, so PW arranged at the beginning of treatment that a psychiatrist see her. He prescribed Prozac.

In the introductory session Dr. Wood had told the patient of PW's long scheduled vacation beginning three weeks later. Usually, of course, going immediately away on one's vacation seems a poor idea when starting treatment with a patient who had had a serious loss in childhood. But interestingly, while PW was away, the patient took dramatic action: she decided to break up with QSO and sustained the decision, threw all three out of her flat, and found new housemates of a more responsible nature. Over the telephone in a newly discovered assertive manner, she scolded her father about his lack of responsibility. She established a romantic sexual connection that was brief but illustrative how poor sex had in fact been with QSO.

The group animatedly discussed how salutory effects seemed to stem from the therapist's unabashedly going away, conjecturing that it was proplan because it contrasted dramatically with the father's dropping everything to care for the kids and trying to preserve things as they had been. How important was the Prozac? Not surprising for a therapy seminar, various people pooh-poohed it. I commented on the serotonergic effects of it, however. Raleigh, et. al., had showed higher serotonin in dominant vervets and later that rank of a subordinate will increase if given Prozac. I wondered if the patient was newly in charge of herself and her surroundings because more serotonin ran in her synapses. Hal Sampson with great diplomacy noted that when success happens, there is plenty of credit to go around. We all agreed that for whatever reason, the "plan" of this patient seemed to be going well with many fewer encumbrances from pathogenic beliefs than was true when the therapy with PW began.

(4) My talk, "Psychoanalysis, Belief Theory, and Sociophysiology: A Three Century Story," held that psychoanalysis relied on machine metaphors of the 19th century (rather than the evolutionary and physiological advances of Darwin and Barnard). Despite this, it held sway in the U.S.A. anyway for the first half of our present century. Then antipsychoanalysis held sway for the century's second half. By antipsychoanalysis I referred to the movement led by Eli Robins who had been treated badly by a psychoanalyst; Robins angrily and persistently countered Freud's movement aided by many colleagues and intellectual descendents who wrote widely and influentially. There were good features of the countermovement but furthering of pathogenesis was not one of them.

That is, antipsychoanalysis disavowed theory so much that along with the bathwater of over-theorizing, it threw out the baby of a medical science model which always operates with theory. I presented ideas that amended that. I presented sociophysiology as a framework for a medical basic science for all those clinical disciplines that appropriately assume the brain to be the central

organ for mediating the behavior and social interactions of their disciplines. While all animal brains prominently include social doings with conspecif-ics, the human brain especially does so with its three-times greater mass and four-times greater cerebral cortical surface compared to ancestors of 2 million years ago or our primate relatives, chimps and gorillas, who share nearly all of our genome.

I talked of PSALICs as a method of comparing our communicational behaviors with those of other species. PSALICs refer to Programmed Spacings and Linkages in Conspecifics. This first acronym highlights the basic functions of intraspecific communication. Another acronym describing PSALIC, Propensity States Antedating Language in Communication, highlights the evolutionary and organismic state qualities of the eight psalics I've so far named: alpha, audience, in-group omega, mating, nurturant, nurturance-recipient, out-group omega, and spacing.[4] The audience joined in with enthusiasm asking about the adaptive features of mania and how its pathogenesis can be divided into those genomic and neural elements that foster the core psalic (alpha) and those that foster its too easy triggering (rendering it maladaptive in patients). This latter component is the topic of the next paper by Dan Wilson, current president of The ASCAP Society.

Audience questions also elicited from me the concepts of Shiver-ATP and Negotiation to Compromise Without Resentment. Thus, I conjectured that pathogenic beliefs are in fact persistent resentments after failures to negotiate to compromise with the powerful other people of the patient's childhood. This connects with alpha psalic. What Joseph Weiss refers to as the plan includes what Jane Goodall discussed about her chimpanzees: she stated that there is an inexorable drive to dominate. When a chimp doesn't show it, she wonders what childhood event intervened to have stopped it (what pathogenic beliefs ensued?). Humans, however, with their big brains have more flexibility than the inflexible need to dominate others. They have the capacity to be in charge of metaphoric others, like self attributes such as time and possessions. We have by and large a push parallel to that of dominance in the chimps, to be in charge of our own affairs, what JW calls a plan for oneself. Elsewhere I have called *"being in charge of oneself* good self esteem; one deploys a muted alpha psalic in the service of getting along in the world.

(5) The final seminar featured LOC's meeting with her research associates. The group featured people from the Wright Institute. Katherine Mann, Ph.D. works with resilient children. She has done research at UCLA on suicide. Bill Meehan, a Ph.D. in history from Berkeley and already an *ASCAP Newsletter* subscriber, focuses on how we can understand primary process, the Freudian concept that stemmed largely from dreams. Kathy Mulhern is doing her dissertation on interpersonal guilt in adolescents. Irene McLaughlin is interested in qualitative analysis of women's diaries collected from published and unpublished sources. She is interested in coping mechanisms, guilt and self-metaphors the women used. Adrienne Ganz, Ph.D., has worked at Berkeley and at NYU on issues of ego functions and resilience. She is building a practice in SF and working to apply Control Mastery in the Berkeley Public Schools. Madeline McGuiley was at her first meeting; she is a first year student just now becoming interested in applying herself to research and LOC paid her special attention.

The chief focus of the meeting involved Rebecca Webster who is doing jealousy research especially in siblings. Her efforts to develop a questionnaire elicited many helpful comments. Interestingly, her personal reluctance to fill out questionnaires was a factor in her thinking through how the project can be successfully conducted.

I spent after-conference time with the first two seminar participants mentioned. Katherine Mann's work with suicide involved 20 interviews with adolescents. We exchanged E-Mail addresses as she generously agreed to share these with myself and Michelle Clark at UTMB. With Michelle I am applying ratings of various sociophysiological dimensions to the stories of people who have elected to suicide

with severe enough consequences that they are hospitalized. We are interested in their state at the time of the act as well as their last interpersonal interaction prior to the attempt.

Bill Meehan provided some exciting conversation with some tour de force summaries of his reading and thinking. He has just finished reading Freud's *Project for a Scientific Psychology* and noted that some of the final concepts resemble Francis Crick's well publicized recent work on consciousness. His current thinking on primary process focuses on how it generalizes from the visual facets of dreamed experience. He compared dream elements to the first versions of the visual representations in the pictographic languages, such as found in Chinese. One such pictograph, for instance, features two women in a house as the symbol of disharmony.

With convention, of course, the meaning becomes fixed and the pictorial elements fade. But with what happens nightly in our rapid eye movement (REM) sleep, pictorial elements of a parallel kind are freshly generated without the constraints of convention. I did recall Howard Roffwarg's work from many years ago that showed middle ear muscle activity (MEMA) can be measured during the night using an acoustic impedance device. REMs are famous, of course, for their ease of measurement and because they were measured first, but we also know that body movement twitches are present. I know it especially as I have done research on that.[5] MEMAs are there too, I recalled, in at least equal abundance though I didn't have the exact reference. Interested, Bill made notes on this, but pointed out that our memory for dreams nevertheless features visual elements more than aural elements.

We went on to talk (I'm not any more exactly sure about how we got there but Bill is an historian) about the history of the discovery of the individual in the European Renaissance. I have been fascinated for years by a book by medieval historian Colin Morris who pinpointed this discovery as happening in the first century of the current millenium.[6] Morris suggests that Cistercian monks who competed in mortifying themselves extended their capacity of this to such an extent that they emphasized their identities as separate individuals. This discovery of the individual was new and spread rapidly in Europe, no longer for individual mortification only but for glorification too. After this cat was out of the bag, biography and individualized works of art became possible. Thus Frederick Barbarossa's statue exemplified not the idealized version of the classical period and the standards set by it for medieval times as well, but featured his individualistic (and somewhat ugly) facial qualities. This topic turned out to be one on which Bill is expert. He has studied Montaigne from the 16th century with this idea in mind. He notes that the idea of the Renaissance invention of individuality is a "trope". (I was later relieved to find that I am not the only person for whom trope was a new term.) Bill explained that it meant a concept that is held in common by many (like a literary trope referred to again and again in Renaissance times with common meaning for all). I invited him to summarize his paper on Montaigne for the newsletter.

Does the excitement of this week in San Francisco comes through this narrative? One must be impressed with Lynn O'Connor's incomparable energy, productivity, enthusiasm, and warmth for all her colleagues and students. And she has been propelled by similar qualities in Joseph Weiss and Harold Sampson in their excellent leadership. The clarity of the Control Mastery ideas (or, as I persist in thinking of them, belief theory) helps one practice better. Not that sociophysiology doesn't have additional features to offer.

Control Mastery or belief theory applies especially to a subset of people, patients who come for therapy of the talking variety. LOC noted, however, that some of their current research involves how in normal life people test their surrounds to see if the pathogenic beliefs or the patient's plan of being in charge holds. She desires anecdotes from any of you who know of people who have gotten better from life experiences independently of treatment. And I suspect that her student, Irene McLaughlin, would appreciate any women's diaries that you might happen to know about. *c8*

ARTICLE:

by Daniel R. Wilson

Evolutionary Epidemiology

1. The paucity of evolutionary genetical analysis in medical and psychiatric research despite its probable utility.

The current state of scientific and philosophical orientation for most biomedical theory and practice is not adequate to even ask, much less answer, deep questions of phylogenetic etiology. Much biomedical science lacks coherence. This case adduced from its mongering of study design, outcome curves and other enthusiasms of the currently reigning, largely inductive philosophy. Conventional wisdom holds that deep concerns are to be pursued only by persons without practical things to say. It is perhaps better to make a minor inductive advance than risk a crashing deductive error. Theory, when robust, can be of sufficient coherence to yield quantitative data or, at least, crisp qualitative incongruences. These, in turn, can lead to insights which, being both counter-intuitive and non-obvious, would never be appreciated by mere experiment, no matter how clever.

Within psychiatric research these problems are only magnified. Psychiatry, lacking as it does, both a foundational theory and cogently integrated intellectual aims, in certain respects has become a pastiche of arid facts, abstruse ideological claims and grandiose speculations. This leads, ineluctably, to the trap in which psychiatry all too often trips up: its surfeit of plausible but contradictory explanations which cannot be properly sorted out for lack of any encompassing framework. Yet psychiatrists have long had available one such framework beginning with Darwin's elegantly reasoned theory of evolution. It is particularly difficult to sort out historical questions (such as the past function of phenotypes and the selection of their genes in the environment of their evolution) since experimental observation is constrained, largely, to modern environmental circumstances. Empirical studies of course would be quite valuable. Unfortunately, ambitious cross-cultural epidemiology of rigorous reliability and validity might constitute a robust data base. These are nigh non-existent. It is, moreover, unlikely the few remaining foraging cultures shall be compared with industrial ones before the former are either extinct or grossly contaminated with diffusionist phenomena.[1] It would be useful to enlarge the comparisons to include cross-genus studies of the primates as well as other relevant ethology. The prospect for such inductive studies is limited. Induction is, in any event, a dubiou/s approach in the sphere of comprehensive biology which is nowhere yet systematized as a science.[2] Darwinism is, therefore, of probable utility in psychiatric research. At the very least it is otherwise quite difficult to experiment with, much less prove, that evolutionary useful features of major disorders exist since these illnesses are viewed with respect to modern environs and cultural circumstances.

One place to begin is with the sure Darwinian deduction that common, genetically simple pathologic syndromes must be the residua of positive adaptation. Such lineages were adaptive at least before the rise of civilization since spontaneous maladaptations cannot surpass thresholds of surprisingly low prevalence. This seems especially true in the realm of disorders that arose phylogenetically from genes expressing a variety of neurobiological sensitivities and talents. The modern environment may sometimes induce among individuals newer, more vulnerable and less adaptive phenotypes.

2. A method of evolutionary epidemiological analysis.

Disorders that are clinically well-validated, nosologically reliable, epigenetic and common

constitutes are amenable to reanalysis within the framework of evolutionary epidemiology.[3,4,5] Indeed, it would seem that any epigenetic medical or psychiatric disorder which attains prevalence higher than basic theorems of evolutionary genetics predict thereby satisfies the two prime conditions of hypothetico-deductive inference at the heart of evolutionary epidemiology. That is, common genes can be generally inferred to have been selected on the basis of advantageous characteristics. The strengthening of such inferences is a major application of evolutionary epidemiology. One such strong inference is the almost inescapable deduction that some syndromes of biomedical pathology held benefits in the course of evolution (and may yet confer advantage).

Epidemiology is, one recalls, a science of disease which specifies rates (illness prevalences, incidences, distributions, etc.). Evolution is a science of life which specifies changes (gene frequencies, generations, forms, functions, etc.). Evolutionary epidemiology is a deductive synthesis of these two sciences which combines the empirical power of classical observations in genetical epidemiology with the interpretive capacities of neo-Darwinian evolutionary genetics. Novel conclusions are thus derived from primary data integrated from these two sciences. In particular, prevalence rates of genetical disease are important data points when reformulated for the purpose of analysis in terms of their evolutionary frequencies. Traits which exceed prevalences beyond frequency of mutation (in Hardy-Weinberg or biometrical calculations and even more complex mixed models) or evidence unusual range of phenotypic reaction are also of special interest.

2.1 The 'algebra' of evolutionary epidemiological analysis.

The integration of evolutionary (population) genetics theory with epidemiology constitutes a new subdiscipline which, in turn, extends basic tools of Darwinian genetics toward an ultimate biological explanation of some 'diseases' as expressions of more normative biological mechanisms. From all this directly follows the hypothesis that much illness is caused by phenotypic 'friction' arising as abiding hominoid genes react with the more recent and brisk rise of human civilization. This appears true because only traits which conferred advantages in the environment of evolutionary adaptation accede to significant rates of genomic prevalence. These deductive methods can be used to test the hypothesis that some 'diseases' have been promoted in the course of natural selection due to intrinsic, if obscure, advantages.

2.2 The relative irrelevance of modes of transmission.

The assumption may arise that evolutionary epidemiological analyses can only be used for similarly Mendelian syndromes. This is not the case. Whether pathologic predispositions are coded as Mendelian dominant, recessive or even multigene systems is not in itself crucial to deductive analysis. Traits need only be epigenetic and common to be made amenable to the analytic tools of evolutionary epidemiology.

Clearly, Mendelian dominance with strong pen-etrance is the most crisp mechanism of putative transmission. Therefore it would also be the most amenable to analyses deducing that positive selection was a needed condition to establish prevalence beyond an estimable threshold. Necessary threshold rates of genetic prevalence are the lowest. Most technical studies are simpler than is the case with other modes of transmission. Implications are the most striking: genes coding for disease vulnerability evolved via selective advantage of other as yet under appreciated traits. A spectrum of trait expression in various pheno-types is largely a function of the degree of pen-etrance.

Recessive transmission is somewhat more complex and requires higher prevalence to substantiate past positive selective advantage. Recessivity also requires modifications of the hypothesis to account for heterosis. An example of such hybrid vigor occurs in the classic phenom-

enon of high sickle-cell anemia with the selective scenario being that a single recessive trait was adaptive (whereas homozygosity was unfortunate maladaptive genetic loading). Trait expression is on a spectrum at two levels and dependent on zygosity as well as phenotypic variation.

More complex polygenic models of transmission are not implausible. However, they do become increasingly cumbersome and less likely relevant in hypothetical positive evolutionary scenarios. The more genes, alleles and complex interactions, the higher the threshold of prevalence needed to establish that positive and non-random selection was responsible. For example, syndromes with complex and weak genetic roots, such as the senile diabetes or dementias, appear to have not accrued through positive evolution. Several evolutionary scenarios by which newly diseased pheno-types may emerge can be modeled. These include (1) discrete Mendelian traits, whether dominant or heterozygotic, (2) continuous polygenic traits, and (3) more complex mixed, composite or multifactorial systems. These models all presuppose that prevalence rates in epidemiologic studies are, with minor adjustments, equivalent to frequency rates for evolutionary calculations.

Therefore, *the frequency threshold which a genetic locus can surpass only via selection* equals the *net prevalence divided by equilibrium.* Rarely, non-Darwinian or other factors may have prevailed, e.g., drift, neutral linkage selection, mutability, pheno-copy, assortative mating, etc.). Otherwise, genes which attain such thresholds were not pathological in the environment of evolutionary adaptation:

Formula 1:

(Pdg)/(Egf) = (Sgt):

(disease gene prevalence)/(gene equilibrium frequency) = (gene selection threshold) With the redundant genetical terms deleted this yields:

(prevalence of disease)/(equilibrium frequency) = (selection threshold) Or

more generally: *P/E = S*

Of course, evolutionary mechanisms typically require aeons of favorable selections for new mutations or simple gene systems to obtain epidemiology prevalence at rates above much above one-half percent. The precise rate of prevalence involves technical adjustments for rates of such things as mutation, back-mutation, fertility, drift, and assumes broadly stable environmental conditions. Similarly, epidemiological prevalence rates must be adjusted by such factors as the degree of identical twin concordance, phenocopy events and so on. Still, as noted above, if a simple gene system occurs to such a degree it was (though not necessarily, is) abidingly adaptive, ipso facto spontaneous maladaptations cannot achieve such prevalence.[6, 7]

In a classic Darwinian system, evolutionary selective value must be presumed to have existed at the genomic population level where genetic alleles of high prevalence co-vary with the manifestation of individual disease. This is the case in the absence of drift due to linkage or similar random, non-Darwinian events. An important deduction follows in consequence of this fact — any common, epigenetic pathology had a likely 'silver-lining' to be best appreciated in the context of ancestral environs. The task of establishing a proper phylo-genetlc perspective, though daunting, is as central to genornic analysis as are the vantages of molecular or cellular biology.

To reveal any such Darwinian advantages, attention must first focus on how genes now expressing pathology operated in the natural environment of past evolutionary adaptation. Subsequently the phylogenetic 'how', 'why', 'when' and 'what' can be considered. All this is difficult to do. Certainly, it is not easy to recalibrate views formed in the contemporary world to the conditions which prevailed in prehistory. Clinicians, in particular, suffer an ethnocentrism of time. It is quite difficult to imagine phenotypes as they would have emerged in the environment of evolutionary adaptation when one knows little about that environment. This is a crucial step before attention can then focus on whether there any salutary features of these genes

are expressed in the current environment. This must be considered in any enlightened clinical practice or public policy (viz., genetic counselling including selective abortion).

Clinicians, in particular often cannot separate evolutionary epidemiological insights from the interesting but separate and far more complex question as to whether genes find adaptive, mal-adaptive or neutral phenotypic expression in the environs of contemporary development. If genes are rather common and simple then there is little question they were positively selected. This is, however, an entirely different matter than how they are now being selected, much less when, where, why, what and how such selection took place. Anthropologists and geneticists commonly are inclined to something of an evolutionary perspective. Physicians rarely are. Having been taught about disease, they cannot readily reorient to the notion that certain syndromes may be more precisely regarded as stories of Darwinian success.

Of course, questions of current selection, if any, are to be answered only by long and painstaking research. Indeed, some of the best validated and reliably diagnosed medical and psychiatric disorders may satisfy the requisite conditions of genetic mediation and high prevalence. So, hypotheses about certain disorders can be posited wherever there exists substantive data on the genetics and epidemiology of a given disease. At this juncture the evolutionary epidemiology of sickle-cell anemia is instructive.

2.3 A Prototype in Medicine: Sickle-Cell Anemia.

An illustrative case might more directly sustain the idea that what is today thought of as disease can have been advantageous. Sickle-cell anemia is a benchmark example in which, counterintuitive though it seems, genes expressing a pathological medical syndrome attained high population frequency due to the Darwinian selection of advantages sustained in the environment of their evolutionary adaptation.

Such a point of reference as this, simple enough to state, has profound consequences. Not the least of these consequences is the way in which the definition of disease itself becomes context-dependent and subject to significant reappraisals within evolutionary perspective. A thorough going review of this as it relates to sickle-cell anemia, neither necessary nor feasible within the present aims, is otherwise available. What is here notable is that research concerning human hemoglobin polymorphisms and related anemia syndromes is now more widely seen as the first and surely the most well known example of what is here termed evolutionary epidemiology.

Reliable and valid epidemiology when coupled with theorems of population genetics, permits a meaningful reconstruction of the evolutionary scenario by which positive selective forces in the past account for the contemporary distribution of alleles. In all of medicine, the investigations concerning sickle-cell hemoglobinopathy exemplifies the materials and methods by which evolutionary epidemiological analysis proceeds. For the present discussion, it is sufficient to briefly outline relevant research on sickle-cell anemia to conclude that, in toto, the syndrome demonstrates much of the increased allelic frequency of anomalous hemoglobins served to counterbalance the selective pressure of malaria.

With the widespread use of modern hematological screening over the past forty years, the popula-tional features of hemoglobin anomalies has become one of the most intensively studied elements of human biochemistry.[8,9,10,11] By the early 1950's it was clear a variety of anomalous hemoglobins existed in high frequencies in specific human populations. These high frequencies were found almost exclusively in tropical and sub-tropical climes. Neel[12] first noted how such high frequencies must be due to either high rates of mutation or conditions favoring heterozygotes.

Allison[13,14,15] provided the first case evidence that such hemoglobinopathies co-varied with population areas in which malaria was endemic. Allison's original work is useful despite the fact that selective

advantage is not definitively proven. While there are residual problems with this model, these are of a technical nature and do not grossly undermine the point that genetic traits regarded as pathological by medical researchers may be the residua of what, in evolutionary terms, were successful products of Darwinian selection. As it happens, work on hemoglobinopathies has advanced well beyond Allison's early reports.

Subsequently, investigations confirmed that sickle-cell heterozygosity is associated with improved resistance to malaria. In tandem with this hematological research has emerged an appreciation for the Darwinian consequences of this resistance. The high frequency of alleles for anomalous hemoglobins is consistent with a selective advantage to carriers which outweighs the disadvantage to homozygote recessives. It is widely assumed there exists a causal connection, however, the mechanism is not known.

This body of work on sickle-cell anemia is relevant as it underscores that contemporary illnesses may be due to genes which were advantageous in evolutionary selection. By this example the further question is raised as to how much of human 'disease' genetics may have been promoted by natural selection of factors conferring Darwinian fitness in the environment of evolutionary adaptation. The evolutionary perspective — so crucial for the full understanding of the coevolution of hemoglobin polymorphisms and parasitical diseases endemic in the environment of evolutionary selection — may well be informative in connection with other disorders, notably manic-depression.

Other 'diseases genes' may come to be seen as not intrinsically pathological or even as expressions of phylogenetic vigor. With this approach, a clearer picture of evolutionary adaptation is possible. A window on the past can be opened. The corpus of medical epidemiology can be readily reformulated as substantive data for reanalysis in evolutionary and paleoanthropological terms. Only recently has this corpus begun to attract the interests of pathologists in a wide variety of clinical fields. Of course, the vast majority of anomalous alleles in a population are either neutral or deleterious. They are not promoted in genomic frequency but are selected against or, in the case of neutral traits, 'ignored'. It is, therefore, crucial the incidence of a trait be high and, further, that it be clearly epigenetic to a great degree (though it need not be a Mendelian character although such traits are more amenable to evolutionary epidemiological analysis). Only in such circumstances of significant genetic causality and prevalence can Darwinian selection be adduced, particularly that of the hetozygotic type.

There are, likewise other less common yet possible non-selectionist causes of sustained polymorphism but heterosis is the primary mechanism in natural systems.[6] Certainly a given gene locus may be (for whatever reasons) highly mutable. Phenomenal mutability, though rare, is a possible cause of high frequency for traits otherwise appear deleterious. Likewise, drift or other non-Darwinian phenomena must be considered.

Heterosis *ala* sickle-cell anemia is not the sole model, it is merely the first and most simple. Much detailed knowledge was marshalled from genetics, medicine, anthropology and other fields to arrive at a sensible explanation of these anomalies. Unfortunately, the genetics of much biomedi-cal pathology are not known in such detail. This is especially true of many major psychiatric disorders. Nonetheless, more definitive answers as to which 'disease' genes positively evolved appear at hand as the human genome is progressively mapped.

3. Evolutionary epidemiological assessment of the operations of natural selection upon the phenotypic spectrum of clinical traits.

The clinical and theoretical importance of evolutionary epidemiology extends to not just the physical aspect of medicine, but to the psychological realm as well. As noted in part two, the body of psychiatric genetic epidemiology accumulated over the past century is large and cogent. Indeed, this indirect

genetic analysis has had a long and prosperous, if unpresupposing, role in psychiatric research.[16] For a variety of reasons this is especially true with respect to manic-depression.[17]

This body of primary data deriving from psychiatric epidemiology is quite amenable to reformulation into terms appropriate for reanalysis with the theorems of population genetics. Of special interest in this body of data are the many genetic polymorphisms with significant population prevalence. Careful examination of these variant alleles may demonstrate some have been sustained by the operations of natural selection rather than transient or even random events.

Indeed, evolutionary epidemiology may require a refinement in the notion of disease itself, at least as such a label might be attached to several of the most common and genetical syndromes in medicine and especially psychiatry. Several important psychiatric conditions (manic-depression, sociopa-thy, obsessive-compulsivity, anxiety and even drug abuse and some disorders of personality) are so common and so strongly epigenetic that their epidemiological frequencies surpass even quite conservative thresholds of evolutionary selection.

The deduction follows that such frequency thresholds were surpassed due to the Darwinian selection of genes advantageous over the course of evolution. Features inherent to these syndromes most certainly served, and perhaps still serve, useful functions in human society. This is not, necessarily, to aver that such genes now express entirely healthy phenotypes. Such would be something of a naturalistic fallacy in reverse. The current environments to which young humans are exposed and in which their phenotypes develop are, by and large, different than those in which much relevant human, primate, mammalian and reptilian ancestry achieved increasing optimal and evolutionarily stable strategies.

This underscores the point that the same genes which conferred advantages in the environment of evolution might, upon ontogenic exposure to new biosocial ecology, lead to deleterious phenotypes. Developmental and social forces become important etiological factors by which the ecological cues of the modem environment nurture nature in emergent, not evolved, ways. The deleterious expressions of such genes are not 'genetic qua genetic' but only the product of gene-environment interactions.

Thus, even a disease phenotype which is a 100% penetrant, twin concordant and Mendelian dominant retains a component of environmental expression. This component is a function of the differences between the ideal and the real phenotypes. These two phenotypes arise, respectively, in the environment of evolutionary adaptation (to which the genome and ideal phenotype are, at equilibrium, adapted) and the environment of ontogenic adjustment (in which the genome is evoked to express the real phenotype).

All this is of importance both for paleoanthropology and the full appreciation of continuing advantages, if any, of these 'disease' genes. Clinically, there must be potential, if latent, benefits of the ideal phenotype residual in genes now more typically expressive of diseased real phenotypes. There are, of course further ethical, legal, social and even theological consequences to be explored with respect to these latencies and potential.

But the main objective here is to explain a method by which standard epidemiological data concerning genetical disease rates can be reanalyzed from an evolutionary point of view. Again, the point of such reanalysis is to establish whether such genetical systems have accumulated over the course of evolution due to the effects of Darwinian natural selection. With the business of "how" specified, attention can be turned in earnest to questions as to who, when, where and why all this happened.[18]

With this comprehensive view of genetic processes by which is expressed the modern extended phenotype,[19] certain major epigenetic diseases — most notably mental illnesses — can be better appreciated as atavisms of previously adaptive hominid biopattems. An improved grasp of the

adaptive essence of mental illness may well lead to their destigmatisation while, also, giving rise to improved methods of rehabilitation.

Evolutionary mechanisms, generally, require eons of favorable selections for new mutations to obtain epidemiological prevalence at substantial rates. The threshold rate is not precisely known for specific genes and involves highly technical adjustments for rates of such things as mutation, back-mutation, fertility, penetrance and dominance. The calculation of threshold rates also assumes broadly stable environmental conditions, i.e., an environment of evolutionary adaptedness.

The mathematical clarification of such evolutionary dynamics is the aim of population genetics. The Hardy-Weinberg equilibrium is perhaps the fundamental theorem of population genetics as every student of evolution may remember. The equation summates genetical fluctuations across generations in a precise way to specify the net effects of evolution via natural selection.[20]

Genes arise by mutation and are selected for or against over time. If a new gene is helpful enough for long enough, it will accumulate. Genes at prevalences well beyond frequency of spontaneous mutation, except in decidedly unusual circumstances, were selected into the genome on the basis of positive characteristics expressed in the pheno-type. They evolved.

As a rule, prevalence above the mutation rate is likely when a gene occurs in the frequency range of 1/10,000 to 1/1,000 members of a population. Therefore, in mammalian systems rates much above 0.001% are suggestive of past positive natural selection and rates beyond 0.01% highly suggestive. Given average mutation rates and neutral fertility effects it is unlikely that a deleterious gene should attain a frequency of much more than 0.01 %. Moreover, to secrete even this random level in the genome might take many generations — up to 10,000. If a simple gene system occurs to such a degree it was, though not necessarily is, abidingly adaptive.

On the other hand, deleterious mutations cannot achieve high prevalences spontaneously nor even via neutral selection.[21] Consequently, the majority of inherited abnormalities should be rare as a function, more or less, of mutation rate divided by fertility and penetrance. Genetic diseases should be, by definition, of very low prevalence (e.g., achondroplasia) and are often enclosed within sporadic idioethnic lines (e.g., Tay-Sachs disease).

Prevalence of even a deleterious gene will equilibrate over generations at a rate balancing new mutations against the selective pressure, e.g., in achondroplasia the equilibrium frequency is one in eight thousand births for what is a classic autoso-mal dominant condition. Tay-Sachs is seen only rarely and in certain lineages: some Ashkenazic Jews have it, Laplanders do not. Neither of these conditions evidence past positive selection and, indeed, such positive attributes are not to be predicted in the established tests of evolutionary epidemiology. Though strongly genetic, they are too rare to have been promoted by natural selection: they are counter-exemplary evolutionary, noise existing, more or less, at equilibrium rates.

As noted earlier, there is a limit to the range of phenotypic reactive adjustment to ecologic change or novel environs. This is true whether the genes concerned were adaptive, neutral or deleterious. Beyond these limits, environmental fluctuations extrude genes which are less flexible in expressing a reproducible phenotype. Heredity does not predict the future but rather transmits the past. While future environments are presupposed to be similar to past ones, they cannot be exactly anticipated by the genome. Some genes are, however, more supple in achieving a phenotype fit to new circumstances. These tensions played out across generations is what natural selection is all about: heredity is specific to population and environs, especially the environment of past evolution. Still, any archetype (including, specifically, evolutionary stable strategies of behavior) was abidingly adapted to life in a past ecosystem.

Indeed, in some cases, elements of the environment were so stable as to have been phylogeneti-cally interiorized into the genome. Given time and stability, diversity converges upon the normative which converges upon the ideal. It is in this frame of thought that the example of the essential amino acids in the human diet comes to mind. We have lost the capacity to construct certain of these molecules even though our lives depend upon them. They have been so consistently available as foodstuffs for so long in the environment of our ancestry that our lineage has lost the capacity to anabolism them *de novo.* These features of the environment of our evolutionary adaptedness are — by means of evolutionary dialectics — now interiorized into our genome. Perhaps the best evidence of such curious interiorization lies in the fact that such deletion mutations induce little evolutionary consequence. The selection which accounts for most current gene prevalences took place in the past environment of evolution. This environment has substantially changed — in the blink of a Darwinian eye — with the rise of complex culture which constrains the genome in ways not anticipated in the Pleistocene environment of human evolution.

Therefore, studies of human behavior which do not vigorously consider these evolutionary parameters are comparable to Zuckerman's[22] early and elegant but erroneous assessments of 'normal' primate behavior as derived from his observations of creatures in captivity. One need not invoke the spirit of Rousseau to acknowledge the parallels between primates in a zoo and the enclosures of human nature brought about by contemporary society. Evolved tendencies are distorted in each. Behavior in the zoo is a property emergent from past selection in evolution. But, selection in the past environment accounts for much persistent human genomic structure and function. Yet the once predominant conditions of this past environment have changed rapidly with the rise of complex culture which increasingly encloses human nature.[23]

In any case, if current phenotypes can be identified as the robust expressions of genes which themselves have population prevalences higher than predicted by Hardy-Weinberg calculations, then the genes evolved via the past natural selection of inherently favorable characteristics. This is true, with only technical exception, no matter how pathologic may be the phenotypes now unfolding from the genes nor how elusive or subtle may be the appreciation of the advantages.

Still, if and when the thresholds of epigenetic vigor and high frequency are simultaneously surpassed, then the two major conditions of the deductive premises upon which evolutionary epidemiological reasoning is based are satisfied. Consequently, the gene locus must have evolved by virtue of beneficial characteristics expressed, at least, in the course of natural selection. This approach, inchoate in Allison's work in sickle-cell anemia, has been recently formalized as a more general system. Genetic loci of 'disease', both somatic and behavioral, can be assessed as to the likelihood of their having been evolved in the environment of their evolution on the basis of their advantageous characteristics in the struggle for existence.

3.1 A prototype in psychiatry: Manic-Depression.

(A) The importance of valid, reliable and common diagnostic categories.

For all the scientific and especially the popular disdain to which psychiatric theory and practice is sometimes subjected, its backbone of epidemiological research is surprisingly strong. Some of the most common, well validated and reliably diagnosed disorders of the human genome have been established within the field of psychiatry. In passing, it is useful to recall that validity and reliability are basic, if technical, terms widely used in epidemiology. The former expresses the mean-ingfulness of a given category of description and the latter expresses the degree to which such descriptions are made by independent observers.

Again, the high prevalence (as population polymorphisms) of such abiding genomic traits points to

intrinsic, if overlooked, positive characteristics that caused them to be so avidly retained by long-term and wide-spread natural selection. These genes and their phenotypic expressions can be said to be highly canalized.[24]

So far, only indirect, phenotypic descriptions of psychopathology have been firmly established. The era of direct, genotypic description is at hand. This era should prove interesting since some diagnostic categories thought to denote discrete diseases may ultimately prove to be mere phenotypic variants of the same etiological genes. Such genome equivalent through phenotypic 'co-morbidity' can only mask much higher aggregate genetic prevalence rates.[5,25,26] If so, the indices of their twin concordance, prevalence and natural selection will be all the higher.

Indeed, on closer examination it appears that several of the variant genes most common in the entire human genome express psychopathology (e.g., manic-depression, sociopathy and obsessive-compulsive disorder). Thus they have been marked Darwinian successes. Moreover, these same diagnoses are universal features of the human genome which evidence little, if any, ontogenic idiosyncrasies of epidemiology due to geographic ethnic, cultural, racial or other influences on the phenotype. Therefore, their Darwinian success was an enduring and universal feature of the evolutionary history of the structure and function of the genome of the entire species.

Still much important psychopathology can already be regarded as the product of natural selection. This is true even without recourse to the greater genetic frequencies which are necessarily involved in concepts of a broader spectrum of extended phenotypes. It is likewise true even without recourse to direct gene analysis. In the era of modem science it is easy to forget that gene characteristics and behavior can be quite usefully scrutinized without direct biochemical technology as the ingenuity of both Darwin and Mendel demonstrated so remarkably. In any case, indirect methods of epidemiology will remain the most useful approach to research in psychiatric research until techniques of direct gene studies are better validated.

A recent, well-designed program has generated indirect population genetics data highly (if unintentionally) amenable to reanalysis in the genetic terms of evolutionary epidemiology. The National Institute of Mental Health Epidemiological Catchment Area Program (US-NIMH-ECA) is an excellent example of highly reliable and valid multicenter data on mental disorders derived from a comprehensive, community-based U.S. sample.[27] The program analyzes data derived from structured interviews utilizing highly systematic diagnostic criteria in the best descriptive tradition established by Kraepelin.[28]

A strong example of how evolutionary epidemiological analysis belies any simplistic notions of 'disease' status can be appreciated with the reconsideration of bipolar disorder, i.e., manic-depression. Prevalence has been estimated at 0.6% to 6.0% depending upon the rigor with which the phenotype is defined. The benchmark ECA it was noted as carrying a lifetime risk of 1.2%.[27] More inclusive diagnostic schemes raise the frequency to some 6%. The former figure is widely accepted as reliable although the latter estimate may have greater genomic validity.

(B) The quasi-Mendelian character of Manic-Depression.

Twin concordance rates, adoptee studies and family risk studies have long suggested a strong genetic contribution in the manic-depressive phenotype.[29a] Even a highly conservative concordance estimate is that at least 65% of the phenotype of identical twins is due to direct genetic expression; moreover, concordance may well exceed 90%. The consensus view from non-molecular studies has emphasized the essentially Mendelian character of manic-depression.[29"]

More recent direct gene studies have begun to trace the chromosomal locale of operative geno-

typy. Such direct studies initially identified pedigrees consistent with autosomal dominance as the mode of inheritance.[30,31] The interpretation of these findings remain somewhat obscured by inconsistencies arising from the application of gene analytic techniques to categories of psychiatric diagnosis. These studies are complicated by terminological problems of 'lod-scoring' but are most promising. Moreover, initial linkage findings have not been sustained.

Nevertheless, more recent direct genomic analyses of bipolar pedigrees appear more promising.[32] While it is not yet clear how many genes are involved in manic-depressive phenotypy, evidence is consistent with an essentially Mendelian (oligo-genic) mode of transmission. There is little support for the notion it is a highly complex, multifactorial or additive trait.

(C) Implausibility of highly complex inheritance.

Quite apart from the question as to whether manic-depression is a Mendelian or even quasi-Mendelian trait, it is sometimes assumed to be a highly complex character which is a continuous or additive factor in genomic terms.[33] There is exceedingly little evidence this is the case.[17] It is true manic-depressive phenotypy constitutes a complex spectrum of phenomenology in a clinical sense. This is not at all the same idea that the trait is an additive trait continuous in the population.[34]

Moreover, this issue has long been a matter settled by the indirect analyses of family risk, adoptees and twins; the trait 'breeds true' along family lines independent of much environmental effect.[17] At the population genomic level, manic-depressive phenotypy is not evident as an additive factor as is, for example, height.[17] It is more consistent with oligogenic — quasi-Mendelian — models of transmission than with continuously variable traits. This is particularly clear where the phenotypes observed by degrees of relatedness have been mapped to Mendelian ratios.[29]

Further, continuous traits are evident in the population as a guassian single modal variation, or bell-curve, whereas polymorphisms are at least bimo-dal.[7] The human genome does not exhibit an obvious bell-curve smoothly linking manic-depressive phenotypy to modal norms. Instead, a strong J-curve is noted. The vast majority of individuals and families are free of manic-depressive phenomena but there are few lineages which genetically transmit manic-depressive traits.[29]

Finally, it is possible that on-going direct genetic studies may alter this picture with new and convincing demonstrations of a highly complex mode of transmission of manic-depressive genes. At this juncture there is no such critical mass of findings and available evidence supports the strong inference that manic-depressive phenotypy is the quasi-Mendelian expression of a few genes.

(D) Implausibility of non-Darwinian mechanisms as a primary factor.

With the inference manic-depressive phenotypy is broadly Mendelian in nature, questions next arise as to why these genes accrued well beyond putative mutation rate prevalence. That is, what may explain the preponderance of evidence which suggests manic-depressive genotypy is a popula-tiorrpolymorphism with selective advantage?

Population genetics offers several possibilities which can explain genomic polymorphisms beginning with the basic Hardy-Weinberg postulate that gene frequencies are stable in the absence of selective forces. The Hardy-Weinberg postulate is useful as a basis to determine aspects of the magnitude and directionality of changes even though assumptions intrinsic to it are not realistic. More realistic extensions of this postulate have been made. The classic selection model and the balanced polymorphism model which each include some elements of evolutionary change.

The standard selection-mutation equilibrium model assumes mutations come and go in a stochastic manner. This is largely the realm of evolutionary

error and inefficiency rather than innovation. Harmful mutations are removed by natural selection at some equilibrium with the occurrence of new mutations. Most traits of this type are not true polymorphisms as they are rare. The presence of mutant forms near the rate of mutation-selection equilibrium is an important way by which genetic diversity is maintained. Such diverse forms may gain advantage in the event of environmental fluctuations as exaptations, but are otherwise merely unfortunate medical liabilities.

Mutation-selection is the default explanation for almost any medical condition linked to genetic etiology. Often rightly but sometimes quite wrongly, an epigenetic disease is presumed to be a non-adaptive, random mistake until proven otherwise. Generally, epigenetic medical conditions due to this driving force exist in the population at low levels approximating the mutation rate itself. Still, equilibrium explains a wide range of rare medical-genetic ailments which occur near mutation rate prevalence, e.g., many deleterious conditions such as albinism, dwarfism and the like. These syndromes are of narrow biomedical or anthropological interest. They do not cast much light on evolutionary process in any but a stochastic sense.

The balanced polymorphism model posits that differential selective advantages exist between individuals with as a function of alternative alleles and zygotic condition. Here certain variant alleles are maintained in the genome at frequencies above mutation rate due to heterozygotic advantage, viz., sickle-cell anemia. Epigenetic medical conditions due to this driving force can attain prevalence well above mutation rate frequency but, thus far, have been demonstrated for only a few traits. Apart from these examples of Darwinian selection, other deterministic or stochastic forces can account for polymorphisms.

i. Neutral Selection.

It has been noted many genetic variations accrue not due to intrinsic Darwinian advantage but because they are proximal to highly advantageous genetic loci. They are, hence, far less likely to be shuffled randomly by the action of polymerases in meiosis. Thus such genetic variants quite simply defy the Mendelian principle of independent segregation. A gene proximal to such an advantageous locus can be swept along in the selective success of the heuristic trait. This accummulation is incidental but can be significant. The accummulation can be particularly significant if the selected locus is highly advantageous, the incidental locus carries little net selective load and the molecular distance separating the two is small. This has been termed "neutral selection" insofar as the incidental locus is typically neither of much benefit or liability.[21]

Neutral selection is difficult to delineate in the absence of detailed knowledge of molecular physiology. It is, however, less likely a causal factor in the persistence of conditions which are clearly deleterious. Should manic-depression be even a classically Mendelian single major locus effect, it might yet have accrued randomly. The point has been made that it is remotely possible that, were such a deleterious gene adjacent to a locus encoding for a major fetal induction (e.g., the notochord or heart), it could attain high, even universal genomic prevalence.[35] Currently, there is, insufficient evidence to prove or disprove the role, if any, of neutral selection in the maintenance of manic-depression at a high level of worldwide population prevalence. However, no empirical evidence demonstrates that manic-depressive genotypy is sustained by neutral selective events.

ii. Genetic Drift and Founder Effects.

Non-random events can produce non-Darwinian results. Small populations can, upon adaptive radiation within new environs, account for high prevalences of genes. The relatively low selective force operative in an unexploited ecosystem coupled with aspects of subsequent inbreeding of the founding stock can induce non-Darwinian fluctuations in genetic frequencies. Likewise, analysis of non-probabilistic genetic samples can

misrepresent the total population. Early medical-anthropological research often relied on non-random opportunistic or judgment sampling. Such sampling renders invalid any statistical analysis based on an assumption of random distributions. If for convenience one were to sample the blood of volunteers at a sickle-cell clinic the prevalence rate obtained could not be usefully ascribed to the universal population. Such events have been advanced in the explanation of rare, idioethnic syndromes (e.g., Tay-Sachs Disease or G-6-PD).

Again, it is difficult to disprove the possibility of this as a factor contributing to the prevalence of manic-depressive genotypy. However, the manic-depressive genetic spectrum has little variation in prevalence world-wide and in no sense appears as an idioethnic entity.[36] As a universal feature of the human genome, it is thus implausible to attribute manic-depressive phenomena to genetic drift or related processes.

iii. Phenocopies.

Phenocopies of manic-depression acquired in the course of ontogenic development may confound genomic analyses. This is a particular problem when the environmentally mediated form is clinically homologous with the classical epigenetic syndrome. Such environmentally engendered clinical equivalents are rare as is evident from studies of twin concordance and adoption outcome. The vast majority of cases of manic-depression are due to familial genetic risk rather than environmental acquisition.[16]

In practical terms, manic-depressive phenocopies are limited to a small set of neuromental dysfunctions in the brain. These dysfunctions, in turn, typically arise as organic impairments in centers which modulate affective neurology.[37,38] Here there is a predictable complement of etiogenic factors ranging from trauma, toxicity, infection, neoplasia, inflammation and the like.[38a]

However, in clinical terms organic-affective syndromes are relatively uncommon. Traumatic brain injury, specifically those involving the frontolimbic cortices, is the most frequent source of non-genetic syndromes which are readily mistaken for epigenetic manic-depression.[39] These constitute less than one percent of the total population prevalence of manic-depressive phenomena. Thus, syndromes acquired in the course of development are not, in evolutionary terms, a significant factor in the population prevalence of manic-depression.

iv. Mutability.

Excessive mutability is a further source of high population prevalence for deleterious genetic traits, as an extreme form of the mutation-selection equilibrium. Genes differ as to their intrinsic propensity to mutate, largely as a function chromosomal conformations some of which render loci susceptible to disruption by electromagnetic radiation or other factors such as oncoviri. A genetic locus which is prone to unusually frequent mutation will exist at a relatively high equilibrium rate.

It is, with the paucity of current data as to mutation rates of specific human loci, difficult to exclude the possibility that manic-depression is sustained at a high population prevalence due to intrinsically common etiogenic mutation. On the other hand, there is no available evidence that genes etiogenic of manic-depression lie at loci prone to high rates of mutagenesis. Here again a non-Darwinian causal factor remains possible, if unlikely.

v. Assortative Mating.

The non-random matings of similar parental stocks is not, strictly speaking, an extra-Darwinian mechanism. It is instead simply a departure from the Mendelian and Hardy-Weinberg postulates of random breeding. However, clinicians sometimes offer assortative mating toward an explanation for the high prevalence of certain disease traits.[34] In fact, the non-random breeding by similar types does not alter population rates of genes, per se.[7]

More precisely, assortative mating can account for variations from expected ratios for some Mendelian characteristics, e.g., recessive homozygotes. This can be further complicated by sampling errors. Assortative mating does not alter the totality of genomic alleles. Rather, as more recessives are sequestered amongst themselves, there are fewer phenotypically obscured by dominants. The population is partitioned or stratified to some phenotypic degree but the overall genotypic ratios are retained. When blue-eyed parents breed preferentially, there are more evidently blue-eyed children bus not more genes for blue eyes in the population as a whole. Recessive traits can thus achieve greater degrees of phenotypic expression without increasing in genomic proportion.

Affective disorders, including manic-depression, subsume considerable assortative mating.[16] This is a significant clinical and research fact and one which has not been exhaustively researched. Clearly, both direct and indirect epidemiological studies must carefully control for assortative matings to maintain valid statistical power. Likewise, clinicians must often contend with complex pedigree dynamics with manifold risks. However, assortative mating cannot account for the prevalence of a genetic trait well beyond its mutation rate threshold. Therefore, it is not a causal factor in the frequency of genes in the manic-depressive spectrum.

There are reasons, then, to move beyond non-Darwinian explanations in a search for the causal factors for the high frequency of genes expressive of the manic-depressive phenotypic spectrum. It is possible and, indeed, likely these genes accumulated in the environment of evolutionary adaptation due in no small part to selective advantage. This possibility can be approached by evolutionary epidemiological inference.

3.3 Calculation of an estimated index of selection for manic-depression.

The manic-depressive phenotype is strongly genetic in a fundamentally Mendelian sense and very common at the population level. By the most conservative estimates its degree of twin concordance of at least 65% with prevalence is at least 0.5% of the human genome world-wide. Taken together, these facts lead to the highly conservative deduction that bipolar disorder is some three hundred times more common than might be calculated from Hardy-Weinberg equilibrium predictions alone:

Calculation 1: (P/E = S) = [0.325]/[0.001] = 325

(Where 'P' is prevalence [adjusted by concordance, oligozygosity, etc., 0.5 x 65%)] and where 'E' is the frequency [known or estimated by Hardy-Weinberg law] then'S' is the coefficient of natural selection). N.B.: Oligozygosity [Z] reduces the selection index by a factor of S/Z where Z is the total constituent loci.

Moreover, with the higher prevalence figures emerging from the ECA (1.2%) and with an extended clinical spectrum (and the higher rates of twin concordance this such a spectrum denotes, i.e., 90%), a more realistic estimate is that the manic-depressive phenotype is beyond one thousand times more common than it would be in the absence of the sustained operations of natural selection:

Calculation 2: (P/E = S) = [1.2]/[0.001] = 1200

If a broader range of psychiatric conditions are, indeed, phenotypic variants of manic-depressive genotypy then frequency may be as high as six percent. This, with a high concordance rate, would sustain a genetic prevalence some six thousand times mutation rate levels alone:

Calculation 3; (P/E = S) + [6]/[0.001] = 6000

In any case, these genes so greatly exceed their predicted rate prevalence as to be best explained with reference to their promotion in the operations of natural selection sustained in the environment of evolutionary adaptation.

3.4 The deductive imperative: if so, then what, when, where, why and how.

Clearly, evolutionary epidemiology is a simple but powerful instrument of medical anthropological investigation based on understanding the term 'prevalence' as used by epidemiological geneticists is, in essential ways, equivalent to the concept of 'frequency' as used by evolutionary geneticists. Given the importance of these terms it is useful to review their technical meaning. Prevalence refers to the rate of existence of a disease (gene) within a population. Frequency similarly refers to the rate of existence of a gene (disease) within a population. These two concepts can be melded in a rigorous fashion to deduce a number of remarkable insights concerning the ultimate origin of genes now predisposing to phenotypic pathologies of body and mind. Darwinian evolution is, after all, a reflection of past intergenerational increases in the demographic representation of healthy reproductive lines and reductions in unhealthy ones. Darwinism offers a rare longitudinal rather than a common cross-sectional perspective.

As noted earlier, Allison's[13,14,15] work on sickle-cell anemia is the founding contribution to what is now emerging as a more systematic approach to diverse questions regarding the evolved basis of epidemiologically prevalent genetic illness. But sickle-cell anemia is not a universal morbidity of the human genome. It is, rather, a special gene system which arose in special environments. It is, to some extent, thought of as an idioethnic curiosity of limited medical interest as, again, Africans have it, Laplanders do not. Moreover, it is essentially a disease of somatic, as opposed to behavioral, pathophysiology. Still, sickle-cell anemia provides the conceptual foundation on which might be built a more considerable research program.[20]

Though the full theoretical and practical implications of such evolutionary epidemiological analyses are only now gaining the attention of medical researchers, the work concerning sickle-cell anemia was the first demonstration that carriers of 'disease' genes were endowed with superior Darwinian fitness in certain ecosystems. The prevalence of what had been thought of as simply 'bad' genes was inexplicably high in such ecosystems. Carriers were, it was soon learned, resistant to the ravages of malaria. The malarial organism and the human blood system had coevolved in the environment of evolutionary adaptation. Sickle-cell anemia, however pathological it is today, was selected into the human genome.

More simply and generally, genes common enough to have evolved by means of natural selection can have done so only by virtue of advantages conferred to lineages which carried such genes even if such genes now express a degree of phenotypic disease.

So it is that techniques of evolutionary epidemiological analysis elucidate whether genes which now express pathological phenotypes nevertheless surpass both their rates of mutation and evolutionary equilibrium and, if so, were promoted by naturaf selection. In some cases they appear to exceed these expected rates by orders of magnitude.

Yet often such genes now seem clearly and rather tightly linked to pathological expression. This seeming paradox that something so 'bad' disappears in light of what we know about the genotypic and phenotypic aspects of genomes in changing environs. Selective parameters shift when an evolutionary stable genomic strategy experiences a new or changed environment. This is why the range of phenotypic reaction emerges as a critical factor in selection as phenotypic capacities are stretched to adapt in the new ecology.

There is, of course, a limit to the amount of genetic stretch in individuals and populations. Less flexible genes are selected against. What was healthy can be made ill. Only such a phenomenon might explain the world-wide excess prevalence of 'disease' genes noted in biomedical pathology. Just as sickled blood cells are no longer needed for resistance to malaria in environs with effective antimalarial agents, culture can also marginalize the value of other somatic and behavioral gene

polymorphisms. It has become harder — in complex, large-scale industrial cultures — to healthfully express some genes which were rather sublime in the more intimate kinship foraging bands and low population density of the paleolithic. The range of phenotypic reaction intrinsic to a genome cannot always or readily adapt to new developmental demands.

Within this framework, much epidemiological data can be reconsidered from an evolutionary genetics standpoint. Such reconsideration will lead to fresh implications about the ancient origins, ongoing processes and current phenotypic modulation of 'disease' genes. There is, then, a vast amount of extant and high quality genetic epidemiological data which will yield new clinical knowledge upon consideration from an explicitly evolutionary point of view.

The body of genetic epidemiology accumulated over the past century of medical studies is quite amenable to reformulation into terms appropriate for analysis by the theorems of population genetics. Of special interest in this considerable body of primary data are the many genetic polymorphisms which evidence significant population prevalence. Studies which synthesize evolution and epidemiology will repay any careful analysis which to clarify how natural selection on these variant alleles. Such studies may not only demonstrate some clinical syndromes to be epiphenomena of highly evolved forms, but will also, necessarily, stimulate new ideas and insights in paleoanthropology.

In any case, such a program of research will eventually expand medical understanding of the theoretical and clinical consequences of evolutionary epidemiology. Central to this expansion is the fact that several important gene systems now expressing 'pathological' phenotypes had — in a Darwinian sense — intrinsic positive qualities that account frequency at the high rates observed today. More immediately, several essential tasks are to demonstrate whether a variety of 'disease' genes:

1. Accrued, via natural selection, as advantageous population polymorphisms.

2. Retain a normative essence which conferred selective advantage in the past.

3. May respond to novel treatments which evoke healthy if latent phenotypies or reduce developmental reactions etiologic of pathologic phenotypy.

3.5 Further Possibilities.

As expanded upon in chapter four, the deduction follows that Darwinian advantages inhered to conditions which surpass specific thresholds of epigenesis and prevalence. Initial attention in general medicine has already turned toward the reassessment of common 'inborn efrors of metabo-lism' (whether Mendelian dominant, recessive, polygenic or mixed). In some cases, Garrod's fine turn of phrase may need to be amended with respect to other highly evolved gene systems which, as has been noted with sickle-cell, cannot be said to be truly erroneous. Cystic fibrosis and the anomalies of alpha-1 -proteases are obvious candidates genes in that they are not only common, but that it can be readily postulated that they conferred resistance to infectious diseases in prehistory.[3] Similarly, further examples are emerging from a range of medical specialties. To name but a few, one notes rheumatology (HLAtype mediating various health liabilities), ophthalmology (myopia, presbyopia), neurology (innate 'wiring' syndromes such as dyslexia and autism) and endocrinology (humoral anomalies notably certain thyroidities) are all specialties now keening on the possibility that some genetic diseases must have definite, if still obscure, advantages.

The clinical and theoretical importance of evolutionary epidemiology extends to not just the physical aspect of medicine, but also to the psychological. The psychiatric genetic epidemiology reviewed in chapter two, collated from indirect studies of the genome as well as from newer direct studies, points to a robust genetic basis for and significant, spe-

cies-general expression of manic-depression. Thus several important psychiatric syndromes, notably manic-depression, likely surpass thresholds of epigenetic frequency.

Meanwhile, radical shifts in sociodevelopmental ecology at the genomic level can induce extensive phenotypic reactivity, e.g., epochal events such as the agricultural or industrial revolutions. Radical shifts from the environment of evolutionary adaptation predispose to conditions of mismatch with the new selective milieu. Reactivity to such shifts can be a factor important in the etiology of epigenetic disease. Thus, deleterious phenotypes now expressed by genes linked to manic-depression may primarily derive from new mismatches between ancestral and current environments rather than an intrinsic 'inborn error of metabolism'. Clinical applications of evolutionary epidemiology therefore provide an opportunity to both better understand and better treat disease states recently emergent from genes that had long been adaptive.

The phylogenetic accumulation of what now constitute etiogenes will be much clarified as the Human Genome Project moves forward.[40] Likewise, such a project shall clarify much more the epidemiology of diseases (both genotypic and phenotypic). The time is nearly at hand when it will be feasible to routinely assess whether a wide range of genes linked to contemporary pathophenotypes were, by the criteria of evolutionary epidemiology, selected into the human genome. Already, it is clear at least some contemporary pathologic syndromes are expressions not of genetic error but of past advantageous selection stretched by the current environment beyond the plasticity of their healthy range of phenotypic reaction. Such knowledge will constitute an unavoidable temptation to therapeutic adventurism and misadventurism. It is important any genetic therapies not assume disease is simply disease. Certain polymorphisms of at least possible utility are at risk of misguided therapy[1]. Surely other gene systems now notable only as causes of individual disease will come to be seen, in the full light of evolutionary epidemiological analysis, as fundamentally salubrious characteristics. Inferences from evolutionary epidemiology will further revise psychopathologic theory and practice as pertains to other syndromes, as well. The deductive methods of evolutionary epidemiology suggest that natural selection promoted genetic lineages now expressing:

1. Sociopathy;
2. Depression;
3. Anxiety-Panic Disorder;
4. Obsessive-Compulsive Disorder;
5. Dyslexiae; as well as the biological underpinnings of some;
6. Personality Disorder;
7. Substance Abuse Syndromes;
8. Psychodynamic Conflicts; **and**
9. Various isolated traits of cognition, personality or temperament. *c8*

ABSTRACTS & EXTRACTS...

van der Kolk B.A.: The psychobiology of posttraumatic stress disorder. *Journal of Clinical Psychiatry,* 1997;58(9):16-24.

Abstract: This review summarizes the current state of our knowledge of the psychobiology of posttraumatic stress disorder (PTSD). People with PTSD develop an enduring vigilance for an sensitivity to environmental threat. They have difficulty in properly evaluating sensory stimuli and responding with appropriate levels of physiologic and neurohormonal arousal. The inappropriate mobilization of biological emergency responses to innocuous stimuli is mirrored psychologically in an inability to properly integrate memories of the trauma and in a fixation on the past. The biological dysregulation of PTSD can be measured on physiologic, neurohormonal, immunologic, and functional neuroanatomical levels. The developmental level at which the trauma occurs affects the nature and extent of psychobiological disruptions. The availability of neuroimaging for documenting structural and functional abnormalities in PTSD, has opened new ways for understanding the neuronal filters concerned with the interpretation of sensory information in PTSD. These studies have produced a number of unexpected findings, which may alter how we conceptualize PTSD and which may force us to re-evaluate appropriate therapeutic interventions.

Price, C.S.C.: Conspecific sperm precedence in *Drosophila. Nature,* 1997;388:663-666.

Abstract: Traits that influence the interactions between males and females can evolve very rapidly through sexual selection or sexually antagonistic co-evolution. Rapid change in the fertilization systems of independent populations can give rise to reproductive incompatibilities between populations, and may contribute to speciation. Here I provide evidence for cryptic reproductive divergence among three sibling species of *Drosophila,* that leads to a form of postmating isolation. When a female mates with both a conspecific and heterospecific male, the conspecific sperms fertilize the vast majority of the eggs, regardless of the order of the matings. Heterospecific sperm fertilize fewer eggs after these double matings than after single matings. Experiments using spermless males show that the seminal fluid of the conspecific male is largely responsible for this conspecific sperm precedence. Moreover, when two males of the same species mate sequentially with a female a different species, a highly variable pattern of sperm precedence replaces the second-male sperm precedence that is consistently found within species. These results indicate that females mediate sperm competition, and that second-male sperm precedence is not an automatic consequence of the mechanics of sperm storage.

Shadmehr, R. & Holcomb, H.H.: Neural correlates of motor memory consolidation. *Science,* 1997;277:821-825.

Abstract: Computational studies suggest that acquisition of a motor skill involves learning an internal model of the dynamics of the task, which enable the brain to predict and compensate for mechanical behavior. During the hours that follow completion of practice, representation of the internal model gradually changes, becoming less fragile with respect to behavioral interference. Here, functional imaging of the brain demonstrates that within 6 hours after completion of practice, while performance remains unchanged, the brain engages new regions to perform the task; there is a shift from pref rontal regions of the cortex to the premotor, posterior parietal, and cerebellar cortex structures. This shift is specific to recall of an established motor skill and suggests that with the passage of time, there is a change in the neural representation of the internal model and that this change may underlie its increased functional stability.

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[1] Attributed to Kupfer, David: address to American Psychiatric Association, San Diego, CA, May, 1997. In *Psychiatric News,* July 4,1997, page 14.

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