In I.I. Gottesman and J. Shields, *Schizophrenia and Genetics: A Twin Study Vantage Point*. New York: Academic Press, 1972. Pp. 367–415.

A CRITICAL AFTERWORD

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Here we have a definitive work, a magnum opus, a beautiful book indeed. It is an absolute *must* for theoreticians and investigators in clinical psychology, psychiatry, sociology, personology, and behavior genetics. It is also, I venture to suggest, required reading for clinical practitioners who feel the need to know something scientific about their patients, although I am aware that in some circles such an impulse is an aberration, viewed almost as a perversion.

This fine book shows what *can* be accomplished by a couple of first-rate intellects when they apply brains, drive, efficiency, thoroughness, and methodological sophistication to a problem, even so fuzzy and intractable a problem as the genetics of schizophrenia. I am pleased to have been invited, along with such a distinguished European psychiatrist as Dr. Eliot Slater, of whose early work at Maudsley the authors' project is a continuation, to comment on this book. And I am proud to think that when coauthor Irving Gottesman was studying for his doctorate at Minnesota in the late 1950's, I perhaps had some small part, directly or indirectly, in shaping and stimulating his mind. But then, he began his career as a physics student, a fact I suspect is relevant. (I am unfamiliar with James Shields' early vocational choice, but I'll take an even bet it wasn't clinical psychology.) There are certain "Minnesota habits of thought"—including some that I am not unwilling to label "prejudices," as I believe them to be good ones!—that are easily discerned herein. It is a pleasure to see a work product like this one emerging partly from one's academic subculture.

I take it to be obvious that the publication of this book "settles" a long-debated question, to wit: Is there something—a fairly "big" something—genetic about schizophrenia? Some of us may have become a trifle bored with the persistence of that debate over recent years, given the sizable and largely consistent research literature summarized and criticized so ably by Gottesman and Shields in Chapter 2, and I would like to urge, in

the light of the present volume, that we now bring that phase of the debate to its long-deserved close. Nothing but American social-science prejudice plus "establishment psychiatry" brainwashing (given the usual dash of plain muddleheadedness) can, I think, lead anyone who has read this book to persist in strong doubt as to the prime importance of genetic factors in schizophrenia. Hence I should now be inclined to adopt Otto Neurath's maxim in the Vienna Circle, when (quoted to me by my friend and philosophy colleague Herbert Feigl) he opined, "Feigl, you know, one can seriously discuss only with those who are in the club." For my part, I am no longer interested in a debate with anyone who continues to believe that we are all born with equal talents for developing schizophrenia, and who is prepared to exercise unlimited theoretical ingenuity (and counter-Bayesian defiance of the reasonable prior probabilities!) in "explaining away" all genetic evidence by this or that *ad hoc* hypothesis (see *infra*). Let us henceforth consider this psychiatric variant of the *tabula rasa* doctrine, which, by the way, never did have anything impressive going for it, to have been now refuted; and let us concentrate our efforts on devising methods for answering the next big questions, namely: (1) What behavioral dispositions (tending to schizophrenia) are inherited?, (2) How (polygenic? one "big gene?" what penetrance?) are they inherited?, (3) How are these inherited dispositions *acted upon* by life experiences to yield schizophrenia versus compensated schizotypy?, and (4) What is the biochemical or neurophysiological *substrate* of those (molar) behavior dispositions?

The second of these, being a "statistical" question in population genetics, may perhaps be researchable without solving any of the other three, although one may be permitted to suspect that for a "geneticist's nightmare" (Neel's characterization of diabetes mellitus), like schizophrenia, this atheoretical development could turn out to be unusually difficult. For example, if, as the authors' MMPI data on discordant MZ twins discouragingly suggest, a molar-level, social-learning-mediated phenotypic indicator such as the schizotype's verbal response to a personality inventory item is just too far removed from the schizogene(s), too many links getting into the causal chain between DNA and laryngeal twitches, then we must "move further back," probably to *non*-behavioral indicators (belonging to the endophenotype) in order to diagnose the subclinical condition with sufficient accuracy to test competing genetic models against one another. I hope this is not the case, as it would (almost) put the "molar-level" behavior geneticist out of the schizophrenia business. But it might be so. We psychologists may have to say to the neurochemists, brain-stimulators, etc., "Look, Gottesman and Shields have now gone as far as we can go while relying on 'psychological' indicators of the schizoid genotype. It appears that no psychometric refinements or souped-up objectification-*cum*-quantification of the Mental Status Examination (or life history) will *ever* be 'valid' enough to do appreciably better. We have skimmed the cream; we are near the research asymptote. Until you can chemically identify the chromatographic Schizotypal

Purple Spot or the schizotaxic single-neurone's hypokrisia, we are at an impasse. Choice between genetic models is, until further notice, not feasible." I consider this molar-level impasse to be a possibility, but in what follows I shall set it aside in favor of more optimistic outcomes.

Even genetically oriented readers lacking the usual (American) social-science bias may have been shocked by my remark *supra* that the "pure environmentalist" theory never did have much of anything going for it. Since this sounds rather high-handed, and since the Gottesman-Shields data (despite their valiant efforts to squeeze blood out of the environmentalist turnip) lend essentially zero support to some of the received theories (e.g., that mother's mental health is so much more important than father's; that having a twin is, per se, a schizophrenogenic factor because of the alleged identity-mixups; that lower social class is primarily a *cause*, rather than an *effect*, of schizoid personality), I should say a few brief words by way of defense of so strong a statement.

1. The initial impetus for a family-dynamics emphasis in schizophrenia theory was largely *theoretical*, to wit, conceptual extrapolation from the Freudian and post-Freudian psychodynamics. (Among American psychologists the environmentalist bias of Watson and his behaviorist successors potentiated this influence.) There is, of course, nothing wrong with relying upon theory to begin one's understanding of a puzzling domain of phenomena, provided the theory is well-corroborated and that it really speaks, without undue ambiguity, to the facts. Further, if—even given those two conditions—the going theory is used to *exclude* a class of factors (as the alleged psychodynamics have been used in preempting the etiological field so as to rule out or down-play genetics) there must be some plausible showing that the received theory is "complete" and that its logical form, content, and *quantitative (parameter) assignments* leave no room for the set of competing causal factors thereby excluded. It should be obvious that these conditions for "exclusionary use" of sociopsychological theory have never been met, or even approached at any time during the entire history of clinical and scientific research on schizophrenia. I am somewhat embarrassed to be writing down these elementary methodological truths, but the intellectual habits of my profession regrettably necessitate it.

As to the Freudian and learning theory influences on extreme environmentalist views of schizophrenia, two comments will suffice, (a) While I myself accept a rather large portion of it, honesty requires admission that the Freudian theoretical corpus remains, three-fourths of a century after its inception, largely uncorroborated (and, on its *clinical* side, as a helping mode, increasingly in disrepute); and (b) The question of "who falls ill" is a learning-function *parameter* question, not a question of the psychosocial *contents* of what is learned—a methodological point on which Freud himself was clear (and, hence, a lifelong "constitutionalist" even as regards the psychoneuroses). The received "laws" of, e.g., object-cathexis or of secondary reinforcement can, of course, be accepted

without thereby settling anything whatever as to the relative potency of genes and early life history on the parameters that play crucial roles in those psycho-dynamisms or learning functions. It really should not be necessary to explain this but, alas, it is.

2. A second powerful influence was the (impressionistic) experience of psychotherapists in working intensively with their schizophrenic patients. I myself can testify to this influence, as a practitioner who has spent thousands of hours trying to help (sometimes successfully, I believe) schizoid and schizophrenic patients by psychotherapeutic means. I do not dispute the "raw data" that so impress clinicians of environmentalist persuasion, although I believe them to be somewhat overdone at times. My schizophrenic patients seem to talk, feel, and think in psychotherapy pretty much the same as those treated by antigenetic helpers. But these "data" are *almost completely ambiguous* as to etiological interpretation. I find it puzzling that so many American psychotherapists fail to understand this methodological point. *Consider*: A schizophrenic patient tells me (and/or acts it out repetitively in the transference) that "Mother—the old bitch—never liked me, she always preferred my brother Seydlitz." If I encourage him, he then "documents" this generalization from his childhood by narrating several pro-Seydlitz, antipatient episodes of maternal behavior. *What does this tell us about schizophrenic etiology?* For a critical mind, next to nothing. The relative importance of contributions by the following causal relations to such intratherapeutic narratives is, of course, simply impossible to assess on the basis of therapy-session evidence.

a. Mother preferred Seydlitz, rejected patient, thereby made him subsequently schizophrenic.

b. Patient got the schizogene from mother (a compensated schizotype of the battle-ax variety) and she preferred Seydlitz (because he didn't)—although this maternal preference played no causal role in the patient's subsequent illness.

c. However mother really behaved to Seydlitz versus patient, the latter (due to his genetic schizotypy) overreacted to all "aversive social inputs" and selectively misperceived things as a child.

d. As an adult, having decompensated, the patient does not now recall accurately what he may have perceived accurately at the time.

e. The patient learns to narrate battle-ax mother episodes because such therapy behavior is what his environmentalist therapist reinforces in the sessions.

f. The therapist selectively remembers these kinds of episodes because of his theoretical prejudices.

Only the most egregious naiveté (not to say arrogance about one's clinical discernment and "factor-unscrambling" powers) could enable a psychotherapist to deny the possibility of these factors operating to produce the received impression of how bad mothers create schizophrenics. In the aggregate, they reduce the *evidentiary* value of one's therapeutic experience to almost nil. *Point*: *The main empirical source of strong*

environmentalist views of schizophrenogenesis was the experience of psychotherapists, and this experience is methodologically next to worthless as to the disputed issue.

3. A third influence, stemming from more sophisticated environmentalists' recognizing the shaky evidentiary status of therapist impressions, consists of systematic, experimental and quantitative file-data research on schizophrenic perception and learning, social class, community isolation, intrafamily dynamics, etc., in an effort to objectify the therapist etiological impressions. Unfortunately, despite many ingenious efforts to smuggle real life into the laboratory, this research suffers from the same kind of causal-arrow ambiguity present in therapist impressions. It is, for example, a relatively pointless enterprise to investigate whether the mothers of schizophrenics "act differently" toward them than toward their nonschizophrenic sibs; or to show that future schizophrenics often do badly in intelligence tests, or flunk fractions; or that schizophrenics tend to be socially isolated or to live in neighborhoods of such-and-such kinds. Such correlations are predictable, of course, from a *wholly* genetic theory, or a *wholly* environmental theory, or *any intermediate mixture* of genetic/environmental emphasis. What then is the point in conducting such investigations?

If the preceding destructive analysis is substantially correct, it is inappropriate for behavior geneticists to adopt a defensive posture *vis-á-vis* the received psychosociodynamic doctrine—to stand on the scientific streetcorner asking timidly, "Who will buy my violets?" The received doctrine stood on very shaky foundations from the beginning. To repeat my challenging remark *supra*, it never did have much going for it—except the zeitgeist. In fact, if one were going to rely on "general background knowledge" and "extrapolated theory" in his personalistic assignment of prior probabilities to etiological notions about mental disorder, the *prima facie* case goes rather the other way—given the massive body of evidence, in both humans and animals (not to mention the folklore of animal breeders, surely admissible in evidence if we admit psychotherapist folklore?) that genes play a role in determining a variety of the individual differences found in any species of animal. One could, of course, have said this with reasonable assurance from the extrapolative armchair. Can it plausibly be supposed that while genes largely determine species characteristics, and mice show pronounced strain differences in dominance behavior, and the Basenji dog breed forms a weak super-ego compared with the spaniel, and the determination of human intelligence is (conservatively) at least 50% genetic—still, differences in potential for major mental breakdown have nothing importantly genetic about them? Why on earth would anyone have bet on such a proposition in the first place?

But enough of polemics. I repeat, we should take the Gottesman-Shields collaboration as a dispositive closing to a discussion that has gone on quite long enough. The burden of proof has been sustained, and from here on it should be shifted to the opposition. He who alleges a particular class of life-history determiners now has the

burden; and he who denies that heredity plays a major etiological role bears a heavy burden indeed. Meanwhile I attempt to dissuade my Minnesota colleague Gottesman from lecturing on the theme, "Genes have a lot to do with schizophrenia." It is too late in the day for that lecture topic. Better he should now lecture on, e.g., "Why Gottesman, Shields, Bleuler, and Co., are betting on a polygenic theory of schizophrenia," and "What evidence shows that Slater, Heston, Meehl and Co., are wrong in pushing a monogenic theory." That is the kind of question worth our serious attention henceforth!

My colleague Professor Gottesman did not ask me to "review the book" in this afterword, but rather to express my overall evaluation, to raise questions for future research, to "needle" the authors wherever I had methodological stomachaches about their design or argument, and—he seductively added—"put in whatever of Meehl's current ideas you think appropriate." Having got some antienvironmentalist polemics out of my system, these things I shall now (briefly and, as a result, perforce a bit dogmatically) proceed to do.

The methodological merits of this work are so clear as to require nothing more than mention here. Among the most important are the care in ascertainment of cases; the clear definition of a population; the accurate determination of zygosity; the tracking down of officially "normal" cotwins; the taperecording of interview sessions; the use of an objective personality test (having respectable evidence in the research literature as to its construct validity); the reliance on blind diagnoses by several expert clinicians; the fact that these clinicians varied widely in their conception of schizophrenia, their etiological persuasions, and their national origins; and the combination of these clinical judgments to form a "best available criterion" for concordance analysis. This on the empirical front, to which one must add the authors' thorough knowledge of the work of their great (and not-so-great) predecessors, their (so rarely found!) fusion of criticality and openness, and their ingenuity in "slicing the pie" of data with various competing hypotheses in mind. I shall make no further remarks on these admirable features, more detailed praise being surely a presumptuous gilding the lily.

At the risk of obscuring the forest with some rather small trees, I present comments and questions in the order they are raised by a reading of the text, expanding with some discussion of my own views here and there. I trust that some of the minor "criticisms"—I simply *have* no major ones—will not appear nit-picking. They are meant as gentle prods to alert the reader that a *caveat* is perhaps in order.

In Chapter 1 a niggling comment: I could wish the authors had not described this fine investigation as an "experiment," a terminology I think better employed, as in the physical and biological sciences, to mean a more controlled situation in which the investigator imposes fixed values of certain variables upon a (relatively) isolated system, and "at his will" manipulates the independent variables of interest.

In their reference to Seymour Kety's review of the failures to date in the search for a specific biochemical lesion, the authors assert that "the frequency of methodological errors and technical limitations prevented finding the needle in the haystack." I would put it otherwise. While these errors and limitations were responsible for investigators' mistakenly supposing they had found the lesion, what presumably "prevented" genuinely finding it—assuming *arguendo* that it exists—would be the very fact of its *being* "a needle in the haystack," i.e., no one knows what kind of biochemical aberration he should be *looking for* in the CNS. One of the functions of an integrated theory of schizophrenia—including a highly speculative one like my own—is to suggest to workers knowledgeable in neurochemistry what general *kind* of substance ought to be involved in order for it to produce the kind of neuro-integrative ("schizotaxic") defect that such theories postulate. A theory that does not attempt, however conjecturally, to sketch in the causal chains leading from a mutated gene to the many-steps-removed clinical phenomenology of schizophrenic disorders just does not say enough about what sort of thing a Seymour Kety might profitably look for. Ever since Kety's important review (and I hasten to add that Dr. Kety himself is not the least bit responsible for this) "sociotropes" have had a tendency to treat the biochemical search problem as though there were some kind of huge statistical population of biochemical culprits, such that the misleadingly positive studies properly criticized by Kety can somehow be viewed as samples from the "biochemical etiology domain." On this strange view, the more negatives you pile up, the less probable it becomes that a positive exists! But we are of course not estimating some hypothetical parameter from a universe of biochemical agents. Rather, we are in the sad state of wondering whether there *is* one schizospecific aberrated neurohumor, an "existential" question that surely has no appreciable light shed upon it by discovering that schizophrenics do not really have an alleged thyroid deficiency or that a reported difference in blood chemistry is an artifact of bad institutional hygiene or peculiar dietary habits. *Point*: If there were some specific neurohumoral substance X whose presence, absence or molecularly aberrant form constituted the first link in the endophenotypic causal chain underlying schizoidia (and, hence, predisposing to schizophrenia), it would not be *expected* that anything other than this substance would turn out to be a specific diagnostic differentiator, given adequate controls.

When they point out that schizophrenia is, by usual geneticists' standards, a remarkably common genetic disorder (compared, say, with the incidence of the many Mendelizing varieties of mental deficiency), being more frequent than these by several orders of magnitude, I wish they had hinted that this extremely high incidence of the clinical syndrome itself ought to alert the geneticist to the possibility that it might be rather "special" or "different" from other main-gene disorders in important respects. For instance, one is repeatedly told that it is methodologically sinful to postulate extremely low penetrance (I don't like that word in this connection anyway,

vide infra, but I will use it here roughly to mean "penetrance of the diagnosable clinical syndrome schizophrenia") suggesting that less than one-fourth or one-fifth or even as few as one-tenth of schizotypes decompensate to the point of being properly labelled "schizophrenia." If you combine the remarkably high incidence of the clinical entity with its persistence in all cultures studied despite its well-documented reproductive disadvantage, you already have reason to suspect that it may have something "special" about it as genetic disorders go, and that the extrapolation of higher-order inductions concerning reasonable penetrance values and the like from the more familiar and well-understood entities should be viewed with caution.

I am unhappy with their fiat statement that "It is obvious from the discussion above that the classical methods of genetics for discrete entities cannot be applied to the study of schizophrenia in order to prove a genetic etiology; the approach must be biometrical and data on frequencies must be converted to measures of similarity between relatives (e.g., Falconer, 1965)," but this involves a perennial hassle between Gottesman and Meehl that cannot be developed here. Suffice it to say that where we differ is in my "faith" that sufficiently powerful statistical taxonomic methods, such as I myself have been working on recently, should theoretically permit the assignment of probability numbers to an individual's being or not being a schizotype, despite the fact that the phenotypic indicators are dimensional variables and that they are all, singly *and collectively*, highly fallible. It remains to be settled whether such a taxonomic procedure generates numerical predictions for, e.g., a dominant monogene of low penetrance (affected by numerous modifiers or, as I prefer to say, for reasons of semantic clarity, "potentiators") differing from a Gottesman-Shields polygenic model enough to permit a definitive empirical test. I surely don't wish to prejudge the issue by dogmatizing that the answer to this question is affirmative; but I am mildly distressed when our authors state so flatly that the "classical methods of genetics for discrete entities *cannot* be applied to the study of schizophrenia in order to prove a genetic etiology." I am still reasonably hopeful that they can, provided that statistics of loose syndromes can be made sufficiently powerful, and especially made to embody enough "internal consistency tests" as to the correctness of the postulated latent model, so that the clear identification of individuals in pedigrees relied on in traditional genetics can be adequately substituted for by trustworthy numerical probability statements. But this is a large and difficult topic beyond the scope of these remarks.

I don't think I am willing to agree unreservedly with their statement that "No one or two clinical symptoms are pathognomonic" unless they mean here "Two-way pathognomonic," i.e., infallible both as an inclusion and an exclusion test. I think—and I rather suspect that Gottesman and Shields would agree if pressed—that you can find at least a one symptom-pair that is *one*-way pathognomonic (the meaning in Dorland's Dictionary), that is, quasi-infallible used as an inclusion test. I proposed one myself

a decade ago, to wit, the clear presence of the characteristic and unique schizoid thought disorder in the absence of clouded sensorium. A patient who is well oriented for time, place, and person and is listening attentively and communicating cooperatively and who says, "Of course, Doctor, you realize that naturally I am growing my father's hair," or who justifies plugging the alarm clock insert into the sidewalk on the Healy Picture Completion II (the frame where the boy is spilling his books) by telling the examiner "That is so he will have time to get to school," is in my view unquestionably schizophrenic. I doubt that any clinically experienced reader would think otherwise. I urge that there is a kind of thought disorder in the calm, oriented and cooperative patient that is a more powerful inclusion test than a positive Wassermann for lues (remember yaws!), and almost as good as the cherry-red retinal spot for Tay-Sachs' Disease. Of course if the authors meant two-way pathognomonicity, I agree with them entirely. It is regrettably as true today, as it was when the great Eugen Bleuler wrote it in 1911, that we have no trustworthy method for excluding schizophrenia.

I should like to have seen, toward the end of this chapter, a fuller exposition of what they intend to claim by alleging a "specific genetic etiology" for schizophrenia. This is one of the few places where I might be inclined to fault them in other than a minor way. It is clear that they have a strong theoretical investment in defending the diagnostic identification of schizophrenia as an entity, of denying the notion of "one (functional) psychosis," and that they want to press for a considerable genetic homogeneity over almost all correctly diagnosed schizophrenics despite the well known variations in momentary symptom picture (the subtypes) and the wide range of clinical status (Rado's compensation, semicompensation, decompensation, disintegration, and deterioration). I rather think they owed it to us to deliver the conceptual goods in a little more detail at this place, even though the empirical evidence is not in. I do not complain, let it be emphasized, of the authors' "pushing" their polygenic theory against a monogenic one. I am a noninductivist neo-Popperian and believe that everybody should "do his own (theoretical) thing" and bet on what he thinks—guesses or intuits!—is the best horse. Rather, I express dissatisfaction with what seems to me an unclarity in *meaning* of their combined doctrine of specific etiology and polygenicity. They do not, if I read them right, want to say that already-named polygenic systems determinative of such non-schizospecific variables as general intelligence, "garden-variety (nonpathological) social introversion," energy-level, or anxiety-readiness are the components of the schizogenotype. That is, I take them to suppose that you don't get to be a schizophrenic just by having an unfortunate combination of high anxiety, low intelligence, low dominance, low energy, low mesomorphic toughness, and high social introversion. There is a *something else* allegedly specific to schizophrenia (better, the disposition thereto) that is, however, not a "big-effect monogene," as postulated by Slater, Heston,

and myself. (This is not, of course, an empty claim on their part, since it has at least a quantitative formal meaning within the already existing general framework of genetics, permitting one to conjecture about a "whatever it is, a not further specified something" that (a) provides the disposition for a recognizable clinical disease, but (b) is nevertheless polygenic.) Do we have a set of genes that all tend to affect the same first-order phenotypic disposition, whatever it is, that is specifically a disposition toward schizophrenia? One understands fairly clearly what it means to conjecture that a "big-effect monogene" is the specific etiology of a disease, and can write a general (albeit useless) mathematical expression for it simply by putting down the function that would characterize all of the genome-*cum*-environment main and interaction effects, and then plugging in as a multiplier on this function a variable that takes on only the two values: 1 [= monogene present] and 0 [= monogene absent]. But once we have excluded that simple situation, the *very meaning* of the phrase "specific etiology" begins to "fuzz up," and I wish the authors had said more about how they conceive it. Furthermore, I cannot suppose that they believe the polygenic systems related to nonspecific variables (like anxiety, social introversion, low energy level, low aggressiveness, or weak social dominance) play no part in contributing to clinical decompensation and, if the patient does decompensate and becomes diagnosably schizophrenic, what form, direction, duration and outlook he has. (I know from conversations that Dr. Gottesman inclines to share my opinions about these potentiators.) But if that is so, we should have some explanation of why these important potentiators of the occurrence of clinical illness, and even of its form and content, its severity and duration, are not considered part of "what is specific" for schizophrenia? I do not assert, nor do I believe, that they would have no interesting and perhaps quite satisfactory answers to these questions. But I wish they had included them in their discussion of specificity.

In Chapter 2 it is not clear to me why they lump alcoholism and general paresis together as examples where cross-cultural stability of rates earlier led to the "false implication of genetic etiology." The two seem to me sufficiently different not to be used for this same purpose. Surely no one, however simple-minded a hereditarian of the old "constitutional school" he may have been, could have thought one could become an alcoholic without drinking alcohol! And if we say, "Well, what we mean by a specific genetic etiology for developing a disorder on the basis of intake of a certain substance is, *of course*, an inherited disposition to react to the substance differently from the great majority of persons who can imbibe it with impunity," then it is not clear why that implication for alcoholism can be called false. There *is* a hereditary component in alcoholism, so far as we can judge on the present evidence; and it may even be "specific" as our authors are willing to use this adjective in their own polygenic view of schizophrenia.

I am bothered, although of course one knows why they say it, to read that a "dominant gene theory would predict that [the risk in second-degree relatives] would be one-half [that in first-degree relatives]." Since no one can possibly hold a dominant gene theory for schizophrenia itself on present evidence, I assume the only live object of their remark here would be a souped-up dominant gene theory with numerous modifiers and potentiators and *in which the phenotype is schizoid disease* (Heston) *or schizotypy* (Rado, Meehl) *rather than schizophrenia*. I have not seen anyone really work out the mathematics of such a souped-up dominant gene theory which (a) involves multiple polygenic potentiators, (b) takes account of the differential fecundity reduction between schizotypes of the two sexes, and (c) includes (as I would still do despite some negative evidence presented by the authors and others) an additional factor of *environmental potentiation* upon a schizotype who has a schizotypal mother (whether she is diagnosed schizophrenic or not) and that is stronger than schizotypy in father as an environmental potentiator. Absent such a mathematical analysis of what I think is certain to be a more complicated situation than the usual kinds of dominant gene, straightforward penetrance-correction setups with which we are familiar, I don't believe one can say quite what a dominant gene theory would "predict" *numerically* about the ratio of diagnosed schizophrenia in first and second-degree relatives. Of course anybody who propounds such a souped-up theory has an obligation to work out the mathematics, a task that is hardly the responsibility of the authors who hold a polygenic theory.

In their discussion of the MZ and DZ rates in Chapter 2, where they discuss measles and the fact that very similar rates are predictable on environmental grounds, an additional comment is in order. Since almost all biological and social dependencies become decelerated functions (and many are quasi-ogival), if the parametric situation is such that over a sizeable range of high (or low, or both!) values of an independent variable we deal with an output variable near asymptote (or near zero), any research method that involves a combination of measurement error, sampling error, and what might be called sheer "crudity of measures" (low construct validity with respect to the focus of our interest) may bring two rates together without telling us much etiologically. It is not clear to me, without knowing what one can postulate about the genetics of the potential for catching measles and having a sufficiently severe case to be diagnosed, what can be inferred etiologically from the fact that both MZ and DZ twins show high concordance. No doubt the authors can explain this, but I wish they had. Suppose, for instance, that what we might call the "typical" measles susceptibility in a genetic population is sufficient so that a child exposed to the virus will get the disease and will have a case severe enough to be diagnosed as such. And suppose that the measles-susceptibility and severity-susceptibility are polygenic. The dizygotic twins average half of these measles-relevant genes in common with the measles-afflicted proband, and on the parametric situation I am imagining this half will be plenty to yield

a very high measles rate. Under such a circumstance MZ-DZ comparisons are simply not illuminating with respect to the contribution of genes to measles susceptibility, are they? It might easily be the case, on a set of rather plausible biometrical assumptions, that a person who carried "counter-measles-genes" at each of, e.g., eight loci would have almost complete resistance to the disease, which would certainly entitle us to say that there were important genetic factors involved; and yet that fact would not be expected to emerge from the usual twin study, would it?

In mentioning my views they appose "schizotypes" to "schizophrenic equivalents," which bothers me because it perpetuates a semantics I consider unfortunate. The received doctrine is understandably (but I argue, wrongly) that the "main concept" is florid schizophrenia and that one should view compensated schizotypes as somehow sort of watered down or subclinical cases of schizophrenia—rather in the sense of the old French psychiatrist's meta-concept *forme fruste*. Now this is a perfectly legitimate way of looking at "latent" or "mild" or "incipient" cases, and I have no wish to impose my theory upon others via semantic stipulations. But the point is that Gottesman and Shields are at this locus referring to Meehl's views, and the language of "schizophrenic equivalents" gives a wrong emphasis to my conception. I do *not* think of the compensated schizotype as, in any usual sense of the word, a "schizophrenic," equivalent or otherwise. I do not consider him a "mild" or "disease-resistant" schizophrenic. He has a certain personality organization developed by social learning on the basis of a subtle neurological (not "psychological!") defect, and so far as I am concerned, *none of the clinical symptoms that enabled descriptive psychiatry to get a foot in the door so as to identify this entity in the first place* are a part of that organization or of that neurological substratum. This seems to be the hardest part of my theory to communicate, so I italicize it—cheerfully admitting that the emphasized sentence is not empirically corroborated (although, I insist, *is* in principle corroborable). If I may use what will seem to some to be a far-fetched analogy (deliberately, so as to drive the point home) it would be rather like saying that an American child who is capable of making a certain kind of nasal sound in his speech more readily than are most other children (on a genetic basis) is a "Gallic equivalent," i.e., he could come under suitable circumstances to acquire the behavior of speaking French well. For emphasis one might start with schizophrenia and then water it down conceptually. I want to start with schizotaxia, and imagine only a minority of schizotaxic persons having other genes and a life history that (conjointly!) lead them to develop a clinically recognizable psychiatric condition, to wit, the schizophrenic psychosis. Of course epistemologically we start with schizophrenia because that is how we find out that there is something here worth looking into. In the same way, in studying the entity "gout," we start with bouts of arthritis of the big toe, attributable to the deposition of certain salts. However, in the gout-free but

genetically gout-prone person, we do not expect to find some kind of attenuated inflammatory tetrad of turgor, rubor, dolor, and calor! I am not poking fun with this example. It really makes the point I want to make. We started our gout research with an inflamed joint; we then got back to the local tissue pathology of deposited urate crystals which are the defining property *locally* of a "gouty" condition; we then begin talking about gout-prone individuals (the great majority of whom never get clinical gout) in terms of their elevated uric acid titer; and even this endophenotypic biochemical dimension is presumably subject to modifiers and environmental factors like consumption of high-purine foods (the "high living" of the folklore) so as to be an imperfect correlate of the gout-disposing genotype. I may be unduly sensitive to the point, but I think not. It is a common complaint, for instance, by European-trained psychiatrists that American clinicians over-diagnose schizophrenia, and that we pay insufficient attention to the "classical (textbook) signs," including those that the great Bleuler made quasi-definitive of the disease. I happen to agree with this criticism, especially when I find some American psychiatrists of "psychodynamic establishment" persuasion calling everybody a schizophrenic who seems to suffer from the adult outcome of a battle-ax double-bind mother! I find that those who favor a more restrictive use of the term "schizophrenia" (I mean, of course, Bleuler's—not Kraepelin's dementia praecox) are surprised to hear me criticize this overuse of "schizophrenia" and then see me clinically identifying "schizotypes" with great clinical abandon. But they should not be surprised. This is a semantic misunderstanding, easy to clear up. The very reason for using words like "schizoid" or "schizotypal" is to permit a distinction between the compensated and the decompensated individual without the necessity for stretching the semantics of the pathology-laden word "schizophrenia" unduly. I don't even feel comfortable labelling a patient with the Hoch-Polatin rubric "pseudoneurotic schizophrenia" if I elicit only the pan-anxiety and anhedonia but not, say, a single micropsychotic episode, or subtle (but still reasonably clear) signs of cognitive slippage, or body image aberrations. How you research something of this sort, and how you assess the evidential weight of family studies, depends intimately upon what it is that you conjecture is inherited. I do not believe that one can, strictly speaking, inherit even a "watered down" or "weak" or "subclinical" schizophrenia. I believe that one can literally inherit Huntington's Disease, and that it makes sense to speak of an early or subclinical case of it, perhaps detectable only psychometrically or by instrumented-and-quantified "soft neurology." I want to put that kind of situation in a different category from what is inherited in the case of the schizophrenia-prone individual. I don't see how one could even "inherit," *stricto sensu*, the elements that enter into the picture of the compensated schizotype as conceived by Rado and myself, inasmuch as these mechanisms, contents and traits are themselves end products of an extraordinarily rich and complicated process of social learning. For this reason I prefer to avoid the

conventional term "modifier" for the various polygenic systems that must surely be involved in altering the probability of clinical decompensation, since they do not "modify" the expression of a phenotypic trait at all in my picture of the situation—not even, necessarily, of an endophenotypic trait such as a parametric peculiarity of the synapse. The polygenic systems that alter the probability that I will decompensate if I inherit the dominant schizogene (on the Slater-Heston-Meehl view) need not have any direct effect upon the early links in the causal chain from gene through biochemical endophenotype to neurophysiological endophenotype (e.g., synaptic slippage) to behavior dispositions to the ultimate adult *learned* behavior. They probably enter in a different way as, for example, polygenically determined primary social introversion or an excessive susceptibility to the anxiety experience or a defective hedonic capacity get into the causal chain (on my theory at least) only when we consider the history of social learning in the schizotype's development and the susceptibility of the adult schizotype to clinical decompensation under current (adult) environmental stressors. On this theory, these nonspecific polygenic factors do not *in the least* "modify" the schizogene's *endo*phenotypic expression as schizotaxia, a CNS parametric aberration. They may not even influence the "neurological" indicators of the *exo*phenotype appreciably. Their causal role is later in the chain, and at a "psychological" (molar) level. It does not seem to me that the usual term "modifier" does justice to this kind of picture, and I notice that when I talk to geneticists they become nervous too. It is for that reason that I prefer my term "potentiator," which has the meaning of "raising, *via the social learning process*, the probability of clinical decompensation into diagnosable schizophrenic disease." A well-compensated schizotype is not, on this interpretation, to be thought of as some sort of "schizophrenic equivalent." He may be a person with negligible probability of developing clinical schizophrenia once he has survived intact to a certain age, i.e., the schizogene has missed its chance to have a psychotic effect, by virtue of the particular development his psychodynamics have taken. I am not criticizing the authors for writing their book instead of a book I might have written, a temptation to book reviewers that we properly deplore. But I do wish to highlight the difference between two ways of looking upon the non-psychotic and even non-neurotic individual who carries the "specific schizogene(s)."

One could wish that the authors had done more with the comparison of concordance rates for like sex versus opposite sex DZ pairs. Ever since an early article in which Rosanoff made methodological hay with this finding, I have found it an impressive counterargument against those environmentalists who try to explain the MZ-DZ concordance difference on the (somewhat *ad hoc* but admittedly plausible) counter theory that the physical resemblance of MZ twins and the recognition of them as "identicals" leads to (a) social expectations of similar behavior and (b) more similar treatment than would be true if they were DZ and easily distinguishable. Part of this environmentalist counter-hypothesis has been rendered quite implausible by the

important research of Sandra Scarr showing that a number of behavioral characteristics of twin children show intrapair similarities that tend to follow the objective zygosity rather than the mother's beliefs about zygosity when the two are in disagreement. And of course any geneticist can tell you that while other people outside the family often mix them up, the mothers of MZ twins are almost infallible in telling them apart. I do not doubt, however, that determined environmentalists will possess sufficient ingenuity to *ad hoc* Professor Scarr's data (so soon as they hear about them, which many of them seem not yet to have done). But consider what an environmentalist explanation of the MZ-DZ concordance difference must face in the light of the small like-sex/opposite-sex DZ difference. The environmentalist must argue that, in a highly sex-typed culture like ours, and one with such very different kinds, times and settings of social and biological stressors as the culture imposes on the two sexes, differential treatment (within the psychodynamically crucial family, remember!) of two DZ boys born at the same time and reared in the same household is so much greater if they share half their genes than it is when they are genetically identical (even though the family members, and especially mothers, can tell them apart) as to reduce the schizophrenia expectancy in an MZ twin of a schizophrenic proband by a factor of three or four to one, that is a drop from, say, 50-60% to, say, no greater than 15%. But despite this dramatic drop attributable to a marked increase in the differential treatment of two male sibs born at the same time and with around 50% overlap in genes, the *increase in differential treatment* when we move from two boy siblings born at the same time to a boy and a girl born at the same time produces a further percentage decline in concordance that is negligible in size. In order to *ad hoc* this finding, it seems to me one would have to be an environmentalist fanatic. Although perhaps not an absolute hammer-blow destruction, these data together with their summary of the (regrettably small) number of known instances of MZ twins reared apart must surely be taken as greatly weakening two of the favorite counter-genetic hypotheses (identity-confusion and similar treatment). I record here, however, my prediction that the same environmentalist arguments that we have heard repeated regularly since Kallmann's findings slowly forced themselves upon the American psychiatric culture will still be invoked twenty years from now, despite these findings.

I cannot resist the impulse, before concluding my comments on this chapter, to say a word about the current popularity of the "spectrum" terminology. I tend to agree with McKusick that, despite its rapid taking hold in the language of behavior geneticists and their environmentalist opposition, it is not a felicitous semantic contribution. If genetic heterogeneity truly obtains among patients labelled "schizophrenic" (I set aside sheer diagnostic unreliability problems for the moment, although goodness knows that presents terrible difficulties for the researcher, which our authors have manfully striven to surmount—and largely succeeded *for the clinical entity*), then we need two

nosological terms, do we not? Until we answer that question about heterogeneity, which presupposes answering the question of specific etiology, especially (see *supra*) how "specificity" is to be construed for a polygenic theory, we do not know whether two labels are needed, let alone to which patients they should be applied. If there is, say, a single nosological entity, disposition toward which was determined by one "big gene," and we then define the concept *diagnostic error* as it would be defined in neurology or internal medicine, i.e., by reference to a specific etiological agent; then, as McKusick points out, there would be little usefulness either clinically or in theoretical understanding, in talking about a "spectrum." Because if you have the specific gene you would be a schizophrenic, although it might be in a *forme fruste*, *forme tarde*, or otherwise "atypical clinical picture," familiar notions which are taken for granted in branches of medicine where one is able to present a quasi-explicit *definition* of the disease entity in terms of its etiology and pathology. A person who has early paresis (paretic gold curve, positive spinal Wassermann, "soft" paretic neurology, early parenchymal changes in the brain associated with *Treponema pallidum*) is not said to belong to a "paretic spectrum," he is simply a paretic who isn't very sick yet. *Point*: We either have a specific etiology or we don't. If we do, there is no need to talk about a "spectrum," it is simply the usual question in medicine of how one treats the variety of clinical pictures and complications that "one and the same disease" may present to the clinician. (Bleuler wrote some very clear and sophisticated things about this in 1911.) Of course one realizes that the "spectrum" terminology caught on precisely because of the present etiological and clinical ambiguities, and perhaps no harm is done by it. But one has a tendency to the illusion that the introduction of this language conveyed something substantively or methodologically interesting and incisive; and I fail to see that it has done so. If memory serves, the term "caught on" at or following one of the first big schizophrenia conferences, when many were astonished at findings reported there to the effect that the families of schizophrenic probands showed some tendency to a heightened incidence of nonschizophrenic psychiatric aberration. I understand from colleagues who attended or participated in those conferences that participants expressed misgivings, fearing that we might have to revive the old-fashioned and long discarded generic "neuropathic diathesis" of continental constitutional psychiatry. I am at a loss to understand this reaction, on *either* a monogenic or polygenic view. With apologies for sounding like "I told you so," this is just what I would expect, and what I have long predicted would happen if the studies were done correctly. Suppose, for instance, that there is a specific dominant schizogene that is completely penetrant for a subtle neurological deficit, upon which is superimposed by social learning a collection of *statistically clustered* personality traits that constitute the loose syndrome "schizotype," and that a minority of such schizotypal individuals decompensate into the

schizophrenic syndrome proper. I cannot imagine that any psychologist, whatever his major theoretical commitments as regards schizophrenia, would suppose that how much anxiety, rage, polymorph-perverse sexuality, energy level, social dominance, garden-variety social introversion, or mesomorphic toughness a person had would be literally irrelevant to the probability of his decompensating into schizophrenia. Granting this, one is also fairly safe in viewing these variables as partly genetic, by extrapolation from animal data, from the theoretical armchair, and through some human data. But these two high-probability assumptions jointly suggest that if I am clinically schizophrenic, the chances are good that in addition to the specific schizogene (or the scars from my schizophrenogenic mother) I carry a batch of polygenic modifiers of these other kinds mentioned, most of which are (in our culture) *themselves* predisposing to social maladroitness, economic marginality, "underachievement," mental distress, neurosis, psychosis, or delinquency. I therefore cannot understand why we should be surprised by the occurrence of "spectrum disorders" in the relatives of schizophrenics, unless we started with an inordinately simple-minded view of what an integrated theory of schizophrenia would look like. If the term "spectrum" encourages conceptual analysis (e.g., what is it that we would require of the potentiators on a theory postulating a specific schizogene?) then it is a healthy bit of semantics; but if it merely makes it easier for us to assimilate what should not have been a surprising familial finding in the first place—without pushing us to ask just *why* we were so surprised—then its introduction will have done us a disservice methodologically.

I shall not comment on the case histories, which make interesting reading but, I believe, contribute less than is often assumed. Despite my being a psychotherapist with (I hope and believe) what is at least the normal fascination with the idiographic question, "How did this unique life develop?," I have rarely been able to persuade myself that case histories are illuminating in considering questions of the present kind, *absent a causal theory-sketch sufficiently rich to generate some sort of quantitative predictions, however crude*. Thus, for instance, the tremendous amount of effort that went into detailed clinical study of the famous Genain quadruplets, about which most behavior geneticists show considerable enthusiasm, leaves me somewhat cold. I really do not know what this kind of material should convince us of, except to bolster something we already know without twin studies, i.e., one and the same patient can present rather strikingly different clinical pictures at different points in time during the "natural history of the disease"; or, perhaps more helpfully, that persons with identical genotypes can differ in varying (and sometimes remarkably great) respects, and the like. For my part, the most important thing about case histories other than their heuristic value (even this, in my jaundiced view, is usually exaggerated), and that's the main value the authors have emphasized, is the fact that a case history, when reliable, can at least show "something is

possible." As Bertrand Russell once jokingly said, "A single occurrence of an event establishes its possibility." How many things were not known to be possible but now are known to be possible from reading these case histories I cannot say, but I incline to be skeptical.

Chapter 5 is one of the most impressive chapters of the book, and one hopes that the obscurantist tradition in American psychiatry, which plays down formal nosology without presenting any respectable evidence for a greater power on the part of *competing* concepts, and which largely ignores the genetic data (themselves among the most powerful indicators that the diagnostic system has a nonarbitrary, nonadministrative meaning, that it "carves Nature at its joints") will be influenced by these results. It is tiresome to hear daily repeated the cliché (a cliché is bad enough when it is true, and unforgivable when it is false!) that "diagnostic categories in psychiatry are completely arbitrary, and besides are utterly unreliable," when this statement is based upon selective attention to studies so badly designed that rely upon diagnoses by such unskilled (or antidiagnostic!) personnel as to be incapable of shedding appreciable light on the question. It should be obvious that unless we had such a huge population of studies of diagnosis that we must worry about "selecting out the accidentally good ones" (as is the case in item analysis of a large pool of potential test items, or the picking of a small number of variables from a very large set in a multiple regression system, not, of course, the case in question), the value of nosology is better judged by the "good" studies than by the "unfavorable" ones. The favorable studies show that major nosological entities can be intersubjectively judged, and that they possess strong implications for prognosis and for treatment choice (e.g., ECT, phenothiazines). It is pointless to emphasize a study with a small sample, relying on the judgments of American psychiatric residents trained to ignore nosology and to doubt its importance (and not even taught the classic textbook differential diagnostic signs, as anyone acquainted with American psychiatry knows is sometimes the case in training settings). Patients are thus seen superficially and without an opportunity for inpatient study over a sufficiently long time; to then analyze the data with respect to subdivisions of the nomenclature that prejudge whether the subtypes of something like schizophrenia represent different diseases (itself counterevidenced by data in the present book) is, again, nonsensical.

Nor is it illuminating to show that quite a few schizophrenics were formerly labeled differently (the diagnostic shift is more often in that direction) when "does schizophrenia exist?" is the controverted issue. Bleuler made that clinical observation 60 years ago, and he also explained why it works that way. If you want to know something about the accuracy of psychiatric diagnoses, you look to see what the results are from the *best* studies, provided their sample size is large enough to have some faith in the figures as not being merely upward direction sampling error. I challenge psychiatrists and psychologists

with an antinosological bias to refute the following claim: The interjudge reliability of a diagnosis of *schizophrenia*—as against other psychiatric diagnoses of functional disorders—is at least as high as typical diagnostic agreements in other branches of medicine; it is higher than the reliability of two clinicians' psychodynamic constructions from interview material or life history data; and it is markedly higher than the reliability of the most popular projective tests relied on by clinical psychologists. (Anyone want to take bets?) In that connection, it is reassuring to note that clinicians Meehl and Mosher, despite the marked difference in their ideological and etiological commitments, showed a reliability as high as that of a well-administered individual intelligence test (r = .88), using the seven-point scale of global psychopathology. I trust it will not seem unduly narcissistic for me to suggest that if you have competent and motivated raters making judgments *from decent data*, their judgments will tend to be reliable, and that will usually be the case despite theoretical divergences.

One of the important things about this chapter is that the authors ingeniously "sliced the pie" in different ways. Some psychologists are so methodologically puristic that they consider it sinful to examine whether one way of classifying the material is better than another, despite the scientific principle that one of the main ways to *find out* whether you are "carving Nature at its joints" is whether a certain way of grouping things increases the total orderliness (lawfulness) of the subject-matter system. Any physical scientist knows this, and psychologists—even Skinnerians, who don't like diagnostic entities much—should reread Skinner's classic discussion about the orderliness of cumulative records in his 1938 book! The problem is again similar to that of item analysis, because you realize that if you permit yourself unlimited cut-and-try procedures, especially "blind, empirical," nontheory-motivated gerrymandering, squeezing all of the blood out of what is a pretty anemic statistical turnip, you are in grave danger of seeing order when there is really nothing but chaos. That is a complicated question which involves a more thorough quantitative metatheory concerning *ad hoc* hypotheses than anyone in philosophy of science or statistics has thus far produced. It is therefore, regrettably, a matter of subjective judgment to a considerable extent. I assume most readers will agree with me that the various ways of classifying the diagnostic categories and dimensions employed by Gottesman and Shields each had an excellent prior probability of being good ones (from the armchair and on the basis of previous research) and that they have not overdone the strategy by riffling through all sorts of oddball nonrationally motivated ways of slicing the pie.

We face here a general problem which, if space permitted and it were appropriate, I would develop at some length. It is naive to object, as one frequently hears done, to selection of one of several data-classifications on the empirical basis that it yields greater genetic orderliness. Psychologists and psychiatrists who make this criticism usually display an undergraduate comprehension of philosophy of science. There is nothing

viciously "circular" about an argument that begins with an observational-statistical finding, to wit, that one way of classifying events or entities leads to markedly greater empirical lawfulness than another way, and infers therefrom that the first classification is "better." *Per contra*, the most general characterization of scientific inference—cutting across all sciences and certainly not peculiar to problems in behavior genetics—is that we seek to maximize the order in phenomena. The bat "goes with" the whale despite the superficial and more common-sense grouping of whale with pickerel, and bat with bird. Consider psychodynamics: There is nothing phenomenologically obvious about a relation between a patient's inability to discard bent paper clips and his overdocility (with subtle, longer-term refractoriness) in responding to a psychotherapist's interpretations, but psychoanalytically we can conceive that these "go together" by virtue of their common (inferential!) factor of *anality*. Or, to take a nonclinical tough-minded example from another species, if one has doubts as to whether a tentative response-class, e.g., one defined by certain effect on a manipulandum (characteristic of the great majority of response classes studied in experimental psychology these days) is dynamically homogeneous, conjecturing that it actually consists of two response classes that are not only topographically identifiable (a pie-slicing job that could be done "blindly" in a number of arbitrary ways), what he does is to study the orderliness (grain of curve, dependence upon certain contingencies, manipulability via state-variables or discriminative stimuli) of the putative subclasses.

Were it not for certain statistical difficulties with the heritability coefficient—arising partly, if I may comment as a nongeneticist, from inadequate attention to the relation between the employed statistic and the postulated causal model that legitimates it and "makes sense" of it—one might, for example, argue that the best way to choose phenotypic indicators of a postulated genotypic variable, whether polygenic or otherwise, and the way to assign weights to such indicators in an indicator-set, would be the basis of *that choice and weight assignment that maximized heritability*. That is to say, if you are interested in a genotypic dimension and you have some combination of armchair theory, background scientific knowledge, common sense, and previous unintegrated factual research which at least permits you to assign certain indicators to the members of a potential indicator-set on a more or less rational basis, then the further screening of those tentative indicators in or out of the set, and the assignment of weights within the retained set, *ought* in consistency to be made on the basis of the genotypic postulate involved. This process may look "circular" to somebody who does not really understand what circularity is, or how science grows by cleverly "saving the appearances." As one philosopher of science said many years ago, "*There is nothing wrong with arguing in a circle, if it is a big enough circle*." But I repeat, the kind of quasi-circularity involved in this sort of process is not even real circularity in the *vicious* circle sense of the logician, i.e., it is not the case, when the inferential structure

is analyzed thoroughly, that one uses a premise in a syllogism which premise is itself the desired conclusion. Finally, while we are on this important topic, it is worth mentioning that the choice of a metric, or the choice of one or another transformation on a phenotypic variable, ought itself to be selected on the basis of some mixture of a causal theory—even a sketchy one—*and the maximizing of order*. It seems to me rather difficult to justify the common practice of picking a more or less arbitrary although conventionally employed nonlinear transformation, such as a log or square root or arc-cosine transformation of phenotypic data, when the latter themselves have a crude and arbitrary metric (e.g., number of pellets hoarded by a rat), and then looking to see whether the offspring of two homozygous strains falls "in the middle." Perhaps I am nitpicking about the mathematics; but it does seem strange that such investigations often attain good results, absent any plausible theory relating the metric of pellet-hoarding via a square-root transformation to a presumed number of genes at a set of loci constituting the polygenic determiners of hoarding behavior.

Similar questions can be raised about the interpretation of MMPI score differences in the present study. The authors' sophistication about diagnosis and about the related problems of "open concepts" and the theory-fact interaction (about which most psychologists are incredibly naive and uninformed) leads one to wish that they had expanded further on this critical point in behavior genetic research on loose syndromes like schizophrenia. There is admittedly a methodological tension between (a) the necessity to avoid a progressive, counterproductive "conceptual drift" via psychometrics or reclassification of patients in the light of selected empirical relationships of increasing orderliness, and (b) the virtues of altering one's initial phenotypic weights on the basis of the empirical relationships observed. There is, for example, nothing wrong with the *concept* involved in saying, "This patient was perhaps not a schizophrenic as we initially thought, as he seems to have made a *complete* recovery." (Bleuler said that schizophrenics often made clinical or social recoveries but insisted that he had never seen so much as one single case in which there was a complete *restitutio ad integrum*; that there would always be some "residual psychic scarring.") Nor is there anything intrinsically wrong in raising the question, "Was co-twin Y a schizotype who remained compensated (hence, "discordant") throughout the risk period?" Those who think there is something illegitimate or "metaphysical" about those questions have, I repeat, not passed beyond an imperfect grasp of scientific method. But of course when a purportedly genetic syndrome is sufficiently loose, or when even the exophenotype held by particular theory to be "definitive" is *not* the full-blown clinical entity, there is a distressingly large element of personal judgment and subjectivity in assigning weights to members of the phenotypic indicator-set. Theoretically this question should, one supposes, have an optimal statistical solution; but none of universal applicability exists at present, to my

knowledge. This is, in my view, one of the most important methodological problems, conceivably *the* most important one, in schizophrenia research. Its "solution" by the development of satisfactory techniques for the necessary bootstrapping of fallible phenotypic patterns should have general applicability in other areas of behavior genetics. Thus, as an example, the subclinical manic-depressive ("compensated cyclothyme") may (I predict will) one of these days come in for as much attention as we are now devoting to the compensated and semicompensated schizotype. Whenever the clinical manifestations of pathology sufficient to bring the patient to psychiatric attention and to attach a certain nosological label are far enough removed *even within the molar behavior domain* from whatever Omniscient Jones would view as "definitive," some combination of internal clustering of phenotypic indicators with maximizing the relation of the entity (thus defined) to the postulated genotypic situation is what is required. It is therefore almost certain that with increasing knowledge, there will occur some degree of shifting in the relative importance given to various phenotypic indicators, sometimes even an introduction of a new one that is weighted heavily, or a dropping of one that is part of the received clinical tradition but that turns out to have too-low construct validity. In the terminology of the epidemiologist, we want phenotypic indicators of high sensitivity and high specificity; and we do not at present know what those indicators are. Although I, as mentioned above, consider the conjunction "thought disorder in the presence of unclouded sensorium" a quasi-pathognomonic inclusion test for clinical schizophrenia, it would be a mistake for me to infer that I must look upon thought disorder as the most powerful indicator (at the molar level) that exists. I consider it not only possible but rather likely—and recent unpublished research from Israel encourages me in this belief—that a sufficiently souped-up "soft neurology" may be a more powerful indicator *of the schizoid genotype* than thought disorder, whether the latter is assessed clinically or psychometrically. But associated with all such thinking is the lurking danger of a conceptual drift (associated, as psychologists go about their work, with psychometric drift) that would mean that we had slowly begun (unwittingly) to study something other than schizophrenia and its psychological or biological substratum. I do not suggest, however, that the authors have fallen victim to this possibility.

The remarkable results achieved by Dr. Essen-Möller might well be assigned reading for all first-year clinical psychology students, as it should almost suffice by itself to counteract the usual undergraduate brainwashing that psychiatric diagnosis is meaningless and that genes are irrelevant to mental illness. This great Swedish clinician evidently knows precisely what he is looking for, and whatever it is, he proves its importance. It seems almost "too good to be true," given the usual correlational baselines we have learned to live with in behavior science, that when an index case was diagnosed as schizophrenic by Dr. Essen-Möller's "solid-gold, hard-core,

dementia-praecox-like" nosological standards, *every single one of the MZ co-twins* was also (blindly) diagnosed as schizophrenic or "schizotypal" by him—and this without an untoward inflation of schizophrenia-rate among the DZs. A truly virtuoso performance!

My scientific joy at this result is not unmixed, since the beautiful MZ concordance (and associated MZ/DZ ratio's potent evidence of heritability) is here attained by Essen-Möller's magisterial application of a (deliberately) "narrow" conception of the nosological entity. The findings put a further burden of proof upon those of us who entertain a broader conception of schizophrenia (*not*, I must reiterate, the same thing as our postulating the entity called "schizotypy"). I would like to work through the statistical implications of Dr. Essen-Möller's amazing display of clinical acumen—implications which I confess are presently unclear to me. On a souped-up dominant gene theory, suppose Essen-Möller's "hard-core," close-to-Kraepelin category were composed entirely of schizotypes who carry, in addition to the schizogene, heavy *multiple* loadings of the (several) nonspecific polygenic potentiators that theory requires. Would a biometrical geneticist predict this subgroup to show a higher MZ/DZ concordance ratio than a more inclusive group who have the dominant schizogene but are clinically more "peripheral" because they carry (on the average) fewer of the malignant polygenic loadings? This theoretical question must be answered, bear in mind, under the constraint that strong environmental influences are holding down the MZ concordance for the broader group by a sizeable amount. Writing under a publisher's deadline, I find that a rigorous causal and mathematical consideration of this important query must, alas, be put aside for now. But I will say at least something about it, at the risk of seeming to "explain away" evidence against my complicated variant of dominant-gene theory. I admit that this evidence does speak, *prima facie*, against that theory, since the MZ/DZ ratio is one crude index of "heritability," so that a clinical diagnostic emphasis which yields a high MZ/DZ index is to that extent an "optimizer of genetic orderliness," following the methodological pie-slicing rule defended *supra*. But I feel justified in qualifying my cheerful admission of counter-evidence by indicating where I think some quantitative ambiguities lie, urging that they deserve thorough biometric scrutiny before we conclude flatly that the continental, quasi-Kraepelinian entity should be the "genetically pure" object of future research efforts.

Adopting *arguendo* my conjecture in the preceding paragraph that the "hard-core" cases *are* hard-core (and, hence, identified by Essen-Möller with confidence and accuracy) *because* they carry a heavy genetic loading on *each of several* polygenic potentiators, his perfect MZ-concordance presents no great puzzle. The more malignant polygenes a schizotype has, the less unfavorable his "environment" (early nurturing regime plus adult stressors) has to be in order for him to decompensate (cf. "essential epilepsy" contrasted with convulsive disorders having a brain-damage etiology, and

remembering that *all* of us have a seizure threshold that can be exceeded to produce a *grand mal* fit given a severe enough environmental insult, e.g., ECT, metrazol). Presumably the causal situation underlying severity-concordance data is an attenuated form of what yielded Essen-Möller's 100% MZ value.

The stomachache comes with the low DZ-value (since he could have achieved a "spurious" MZ rate by the strategy of calling everybody schizophrenic—but trivially reducing to nothing the conventional index of heritability). What might we expect, speaking quasi-quantitatively in the absence of a powerful statistical model for the complexities of a "souped-up" dominant-gene theory? I (timidly) commend the following rough conjectures to the attention of those who possess competencies in statistical genetics that I lack as yet: The "soft" or "peripheral" schizotypes are those who carry the dominant schizogene but relatively fewer of the polygenic potentiators. Further, on this complex theory, the word "fewer" refers not merely to an overall *count* of "favorable/adverse" alleles at all relevant loci. On my "psychologically"-oriented views, an equally important quantitative question is the *distribution* of these "bad genes" over *different polygenic systems*. These systems are "different" in that they control higher-order molar-behavior dispositions that may have nothing "physiologically" in common, but nevertheless converge causally—in the patient's *psychological* development and *social* history—to potentiate schizophrenia [= to raise the probability of a schizotype's decompensating]. I trust that my thus denying the fungibility of multiple polygenic potentiators does not seem contrived or fanciful. While it is not, I gather, a common mode of thinking among *non*behavior geneticists, it seems to me quite plausible in the behavior domain. Suppose, to put some flesh on the bones, we assume that both the rage-parameter and the anxiety-parameter are important polygenic potentiators tending, *ceteris paribus*, to decompensation in one who carries the dominant schizogene. A schizotype inheriting a +2 sigma hostility-parameter and a –1 sigma anxiety-parameter may remain compensated (albeit a somewhat cranky, litigious pain in the neck to employers and landlords!). Another, with these two temperamental parameters reversed, resigns himself to a menial job and a passive, withdrawn social existence, remaining "adjusted" at that marginal level. But a third schizotype has the bad genetic luck to inherit +1 sigma parameters for both rage and fear, and this one is in for trouble. He is less able than average to fight, but also less able to "give in." He will resent his incapacity to relate and achieve, but he will be anxiously inhibited from doing anything effective about it. The (rage → fear) sequence of traditional psychodynamics will be a chronic problem for him ("I am afraid that I will hurt somebody"), as will the less-recognized but equally important (fear → rage) sequence emphasized by Rado ("I am almost always fearful, except when I get angry,"—cf. schizotype Hitler's seemingly deliberate use of this autotherapeutic technique, working himself into a rage in order to counteract the massive inhibition of thought and

speech that often threatened to impair his functioning when conferring with a visiting diplomat.)

The index case of a twin study, *being* a schizophrenic, is more likely to resemble our third example than either of the other two, despite the fact that our third man's "mean sigma score" (treating the polygenes wrongly as fungible) is the same as theirs (= +1 sigma). Where did our index case get his two +1 sigma polygenic potentiators? More probably than not, either (a) both were largely inherited from the same parent (*not* the parent from whom he got the schizogene, because that parent was very likely a compensated schizotype, as the proband → parent figures and the fecundity statistics show); or (b) the genes for the two affective parameters came from both parents, but not "randomly" distributed across systems, e.g., he may have received the big dose of rage-parameter polygenes from his schizotypal mother—the battle-ax compensated type—and the big dose of fear-parameter polygenes from his non-schizotypal (but somewhat neurotic) father. As I understand what the geneticists tell me, such a "piling-up" of relevant polygenes on one side (rather than a more symmetrical "mix" in parental origin) will tend to yield higher average values in the sibship than would be true for the fungible situation. Hence, on the average, this theory leads to a "boosted" DZ concordance, moving the DZ value up closer to the MZ for those clinical judges who diagnose "schizophrenia" more freely than continental practitioners, there being no systematic influence tending to raise their MZ figure correspondingly. (Side comment for geneticists: Do these causal conjectures fit the traditional conception of a "modifier" closely enough to justify using that word?)

Taking a different tack, what would happen if a super-Radovian clinician *could* spot schizotypy perfectly (i.e., regardless of decompensation): On a dominant gene model, the MZ concordance would be 100%, and the DZ 50%. But such a clinician might nevertheless "do worse" than Essen-Möller, since they both hit 100% on the MZs whereas Essen-Möller would—*even if the dominant gene theory of schizotypy were correct*—run considerably lower than 50% for the DZ cases, not labeling those (among the schizotypal 50%) with "good polygenic luck" as schizophrenic by his strict clinical criteria. So an MZ/DZ or (MZ – DZ) index would favor Essen-Möller even if the compensated schizotype were a real entity and were accurately diagnosable.

In that connection, there is a serious problem about the index to be used. In comparing the six clinical judges, Gottesman and Shields employ the simple *ratio* MZ:DZ of concordances. I do not suggest that this is "wrong"; but I should like to have seen more discussion of their basis for choosing it (over, say, the MZ – DZ difference). Not only can the "distance" between two judges be different as between these indexes, but even the *order* of judges can rather easily be re-arranged by one's index choice. In Table 5.3, consider the concordance for (a) "definite schizophrenia in both twins." To get the six-judge order determined by index (MZ – DZ) into the

authors' MZ:DZ index order requires two permutings (and, I note egocentrically, shifts Judge PM from fifth place to the middle position). Employing concordance (b), "inclusive of ? Sc in either twin," the MZ:DZ and (MZ – DZ) orders again differ by two permutings. We note further that the indexes differ from each other by the same permutation number as MZ:DZ does from DZ-rate itself in cases (a), and in cases (b) the (low) DZ-rate order is exactly the same as that of MZ:DZ but for a paired ranking (1.5 for judges KA and LM). The denominator DZ exerts heavy influence on a ratio index, of course; we recall the theorem of elementary calculus that the derivative of a quotient has its denominator *squared* in the denominator. These problems of choosing the "optimum" index relating two concordances are as difficult as they are important, and we must try to avoid indexes that have a mathematically built-in feature capable of loading the dice. My suspicion is that a ratio index inflates the significance of DZ-concordance interpretively, but I primarily want to raise the question for thorough analysis. Its importance is enhanced by Gottesman and Shields' suggesting (from Table 5.3 orderings) that either a "narrow" (Judge JB) or "wide" (Judge PM) diagnostic usage leads to a poor heritability result.

Of course the ratio index is a linear function of the difference index *for fixed DZ base*; but it is both nonlinear and *nonmonotonic* when we allow both MZ and DZ to move around considerably. To give the reader some notion of the complexity of this "index" issue, suppose that x = MZ concordance; y = DZ concordance; $u = x/y$, i.e., Gottesman-Shields' choice of index, MZ/DZ; and $v = x - y$ simple (MZ – DZ) difference. How does the ratio index change with changes in the difference index? The derivative of the former with respect to the latter turns out to be

$$\frac{du}{dv} = \frac{1}{y}\,\frac{1-(x/y)(dy/dx)}{1-(dy/dx)}$$

which is a can of worms, especially when we remind ourselves that dy/dx will surely depend in no *simple* fashion upon the value of x (the DZ concordance). To put in my psychologist's two cents worth again (since I don't belong to their trade union, the geneticists can ignore me with a clear conscience), it seems to me that adoption of indexes like MZ/DZ or MZ – DZ (or, for that matter, the ubiquitous and sometimes strangely behaved heritability coefficients—and why *two*?) ought ideally to be itself based on theory. And by "theory" here I mean something more substantive than a statistician's discussion of how components of variance can be algebraically separated and pooled. The choice of a numerical index is rather like the choice of a scientific instrument for a certain purpose; and we understand how that purpose is rationally served by the chosen instrument in terms of a substantive theory concerning the causal structure of the domain. It may be that I am poorly instructed as to the "causal-theoretical" rationale underlying an index like MZ:DZ, and that the genetics literature

somewhere explains it all quite clearly. If so, reviewers of this book will no doubt enlighten me, and in the process others (some of whom seem to me almost equally unclear but not as distressed about it) will have their education furthered along with mine.

A final comment on Essen-Möller's results is to reassure ourselves that bootstrapping from clinical judgment (when the clinicians "believe in diagnosis" and have bothered learning how to do it) is not a foolish way to spend research time and money.

My only criticism of this chapter is a minor literature disagreement which, if anything, favors the authors' own position. They mention the 1956 work by Schmidt and Fonda as one of the studies taken to suggest that psychiatric diagnosis is unreliable, and while no doubt some muddleheads have cited it for that purpose, that is *not* the burden of Schmidt and Fonda's own conclusion, as the reader will find if he goes back to the original paper. As indicated by Schmidt and Fonda's title, "The reliability of psychiatric diagnosis: A new look," and the introduction of the paper which points out that they themselves, having previously asserted without documentation that psychiatric diagnosis is unreliable, thought better of this statement and decided to investigate it more thoroughly, their interpretation is distinctly pro-nosology. The last sentence of their article reads: "It is concluded that satisfactory reliability has been demonstrated for some of the psychiatric diagnoses, but that this carries no implications regarding their semantic validity or usefulness." Quite apart from what Schmidt and Fonda thought they had shown, when schizophrenia is the subject matter, it would be inappropriate to cite their study on the "unreliable" side of the argument, since a tetrachoric *r* they computed on the dichotomy "schizophrenia/nonschizophrenia" came to .95. This is surely better than many diagnoses in internal medicine, and vastly better than the kinds of personological judgments and psychodynamic inferences (not to mention predictions about psychotherapy!) which are routinely relied on in clinical psychology and psychiatry in the United States. The Schmidt and Fonda study, either in terms of its data or in terms of those authors' conclusions, should not be cited with studies indicating unreliability.

In Chapter 6, I understand why the authors say, "It would seem appropriate to use more than one criterion for severity in any one study so long as the construct remains incompletely defined." But I am troubled by that language, which seems to suggest that severity is some sort of "construct," comparable methodologically to the postulated schizogene(s) or a postulated schizophrenogenic mother or a postulated virus for multiple sclerosis. There isn't any good reason I can think of, or that the authors present, for supposing "severity" to be that kind of construct at all. It is not that kind of construct in nonpsychiatric medicine. "Severity," which can range from a patient who is accidentally discovered in the course of an insurance examination or a mass tuberculosis or cancer

screening, to have an unsuspected pathology even though he had no complaints (or, more dramatically, the man who is killed by a truck and who, when autopsied, is found to have one kidney's lumen completely occluded by a gigantic renal calculus filling it, the famous "staghorn kidney," without so much as a history of complaints of mild backache!) to an individual who is moribund and receiving the last rites. We need not assume that "severity," which is basically an administrative or "clinical handling" type of concept to begin with, designates any theoretically homogeneous entity. For this reason, the authors' language in speaking of using more than one "criterion *for* severity" strikes me as possibly misleading. It sounds as though the methodological problem presented by the severity concept is on all fours with the methodological problem of assigning differential indicator weights for the presence of the schizogene, or of deciding whether the colloidal gold curve should be thrown into the clinical hopper along with the blood and spinal Wassermann and washed-out nasolabial folds and Argyll-Robertson pupils as different indicators of the presence of general paresis. In fact, I think the word "criterion" is undesirable in this kind of situation, whether we have a hypothetical construct (such as a disease entity or germ or gene) in mind or not. "Criterion" means that which defines or which suffices definitively to include or exclude. (In psychometrics, it also has the weaker meaning of "used to validate.") That is not the situation with loose genetic syndromes or, for that matter, with any kind of syndrome in which the underlying pathology is either unknown or unreliably judgeable, and consequently is not useable "operationally" as an explicit definition of the entity. Any time we deal with open concepts, whether in behavior genetics or elsewhere, we ought to use some more modest word like "indicator" rather than the strong word "criterion."

I do not mean to suggest that the study of correlations in severity between twins or other family members is unprofitable—far from it. Such correlations are illuminating as to the proper theoretical model; and any kind of theory—whether genetic or non-genetic—explaining concordance and discordance values in the clinical entity as diagnosed must do justice to more detailed and refined assessments of severity. (Even this remark requires a caveat, however: In other branches of medical genetics, and in medicine generally, "how sick" somebody is with Disease X is not the focus of much attention when the disease as yet is hardly understood. And even diseases whose etiology and pathology are very well understood, such as those due to a known invading microorganism, exhibit wide variation in severity, most of which attracts rather little interest on the part of medical researchers.) All I am objecting to is the language labeling severity a "construct" and implying that the various administrative, social and psychological variables that have been employed in studying it are fruitfully viewed as multiple criteria for severity. The point is that there is no strong reason to believe that severity is a "theoretical" dimension at all. Rather than being a dimension for which we desire good

indicators, *it* is itself in the role of a (global, best-available) "indicator" of the known and unknown theoretical entities underlying it. As such, of course, it is presently a worthwhile thing to study. But it will not, I presume, be found occurring in a full-fledged nomological network explaining schizophrenia, having been replaced by the genetic and environmental variables it now does duty for in our state of incomplete knowledge. The problem is analogous to the vexed problem of psychotherapy outcome criteria, which some psychologists persist in treating as though it were a problem of assigning some kind of optimal weights in an outcome "index." Absent a theoretical or empirical showing that some such variable as "outcome" has homogeneity, that there is in fact some sort of entity (whether taxonomic or continuous) that is being "estimated" or "approximated" by the various outcome measures, it is not clear why anybody wants to make a composite "outcome" measure. If the effect of psychotherapy is to make Jones feel less anxious because he is more openly aggressive to his father, as a result of which an MMPI anxiety measure will show him to be improved and a family's rating on "pleasantness" will show him to have become worse, this does not present any kind of problem in "weighting" these two measures, nor any paradox in theoretically understanding them. They are simply not indicators of some generic "good" or "bad" outcome; one of them is a measure of anxiety and the other is a measure of overt hostility. Whether or not this is an improvement depends upon the therapeutic contract. It is not subject to empirical study of the sort we would do when trying to find out whether spilling gravy on your vest or having grandiose delusions are as powerful indicators of the disease entity "G.P.I." as was stated in the old neurology textbooks prior to the development of accurate serological methods for identifying the paretic patient with high validity. In the theory of schizophrenia, for instance, I conceive of several polygenic modifiers or potentiators that may contribute to a patient's "holding together" until his thirties or forties (as in the paranoid subtype) and hence contribute to a rating of "lesser severity" by *one* set of clinical criteria (e.g., later age of onset, less psychometric evidence of severe overinclusiveness, or other types of gross hebephreniclike thought), such as high intelligence plus mesomorphic toughness plus high aggressiveness plus high social dominance plus relatively low social fear. Yet these factors can all be responsible for the tendency to act out aggressively by taking a shot at the President of the United States—presumably another indicator of "severity." This reasoning suggests that rather than studying concordance of severity, or treating various indicators as somehow "competing" or "alternative" *measures* of a putative construct "severity," what we really want would be a rather extensive set of clinical and psychometric measures of avowedly different theoretical entities. No doubt such a list would show that some cases presently considered discordant as to "severity" were in fact concordant psychologically, others not; and *most* cases (whether

concordant or discordant using present indexes of global "severity") would be concordant for some variables and discordant for others. (I pass by the obvious point that on that kind of multivariate profile basis, "discordance" would be a quite arbitrary cut on each dimension measured, as it would also on any profile-similarity index adopted.) For example, suppose a patient manages to stay out of a mental hospital for ten years because he employs extrapunitive, socially dominant, counteraggressive defensive techniques (along with just a dash of sub-clinical paranoid ideation) and is therefore able to manage his anxiety and prevent himself from a gross, socially observed psychotic breakdown. Would we call him concordant or discordant for "severity" with a twin who spent those intervening ten years in a psychiatric hospital? I think this kind of example shows us why the severity concept does not deserve to be treated as a *theoretical* construct with respect to which we must find optimal indicators for genetic research purposes.

In this chapter the authors say that "It is not merely a tendency to be schizoid that is inherited and is in some way causally related to schizophrenia, but something more besides." I confess I do not fully understand this statement, or the sentences that follow it. The tendency to be schizoid is a dispositional concept and I don't know just what it would mean to speak of "something else" as being an important contributory factor, when that something else is also said to be "under considerable genetic control." Is there perhaps some sort of conceptual confusion here? If being schizoid is having a personality makeup predisposed to schizophrenia, and what is inherited is a disposition [= "tendency," they call it] to that state or condition, I find it hard to grasp what a something else, also under genetic control, and also *disposing to* being schizoid or to being schizophrenic (either one!) means conceptually. But this may be partly because I cannot conceive, as mentioned *supra*, that even being schizoid is inherited. Being schizoid is having certain kinds of behavior and mental life, which include form (e.g., type of defense mechanism, parameters of various sorts) and content (e.g., social fear, apprehension about being disliked, deficient basic oral trust, low feelings of personal worth); none of this could possibly be "in the genes." One of the reasons we need an additional terminology for designating individuals who are neither clinically schizophrenic (even "pseudoneurotic") or phenotypically schizoid—I set aside here entirely the reliability and validity of those assessments—is precisely that if such a person is the MZ twin of a clearly schizophrenic individual, we need a term to refer to whatever he is dispositionally that is not the same as being either schizophrenic *or having a schizoid personality in terms of the usual nomenclature*. What term should be used for this purpose unfortunately hinges upon something not entirely conventional or stipulative, to wit, a tentative decision as to whether MZ co-twins who seem not to be schizoid would still be judged non-schizoid given a sufficiently thorough and high construct-valid assessment. Of course nobody knows, and the authors do not claim to know, the answer to this question.

With regard to their interesting suggestion that not all relevant genes get "switched on" until certain psychosomatic states are reached, I have no expertise to evaluate that within the received causal frame of physiological genetics; but I don't quite see how it follows from their empirical findings under discussion at that place in the text. I think the hooker comes from the previous sentence, where they speak of ". . . something more besides." Why does it have to be *besides*? Wouldn't it be better to say something else instead? If (as I believe Professor Gottesman has agreed in conversations with me) delusions and hallucinations and catatonic posturizing cannot possibly be transmitted by the genes, and if the Radovian "scarcity economy of pleasure" and exaggerated social fear of the schizothyme cannot, strictly speaking, be inherited either; then what is inherited is not "something else besides" a disposition to schizophrenia or schizoidness. Rather the genes determine something else instead, to wit, the underlying neurological or biochemical aberration (or whatever else it is) that is the biological substructure corresponding endophenotypically to a *higher-order disposition to acquire the disposition: schizoid personality makeup*. We can hardly suppose that the switching on or off of the schizogene(s) can switch on or off the acculturated, developed, organized adult schizoid personality, can we?

One understands why, toward the end of this chapter, they agree with Slater in excluding the alcoholic hallucinosis of one MZ co-twin, and I do not quarrel with that decision. On the other hand, one can raise here a question similar (perhaps identical?) with the question I raised *supra* in discussing such factors as influenza or brain damage in the precipitation of a schizophrenic break, from which the patient may subsequently fail to recover after he has recovered from the acute infectious disease. Not wishing to beg any genetic question, it is not clear what should be done with alcoholic hallucinosis, which is—even by clinicians who employ the term, and many do not recognize it despite its listing in DSM-II—seen as importantly different from delirium tremens or alcoholic Korsakoff syndrome. We are not today in a position to say that prolonged excessive use of alcohol *cannot* be a stressor leading to a schizophrenic psychosis in a genetically predisposed individual, who might or might not have remained compensated without overindulgence, and had he decompensated, might instead have done so *with a different clinical picture*. There simply isn't any good evidential basis for us to decide whether or not the alcoholic hallucinosis syndrome is an atypical schizophrenia whose atypicality is due to the particular chemical mode of its precipitation. For all we know, everybody with alcoholic hallucinosis, if the syndrome were optimally defined as in the eyes of Omniscient Jones, would be an "alcoholically precipitated atypical paranoid schizophrenia." I don't assert this, I simply say that nobody knows whether it is so or not. If a college student develops an irreversible schizophrenia following use of LSD, he is nonetheless a schizophrenic. Some people become almost psychotically paranoid under the influence of the amphetamines, and my impression has been that many of such are rather obvious schizotypes, although not all. The causal

chain might very well run: Schizotypy → alcoholism → brain damage → "alcoholic hallucinosis," this last event being converged upon by two causal arrows, one from the (penultimate) brain damage and the other from the schizotypy that initiated the whole chain. It is a nice example where neither fact nor theory nor an optimal bootstrapping procedure for cleaning up a loose clinical syndrome of unknown multiple etiology suffice to tell us how a case ought to be classified. Which illustrates the Feyerabendian point that our theories play a critical role in how we classify our "facts."

For myself, Chapter 7 on psychometric contributions to genetic analysis elicited the most ambivalent affective responses. I will not dilate upon the obvious advantages of employing psychometrics in genetic research, since it is perfectly clear from the authors' MMPI profiles how useful it was. One hopes that this chapter will lead psychologists and psychiatrists who study the genetics of mental disorder in the future to employ an objective instrument of respectable validity like the MMPI, instead of relying upon clinically popular devices of low objectivity whose validity is not corroborated (in some instances one should rather say, whose *in*validity has been strongly evidenced by the research literature). One must consider the fact that the MMPI is an objectively scorable and to considerable degree even objectively interpretable psychometric device; that it requires negligible time on the part of the investigator and only an hour or so by the typical examinee; that its construct validity is supported by a vast empirical literature; and that it is (to an unprejudiced reader of the record) at least as valid as any existing personality assessment device—considerably more valid than most of them. I here permit myself a dogmatic remark: There is little excuse for anybody subsequently to enter upon a costly and difficult study in human behavior genetics and fail to include the MMPI in his battery. I should opine that although that was already fairly obvious 15 years ago, Gottesman and Shields' work in Chapter 7 makes it blindingly clear.

With respect to the problem of circularity, the chapter provides us with a beautiful example of mutual support between claims of (a) psychometric validity, (b) the empirical meaningfulness or legitimacy of an open concept, and (c) the verisimilitude of a substantive theory. Many psychologists still evince a rather low level of sophistication about this extremely important methodological matter, despite the (unanswered) arguments by Cronbach and myself of 17 years ago that one cannot, except quite artificially, disentangle the logical and evidential problems of validating an instrument and corroborating a substantive theory about a construct variable, which the instrument purports to measure. One still hears it argued that you either have to validate the measuring instrument "independently" (whatever that means!) before you can plug it into a theoretical network, or you have to (again, "independently") corroborate the theory and then go about "validating" the measuring device. If this can be done, it is of course a delightful state of affairs; although one must point out that the alleged "independence"

will not, when closely scrutinized, ever turn out to be "theory independent," at most it may be a relative independence of the particular *portion* of theory that we have our eye on for the present purpose. But a realistic and sophisticated methodological appraisal of the research situation, especially in the case of open concepts and loose syndromes in behavior genetics, shows it usually to be otherwise. What we have is an interconnected set of constructs in which validity claims for an instrument and verisimilitude claims for a substantive theory concerning a variable, which the instrument supposedly measures (and which, note well, the theory "contextually" defines!) are all one ball of wax. It is thoroughly misleading to ask what appears to be the sophisticated question, "Do these impressive MMPI findings on schizophrenic co-twins tend to support the construct validity of the MMPI Sc scale, or do they tend to support the nosological claim that such an entity as schizophrenia exists, or do they tend to support the conjecture that genes have something to do with schizophrenia?" There is no either-or about it. The point is that the findings support all three of these things at once. Neither the logic nor the statistics of this should cause any intellectual distress, although I gather they often do. Again, there is nothing "viciously circular" about the factual claims, nor is there anything "circular" or "tautologous" about the definition—objections we still meet within this area, despite repeated efforts by numerous writers to clarify the matter.

As a result of the analyses carried out by Gottesman and Shields in this chapter on psychometrics, we now have better reasons than we had before for believing that there is such an entity as schizophrenia, that the MMPI has respectable construct validity for detecting it, and that genes have something to do with it. I would not even be prepared to say whether one of these three assertions receives more incremental support from the chapter's data than one of the others. Of course, one must play fair about it. By the same token, the negative psychometric results on thought disorder in nondiagnosed relatives tend to discorroborate a conjunction of assertions, to wit, that thought disorder is a "core" aspect of the schizotypal makeup (absent clinical decompensation), that schizotypal thought disorder is genetic, and that the Object Sorting Test has moderate to strong construct validity for schizotypal thought disorder. At least one of these antecedently plausible assertions would seem, given the authors' discouraging data, to be false. I leave the choice to the reader. One notices an asymmetry here (which Sir Karl Popper would find displeasing, but I cannot help that, until his fellow logicians clean it up); the positive findings on the MMPI are taken to corroborate all three assertions, whereas the negative findings on OST [Object Sorting Test] clearly refute only the conjunction of three. This being a consequence of the logic of conjunction, negation, and *modus tollens*, I am afraid I cannot be held responsible for it! There is a "heads-I-win-tails-you-lose" aspect here which is, I suggest, built into the very nature of the research

situation. What are we to do with a psychometric device that characteristically indicates a relatively lesser amount of "thought disorder" in schizophrenic patients who have paranoid ideation, since for a high IQ person to think so "crazily" as to have delusions (and in some instances to "support" them by hallucinations) can hardly be considered, from a *clinician's* standpoint, to be other than a "disorder of thought?" Until that still disputed matter is cleaned up one does not know just what to think about the authors' findings on the Object Sorting Test. I believe that we do not have at present any psychometric device for detecting mild amounts of thought disorder in the schizotype, just as we do not have any accurate means of measuring schizoid anhedonia. Until we do, we won't know what to make of this kind of negative result. But lest I seem to *ad hoc* the unexpected negative findings, I must record the judgment that these results do argue somewhat against my inclusion of "cognitive slippage" as a fundamental feature of the schizotypal makeup. To that extent the chapter must be received in evidence as against some of my theoretical opinions.

The apparent insensitivity of the MMPI to well compensated schizotypy was disappointing. One does not, of course, know exactly what to predict psychometrically about the DZ co-twins, even on a (modifier-and-potentiator) dominant gene theory, unless he relies upon the *non*psychometric diagnosis of schizotypy, which would rather defeat the purpose of including psychometrics as a separate, and putatively more sensitive, schizotypal indicator. Setting aside that possibility (which, however, the authors quite properly include as one way of looking at their data), let me spell out somewhat the source of the DZ unpredictability. There were 26 DZ co-twins on whom MMPI profiles were available. Let us neglect any influence of selective attrition, keeping in mind that this influence has a reasonably good chance of pulling down the DZ scores because of noncooperation of schizotypal co-twins, but also pushing in the opposite direction because of the greater likelihood of a decompensated DZ co-twin being available by virtue of his clinical status (e.g., in hospital). We are neglecting clinical status. Proportions are, alas, among the most unstable statistical estimators, although not as bad as correlation coefficients and beta weights. If there were no selective attrition, and ignoring clinical status of the 26 DZ co-twins, one has a theoretical expectancy of 13 schizotypes on a dominant gene model. If we compute the standard error of this expected number np by the usual formula $\sqrt{npq} = 2.6$, we see that a single standard error random sampling fluctuation of $(k - np)$ ranges from 10.4 to 15.6 schizotypes among the DZ co-twins. There is one chance in three that we are even outside these numerical limits in the schizotype rate. Now let us suppose averages of a T-score approximately 70 (higher than that suggested by previous research or by the MZ data) for schizotypes, and $T = 50$ for "normals." The expected mean T-score for all DZ co-twins would then run around 60, but the above computation in sampling

fluctuation on a dominant gene hypothesis could easily take us down to the limits of one standard error fluctuation, and that would be only around $T = 56$. Of course if one sets up a more traditional "confidence interval" for the purpose of refuting the dominant gene hypothesis psychometrically, and were on that basis to expand his range of tolerance around the theoretical expectancy of 60 to a 2-sigma fluctuation (95% confidence), the mean value of the DZ's could go down almost to the Minnesota norm $T = 50$, without postulating an outlandish sampling fluctuation. Let me emphasize that I am not in any way trying to make out the psychometrics to be better than they are. They are quite good enough to make the authors' point without any statistical finagling or fudging on my part. But one could be tempted to argue strongly against a dominant gene model on the basis of these results, unless he thought through the actual numerical situation that obtains when working with samples of this size. I am not greatly distressed about my own monogenic theory in looking at the DZ values, since extrapolating (very roughly!) from previous research it is not to be firmly expected that the Sc scale would yield a mean any higher than 1 standard deviation above the Minnesota normals.

What is discouraging, to anyone (like myself) contemplating the use of Minnesota's huge mass of MMPI file data ($N = 10{,}000$ patients) in an intermediate-stage reliance on MMPI to "bootstraps" other more direct indicators of the schizotaxic nervous system, is the fact that the MZ co-twins who were clinically normal, or diagnosed something other than schizophrenia, only managed to eke out a *T*-score on Scale 8 of 63 (Table 6.7). That suggests rather strongly that the extant MMPI Sc scale is insufficiently responsive to schizotypy as such, i.e., that the discriminations are achieved by virtue of "psychopathology" items.

Of course, however disappointed one may be about this he is not entitled to be too surprised. The Sc scale was derived using patients diagnosed in the late 1930's on the basis of formal diagnoses by a fairly conservative psychiatric staff, prior to the publication of such influential papers as Hoch and Polatin or Eisenstein, or the work by Rado on the schizotypal organization. Inspection of the item content tells us how important some rather florid psychotic items are in contributing to the Sc score. But let us not overdo that argument. The scale does contain quite a number of "subclinical" items that seem to reflect the phenomenology of the schizotype and that one would expect to show at least an average trend even in compensated cases. But these items are definitely in the minority, so we are requiring that a rather small tail wag the psychometric dog. *Suggestion*: Break Scale 8 up for genetic research. Whether the MMPI pool is qualitatively rich enough to permit construction of a "schizotypal key" that will reflect the personality organization and the subclinical phenomenology without requiring presence of any of the classical textbook diagnostic signs of diagnosable schizophrenia is doubtful. And, pushing the argument further, it is also by no

means assured that any item pool composed of verbal responses is in principle constructable that would have sufficiently high discriminative validity for the compensated schizotypal condition to be satisfactory in behavior genetics research. But I intend to try it.

Chapter 8 on the environment will doubtless elicit complaints against the authors because of its relative brevity, but it does not appear from what they *did* do by way of unscrambling environmental stressors or nurturing factors that spinning it out further would have been profitable. No doubt the qualitative impressions from the case studies helped make this a short chapter, as would the overall implications of the research they review (e.g., foster child data, MZ twins separated, father versus mother, and the like). I am gratified by the appearance of social dominance as a predictor variable, it being one of the important polygenic potentiators on my conjectural list of factors that determine whether a schizotype remains clinically compensated. I here record a high-confidence prophecy that the same will be found when such variables as anxiety-proneness, polymorph perverse sexuality, "garden variety social introversion," rage-readiness, sex drive, energy level, mesomorphy, and hedonic potential are adequately researched. We already know that heterosexual aggressiveness in one of its aspects, to wit, marriage behavior, is the biggest single element on premorbid adjustment scales—almost enough by itself to be used as a scale-surrogate.

I think it important that we regularly distinguish between (a) those environmental factors that are part of the early nurturing environment and therefore play a role in forming the schizotypal organization that emerges from the patient's childhood (these being the factors customarily stressed by antigenetic psychodynamicists); and (b) those stressors that are exerted in adolescence and adult life upon the schizotypal organization resulting from the sequence of child development as influenced by factors (a). One must be careful not to infer anything about one of these "environmental domains" on the basis of research findings concerning the other. Here again, what sort of causal theory you have in mind for the relations between schizophrenia, schizoid disposition, and the genes will properly influence how you draw your causal arrow diagram.

I think the establishment psychodynamicist might justly complain that the authors do not sufficiently allow for the richness and subtlety of the psychodynamic theory in their discussion. When we criticize the theory, we have to allow it its own inner coherency and not require it to predict facts that it really doesn't claim to predict. One may be skeptical about whether the subtle intrafamily psychodynamisms play the critical role that establishment psychodynamics gives them in the causation of mental disorder, but if they did, the kind of information one can get from formal diagnosis plus psychometrics plus even a respectable clinical case history would not have any guarantee to reveal it.

We do have a fascinating paradox that presents itself to us, given the total body of evidence of all kinds available today: How is it that almost half of the MZ twins of

schizophrenics will manage to live out their lives without developing schizophrenia but the "obvious causal candidates" among neither socio- and psychodynamic factors in a nurturing environment, nor situational stressors imposed upon the adult schizotype appear, whether looked at statistically or idiographically, to be clearly identifiable as making the difference between the schizophrenic proband and his compensated MZ co-twin of identical genotype? *Point*: The concordance statistics themselves prove a major influence upon clinical status to be *non*genetic; but when we look in a variety of ways for conceptually treatable aspects of the "environment," we draw practically a blank. This is surely a puzzler for the theoretician. The first possibility—and here, as I indicated *supra*, I tend to line up somewhat with the psychodynamicist "against" our authors—is that nothing but a very detailed knowledge of the life history in its unique idiographic sequence of events (including *inner* events!) would provide the evidentiary material for a causal understanding of the difference. If this were so, and I am willing to assume that it is at least sometimes so for the discordant pairs, one cannot infer that a more thorough going study by intensive depth interview methods of the psychotic and nonpsychotic adult pairs would even give us the information. My own determinist beliefs lead to an unjustified optimism about reconstructing the past when "history" (whether of a life, a nation, or a religious or political movement) is the subject matter. It is not obscurantist, nor incompatible with a faith in determinism, to have doubts about the feasibility of such reconstruction. There may be critical events, in systems involving what Langmuir called "divergent causality," that are literally unavailable to the investigator from a study of the patients, or any kind of documents, twenty years after the critical event occurred. If a geologist finds a somewhat unusual kind of formation occurring in a given type of rock, he may or may not be able to spin out some plausible causal hypotheses within his overall theoretical framework; but even if he can do so, the most detailed knowledge of physics and chemistry plus the overall generalizations about the history of the earth, about how igneous, metamorphic, and sedimentary rocks are formed, and the like, will not enable him to infer with confidence just how this one strange chunk of rock got the way it is.

I do not think this kind of analogy is far-fetched, given a theory of schizophrenic decompensation as complicated as I believe we are going to need even to deal with "the general case." A major difficulty is that we have to conceptualize "the environment," which is literally "everything causally efficacious except the genome proper," largely by *parameters* or by *classes* of events. Whereas a filled-out psychodynamic comprehension of why Jones underwent an acute schizophrenic break at age 23 but his genetically identical twin did not, would be to know the full psychological details of a particular event in the decompensated twin's life history, *and that we may never know, even on the basis of a thousand hours of intensive psychotherapy*. Thus, for example, one interested in

the role of sexual conflict in producing schizophrenic decompensation might do a statistical study of "familial puritanism" in relation to diagnostic concordance, and find nothing. Frustrated in this nomothetic parametric effort, he might shift to a more intensive study of families e.g., whether a seductive compensated schizotype mother tended to put the one twin in more frequent or intense oedipal binds than she did the other. But even this might not yield anything, whether treated statistically over sets of families, or strictly idiographically. After spending thousands of hours of his brain power and perhaps thousands of dollars of taxpayer money, our eager-beaver investigator reluctantly concludes that "There seems to be nothing about the sexual environment that helps to explain the difference." Suppose that similar investigations are conducted by many competent persons into other aspects of both the nurturing and adult stressing environments, covering such plausible sectors as academic achievement, social acceptability, neighborhood atmosphere, financial success, and inter-current disease, with similar negative results. If such should be the long-term outcome of numerous similar investigations, one might be tempted to conclude that there is "nothing environmental" that bears upon the question of compensation versus decompensation, an obviously preposterous conclusion given the high discordance rate for MZ twins! This dreadful fantasy of negative results "no matter what we look at in the environment" is not likely to materialize, but it hardly seems excludable on the basis of the evidence thus far gathered by our authors and others.

Consequently we should set our switches in advance not to be completely baffled by a paradox: Failure to find positive environmental correlates of decompensation, despite the clearly established power of environmental influences collectively as shown by the genetic statistics themselves. I don't think it will be too hard for a genetically oriented psychotherapist to make sense of these facts, scientifically frustrating though they would be. Neither a rough measure of familial puritanism, nor a measure of a schizotypal mother's differential seductiveness as between two MZ twin boys, covers the possibility of a critical event such as Twin *A* receiving a completely unexpected low grade in his physical education class (due—let's really run it into the ground—to a clerical error!) several months following his first heterosexual experience. It doesn't take much for a schizotypal mind to connect up these two happenings in some sort of crazy, hypochondriacal, and guilt-ridden fashion. *Without anything else* being "systematically" different between him and his MZ co-twin, his aberrated CNS may take it from there and snowball it into a psychosis that appears, say, a year later. I do not myself find this kind of "happenstance" at all implausible, and therefore I was pleased to see our authors' explicit emphasis upon "chance" factors in their discussion of the environment. The causal model for an integrated theory of schizophrenia would surely involve social feedback loops, autocatalytic processes, and powerful critical episodes initiating chains of divergent causality, perhaps the most important of this third kind of causal relation

being idiographic content features that alter the subsequent psychological meaning of interpersonal events *that may have the same sort of "average value," parametrically speaking, for both members of a discordant MZ pair*. Thus, for example, 6 months after our hypothetical Twin *A* in the preceding example has schizotypically concluded that "sexual drainage" caused him to fail the gym course, both twins are present at a dinner table conversation. The father says, innocently and with no notion of his critical schizophrenogenic role, "If there is anything I cannot stand, it is a boy who is a sissy." Now the schizotypal snowball really gets going for Twin *A*, whereas father's casual remark has negligible psychological significance for co-twin *B* (who has neither failed in gym nor visited a prostitute). I find it hard to think of any kind of statistical analysis of case history material or neighborhood characteristics that would tease out this kind of thing. And if one combines these "chance" factors with the possibility (some would say likelihood) that the schizogene(s) can "switch on and off" as a function of intercurrent biochemical states, quite possibly including states induced by momentary stressors, the elements of "psychological-social coincidence" can loom very large indeed. Every psychotherapist who has treated schizophrenics knows that the patients themselves sometimes connect a momentary resurgence of anxiety or confusion with what would to a normal mind be a very minor happenstance; and while I certainly do not wish to rely heavily on these anecdotal connections (see *supra*), neither would I be willing to dismiss them as of no evidential weight. Following close upon father's "sissy" remark, random episode E_1 (a waitress momentarily ignores him in favor of a customer that she knows well) ticks off in our Twin *A* a 2-hour increase in the blood level of norepinephrine. Due to his oddball dietary obsessions, which in turn went back to his reading a pamphlet (which didn't *happen* to fall into co-twin *B*'s hands) at age 14, he also is running an unusually high level of organic acid X at the time. These concurrent alterations in the intracellular milieu of the schizogene, and note that they are neither physiologically nor psychologically related, nor attributable to any *systematic* characteristics of the environment, "switch on" the cerebral schizogenes and as a result the patient undergoes an increase in his pan-anxiety, his anhedonia, and his tendency to cognitive slippage. The last straw: While he is in this state, which is a deviation from his usual schizotypal norm, his girlfriend breaks a date with him, speaking rather roughly on the telephone (because she is embarrassed, and in order not to feel defensive she becomes aggressive). *Result*: snowballing in the aversive direction, dangerously consolidating the mixed-up schizoid complex: "I am bad and weak because being sexually drained I have become a sissy as my father said, which is why waitresses prefer others to me, as does my girlfriend, and hence all women. I'm a hopeless nothing." Twin *A* is now well on the way to clinical decompensation.

I must emphasize that envisioning these kinds of "idiographic unpredictabilities" and even after-the-fact "unexplainabilities"—not quite the same thing, as Scriven and others have convincingly shown—does not require that we postulate any sort of radical

biological or psychological indeterminism. We just have to recognize unblinkingly the rather obvious fact that even a so-called "thorough in-depth" life history is extremely deficient as regards details, and that we have nothing to guarantee that this deficiency could be made up by *any* amount of ingenuity or expenditure on the part of an investigator concerned to reconstruct the past. The kinds of "influences," "variables" and "factors" that social scientists are usually able to assess are almost always, when carefully scrutinized, classes of variables or kinds of episodes. In terms of learning theory, we deal in most psychological and sociological research with parameters of the elaborate "social Skinner box" that constitute a person's nurturing environment and adult life. The numbers we can correlate with outcome (e.g., psychosis) are in the nature of average values, they do not point to what may be critical events but rather to stochastic features of discriminative and eliciting stimuli or schedules of reinforcement contingencies.

If I were to present an engineer or physicist with a "molar" problem involving a chair made out of a specific kind of metal, riveted or welded in a specified way, telling him I was going to catapult it from the roof of the Physics Building at 12:32 P.M. in a direction so it would land on the stone steps of the Administration Building, and require him to predict whether and how it would fracture, he would probably decline the invitation. *A fortiori*, he would decline if the object to be catapulted were a century old oak-case grandfather clock! But that, brethren, is about the situation when we are trying to understand why Twin *A* became schizophrenic and MZ Twin *B* did not.

I may conclude this discussion of "chance" factors determining which twin decompensates by quoting from my paper read at the 1971 MIT Conference on Prospects for Schizophrenia Research, where I said

> But that there are *some* schizophrenics who act more like *some* anxiety-neurotics than they do like *other* schizophrenics is an important fact to think about and to explain. It is, however, very weak evidence against anybody's theory of schizophrenia, genetic or otherwise. I understand from the mathematicians that there is a clear negative answer to this question; and it is found, for example, in the theory of certain stochastic processes such as random walks. Whether a particle pursuing a random walk ends up (after a specific finite time) in a so-called "absorbing state" [=a state which it cannot leave] is a "dichotomous end-result" comparable to whether a schizotype ends up in a state hospital, enters and leaves, or wins the Pulitzer Prize for poetry; but the mathematics of such situations teaches us that it would be a mistake to presume a dichotomous etiological basis for this important outcome difference. In that connection, I mention in passing that we should not assume, even in the case of MZ twins, that a clinical discordance must always have some "big" life-history factor discernible. That Twin *A* becomes schizophrenic and Twin *B* remains "healthy" may be a random walk problem—I myself would bet that *many* of them are.

I am not, in the light of these reasonings, entirely happy with the authors' statement "MZ 22*A* spoke convincingly of how ordinary contact with a young man at work

reawakened sexual conflicts which then escalated into overt thought disorder and a relapse. We can hardly call a happening as subjectively apperceived and idiosyncratically elaborated as this an objective etiological stress. It would not be feasible to design environments so as to insulate people against these kinds of stresses." It seems to me that this conflates a technological problem in social engineering (admittedly important to be clear about) with what is primarily a theoretical issue. I do not see any reason why the girl's contact with the young man should not be considered an "objective" etiological stress, if it is the objective condition for the actualization of (an also objective) disposition. The disposition is admittedly aberrated, because the individual is schizotypal; but its activation is nonetheless "objective," is it not? I think that the behavior geneticist should take these kinds of situations as the tort lawyer takes them: It is no defense, in an action for damages produced by a light blow on the head, for the defendant to show that plaintiff had a rare disease called "eggshell-skull." The tort lawyer's maxim is, "You must take the plaintiff as you find him."

As a final comment on this chapter, it may be that the customary distinction between "necessary" and "sufficient" factors requires more detailed methodological analysis before it can be powerfully applied in behavior genetics, especially to the examination of a polygenic theory. I venture the opinion that this is one of the rare instances in which the technical contributions of philosophers of science may actually be of some positive value to the scientific theorist or investigator. Both in law and in medicine, examples are currently being subjected to intensive philosophical analysis, and the outcome of these investigations is not presently foreseeable. But for reasons similar to those that led me to needle the authors gently on ambiguities I discern in what "specific genetic etiology" means for the polygenic case, I would say that there is a slight conceptual murkiness in the distinction between necessary and sufficient causal factors in their chapter on environment. To detail that argument would go too far afield so I shall content myself with noting that, in a fascinating transatlantic exchange with Professors Gottesman and Shields, I found myself delineating some half-dozen possible mathematical meanings of the term "specific etiology" (not, by the way, confined to the genetic case), any one of which is semantically defensible and which might have a methodologically fruitful application, extending from the crystal-clear case of a dichotomous factor (e.g., the mutated gene at the Huntington's chorea locus) to an attenuated meaning (formulable only in terms of mixed partial derivatives) that is *so* weak one hesitates to apply the term "specific etiology" at all. I hope shortly to publish the results of this analysis.[*]

My only comments on Chapter 9 concern the question of "other diagnoses." Had they been classified as part of a continuum of schizophrenic psychopathology, the authors would have been severely criticized for "loading the dice" in favor of a genetic emphasis,

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[*] Meehl, P. E. (1977). Specific etiology and other forms of strong influence: Some quantitative meanings. *Journal of Medicine and Philosophy*, *2*, 33-53. See also: Meehl, P. E. (1972). Specific genetic etiology, psychodynamics and therapeutic nihilism. *International Journal of Mental Health*, *1,* 10-27. Reprinted in Meehl, *Psychodiagnosis: selected papers* (pp. 182-199). Minneapolis: University of Minnesota Press, 1973.

and I certainly do not want to suggest that *for their purposes* these other diagnoses should be thus subsumed. But lacking any substantive specification of what it is that is schizo-specific in their polygenic model, we cannot be sure that such cases would be excluded by Omniscient Jones. On a big-gene model with numerous modifiers and potentiators, one may be in doubt as to whether this or that individual case is "atypical schizophrenia" or any of the other official and unofficial labels that some of us are fond of employing, perhaps carelessly at times (e.g., "pseudoneurotic schizophrenia," "pseudopsychopathic schizophrenia"); but one does have a fairly clear *meaning* for the monogenic concept, in the sense that whatever the ambiguities of the clinical phenotype, even including a beautifully compensated schizotype detectable by no presently available methods, the individual belongs to the group if he has the schizogene, otherwise not. I want to urge, not that a polygenic model *could* not provide such a basis (would it be genuinely taxonomic?), but that when the psychological or biochemical *nature* of what is allegedly schizo-specific but nevertheless polygenic has not been even speculatively indicated, one has no rational basis for deciding whether a severely depressed or chronically delinquent or episodically alcoholic person does or does not "belong," does one?

I have less to say about the final chapter on genetic theorizing, because most of what occurs to me upon reading it would be repetition of methodological or substantive issues that have arisen in my comments on the previous chapters. For reasons given *supra*, I think the authors concede too much by saying "On the face of it, such observations [of a disproportionally higher incidence and prevalence of schizophrenia in the lowest social classes] provide strong support for the role of social stressors as causes of schizophrenia." While they go on to criticize that interpretation, I cannot agree that this correlation provides even "on the face of it" strong support for much of anything. It is as it stands an ambiguous fact, so far as etiology is concerned. I trust I have given sufficient reasons for that opinion above.

In their discussion of our colleague Dr. Leonard Heston's view that about 50% of the first-degree relatives of schizophrenics have a mental abnormality and that these are cases of "schizoid disease," the authors are, of course, correct in mentioning the difficulty that arises from our having no reliable way to identify a *case* of such "schizoid disease" without reference to his relatedness to a schizophrenic. But they go on to say, "If the concept is defined broadly enough to encompass abnormalities in 50% of schizophrenics' parents, sibs, and children, and then generalized, the population base rate will be exaggerated and include many false positives." While Dr. Heston would of course agree that his interpretation is at present speculative—betting on our mono-genic horse!—in examining the merits of that substantive position, are we really entitled to assert confidently that the population base rate will be "exaggerated" and include many false positives? That depends upon the gene frequency, and on a view such as

Heston's or mine, the "clinical penetrance" will run very low. Although there would be a vicious circularity in *arguing* that two actual cases of apparently "anxiety neurosis" syndrome are nevertheless different because one is manifested by the MZ co-twin of a known schizophrenic and the other not, *speculating* that this is in reality always the situation (although we do not presently know how to corroborate or discorroborate it) does not commit us (substantively) to an *impossibly* high base rate, does it? Apart from genetic investigations, we already know (e.g., from Piotrowski and Lewis' follow-up studies of rediagnosis, or from Peterson's work on the MMPI profiles of misdiagnosed VA patients) that some schizotypes do appear clinically indistinguishable from, say, "anxiety neurosis" or "depression" when first seen by a psychiatrist. The point is that one does not know how many "false positives" would exist among the patients that Heston considers "schizoid disease," let alone those that Rado or I would label "compensated schizotypes" (some of these not even showing the pseudoneurotic schizophrenia syndrome) unless he already has somehow assigned a numerical value to the hypothetical dominant gene population frequency.

In discussing the psychotic relatives in Ødegaard's study the authors say: "If transmission were monogenic, we would usually expect to find (a) an excess of schizophrenia and no excess of any other abnormality and (b) an unambiguous bimodal distribution of affected and unaffected in the relatives of probands." As a literal statement, if "monogenic" is taken to mean one "big gene" whose "clinical penetrance" is being held down *by modifiers that have no other behavioral relevance*, this statement is unexceptionable. But nobody holds such a theory. We already realize that you can't make a dominant gene theory fit the facts without finageling with penetrance (or, saying it a different way, but one that comes in my view to the same thing, my not making my theoretical distinction between schizophrenia and schizoid disease, schizoidia, or schizotypy); and that is what the pushers of a monogenic theory, such as Slater, Heston and myself have regularly done. So we begin by arguing that the facts require modifiers (in my terminology, schizophrenic potentiators). Now is there any plausible basis to suppose that these modifiers and potentiators are *psychologically irrelevant* when found in nonschizotypes? I cannot conceive that this would be the case. It seems to me that the theoretical and clinical grounds for denying it are, in the aggregate, so massive and interlocking that it would take a fair amount of research of above-average caliber to convince me of the contrary. As to their role in the schizotype, surely no one, whatever his etiological view of schizophrenia, believes that the major human emotions—even in their "nonpathological" form and intensity—have *nothing* to do with the phenomena of schizophrenia. All you have to do is go through a state hospital or treat a schizophrenic patient to know that rage, fear, sex, dependency, shyness, pride and so forth play a role in the character and intensity of his symptoms. Of course this recognition does not

contradict an etiological theory making the schizogene(s) a necessary condition for developing the disorder. It just recognizes the rather trivial and unexciting fact that schizophrenics, being people, tend by and large to have pretty much the same things on their minds that the rest of us do! (It takes a psychiatrist or psychologist to make a theoretical mountain out of this particular molehill.)

Gottesman and Shields' own data, taken together with the other studies they review, indicate at least one psychological variable—not identifiable as such with schizophrenia or schizoidia—to wit, social dominance, that plays an important role in concordance, course and severity. But we have independent evidence, both in humans and in animals, that social dominance is to some considerable degree inherited, presumably on a polygenic basis. Hence I conclude, until further notice, that one of the potentiators of schizophrenia (given schizotypy) is very probably social dominance. And I cannot imagine that anxiety proneness, rage readiness, social introversion, and the whole list of variables which we already know something about, have some ability to measure psychometrically, and have some evidence (on humans and animals) to consider partly hereditary, are utterly beside the point in potentiating a schizophrenia. (It seems to me that this might be considered even more plausible on a polygenic theory, although I do not wish to press the point). Now, unless the authors believe that these temperamental dispositions have nothing to do with mental disorder *outside* "the schizophrenic spectrum," why would they want to say what they say in the sentence quoted? I would expect the contrary, either on a polygenic view or on a main-gene view with multiple potentiators, namely: The collaterals of schizophrenic individuals ought to be expected, given sufficiently accurate assessment, to show a heightened incidence of practically every kind of behavior aberration except possibly any that might result from abnormally low contributors to "social fear," e.g., the true, Cleckley-type hard-core psychopathic deviate.

As to the second half of their sentence, that one ought to find an unambiguous bimodal distribution of affected and unaffected in the relatives of probands, I do not believe this has been shown by the authors, or by anybody else. How "unambiguous" a bimodal distribution looks depends upon the degree of latent curve separation, and very importantly on the unreliability of the continuous variable employed as an indicator. It takes a separation of around three standard deviations to produce a clear "valley" in a joint distribution having equal base rates, and with a separation of two standard deviations, inspection will just barely detect the bimodality with infallible measures. With asymmetry of base-rates it becomes still harder to discern. So far as I am aware, detailed working out of the relationship between observed bimodality and a latent taxonomic situation has yet to be rigorously done; and the occurrence of bimodality has been shown by Murphy to be neither a necessary nor a sufficient condition for a single (qualitative, dichotomous) etiology. I don't mean to push my dominant gene view *a priori*; I merely want to assure that no factual implications are improperly drawn

from a dominant gene theory that is sufficiently complex to remain in the running given the present data. I will go a little farther than this, hoping thereby to shape the direction of future research on the competing genetic models. The differential impact of schizophrenia on fecundity between the sexes, taken together with clinical experience working with compensated and pseudoneurotic schizotypes of the two sexes, leads me to the conjecture that on a dominant gene theory, there ought to be quite a few more schizophrenics who got the schizogene from mother than from father. Speaking of the schizogene and not clinical schizophrenia, I am going to stick by that conjecture awhile yet, despite some evidence to the contrary. As I suggested in my 1962 APA presidential address, a plausible family pattern (which also explains much of the intrafamily dynamics commonly assigned etiological status) is that of a compensated schizotypal mother—especially one with a heavy dose of dominance and aggressiveness, *which is partly what keeps her compensated*—and a neurotic father, who provides high anxiety and low dominance polygenes (along with poor identification for a male child). Be that as it may, one does not need such speculations to draw some tentative inferences from the well-corroborated sex difference in schizophrenia's effect on fecundity. I have enough of the psychodynamicist in me to find it incredible that a schizotypal mother is, on the average, no more psychologically malignant a feature of the nurturing environment than is a schizotypal father. I say this despite the authors' summary of evidence, with the exception of Reed *et al.*, suggesting the contrary. (I must once again remind the reader that schizotypy is not the same as clinical schizophrenia.) I have been unable to find in the literature—my local geneticist colleagues, including Professor Gottesman, tell me that the reason I cannot find it is that it doesn't exist—a mathematical analysis of the expected situation when we conceive a dominant gene to be potentiated by polygenic systems that tend more often to come from the *other* parent rather than from the one from whom the dominant gene is inherited. Because if the schizotypal parent also had many of the potentiating polygenes, he would tend to have been schizophrenic, and consequently would tend not to have *been* a parent at all! We then postulate the psychodynamic hypothesis of a greater environmental potentiating factor if mother is a schizotype than if father is. I predict that nothing less complicated than this model will do justice to the facts when we have (a) sufficiently accurate taxonomic statistics, and (b) applied them to respectably valid indicators of compensated schizotypy. The sort of causal model I have in mind is just too complicated to permit the kinds of traditional geneticist implications of monogenicity that the authors express in the quoted sentence.

I seem to have a blind spot for an argument that my geneticist friends keep giving me, which relies on the low gene frequency for nonpsychiatric disorders with single gene inheritance. Gottesman and Shields repeat this argument using the example of cystic fibrosis, pointing out that it is 20 times rarer than schizophrenia. Since everybody makes

this argument, I feel considerable pressure to accept it (especially from experts in a field where I have no real expertise), despite my persisting inability to fully understand its logical structure. As mentioned *supra*, I think we ought to be prepared to find that schizophrenia is kind of "funny" from a geneticist's standpoint, i.e., that it violates some of his ordinary numerical expectations. And nobody cites to me any actual laws of either population genetics or physiological genetics that will assure me that a gene for subtle neurological integrative defect could not occur 20 times as frequently as the gene for cystic fibrosis. I suspect that the whole set of analogies to other genetic conditions may be misleading us, because their application to schizophrenia is not based upon a sufficient recognition of the differences that are quite likely to arise between behavior genetics and other branches of genetics by virtue of the complex social learning involved—that what is inherited is not merely the first step in a three, four or five link metabolic chain (of the kind with which we are familiar in the physiological genetics of Mendelizing mental deficiencies), but a "something" that affects certain functional parameters of the CNS (and in a rather subtle way, initially) *so that what we call the "pathology" of the clinical disease is learned social pathology*, related only derivatively to the fourth or fifth order dispositions that are, strictly speaking, "heritable." I have such a hard time conveying that point of view to geneticists and psychologists that I am almost ready to conclude that my thinking is haywire. But for the record, I rashly record here the prediction that it will be necessary to "think differently" about not only schizophrenia but manic-depression, unipolar depression, compulsion neurosis and all other learned behavior disorders whose syndromes are defined by certain *psychological* contents, themes, object-cathexes, self-concepts, and preferred mental mechanisms. The causal and statistical model needed is, I predict, just not the same *sort* of model as is involved when we deal with the diabetic's defect in carbohydrate metabolism or the PKU child's inability to handle a normal phenylalanine dietary intake.

In this chapter, which to one with my concerns is one of the most fascinating and stimulating in the book, I wish the authors had permitted themselves to speculate a bit on what kinds of psychological dispositions they believe to be polygenically inherited and yet schizospecific, especially since elsewhere in the book—including the remarks in this chapter mentioned immediately above—they seem to exclude from the list of polygenic loci those that bear on psychological dimensions of the kind that we know are important in other kinds of behavior disorder. If whatever is the polygenic system that makes specifically for schizophrenia does not overlap with whatever makes people anxious or angry or depressed or sexually perverse or shy or submissive or whatever, what *is* it behaviorally? On my view that is part of the difficulty in any formulation that makes the inherited trait(s) *behavioral at all*, which I think they are not. They

get to be behavioral only as a result of several further processes. Basically, they are "neurological," in a sufficiently sophisticated sense of that term. I daresay that Gottesman and Shields would reply to this criticism that we have only a little evidence to make such speculations fruitful at the present time. I cannot quarrel with that response, since I am not one to tell others that they have to adopt the same philosophy of science as I do. But with so beautiful a set of data, and such a mastery of the empirical research literature, I think they could have permitted themselves somewhat more free-wheeling speculation in their final chapter. And—trusting that this is not hitting below the belt—I entertain the dark suspicion that one reason they did not speculate about what the specifically schizoid disposition is (in its inheritable component) is that had they done so, they would have been in somewhat of a conceptual bind because of the combination of their polygenic view, their schizospecific view, and their exclusion from the list of what would otherwise be the most plausible candidates. As to their discussion of the "trajectories" of two hypothetical twins, all I need say is "Good!—and matters must be at least as complicated as this, in the eyes of Omniscient Jones."

Well, this afterword has almost become a book review. I have devoted space very largely to caveats, queries, obscurities, challenges, and (very few) real "complaints." I trust this approach does not convey a negative, carping impression. The great merits of this book, reflecting the talent and dedication of its authors, are sufficiently obvious, so I stated at the beginning that only a brief summary of them would be appropriate. The highest praise of a scientific work is to take it seriously; and that means, especially for us neo-Popperians, to *criticize* it, in Sir Karl's honorific sense of that word. The history of science is a history of errors, since all theories are lies. The point is to abandon the black lies as quickly as possible, and to change the gray lies in the direction of lighter grays—to improve a decent theory's "verisimilitude." If, as I believe, a genetic theory of schizophrenia has (by this book) been definitively corroborated, the task now put before us is to determine what is inherited and how. Empirical research on these difficult questions will, I think, be wasteful unless we explore the *conceptual* possibilities imaginatively, and prepare ourselves for some "new problems" for which the received models and methods of genetics may not be adequate, because of the socio-psychologjcal learning processes that enter the picture. My belief in the importance of that methodological thesis is what led me (given Professor Gottesman's highly "permissive" invitation) to indulge so freely in unresearched substantive conjectures.

To repeat what I said initially, this book, definitive for its purpose, perhaps represents the final step in a purely "behavioral" study of the genetics of schizophrenia. I do not myself believe that further twin or other family studies will add materially to what is surely a sufficient body of evidence for a genetic interpretation of this disease. And I cannot convince myself that further studies will add significantly to our ability to choose

between competing genetic models, unless and until more powerful phenotypic indicators of the relevant gene(s) become available. The "validation" of such indicators will involve complicated methodological issues, including the Cronbach-Meehl "bootstraps effect," about which many of my brethren are still regrettably unclear. At the strictly "psychological" level, there may be some merit in pursuing the construction of personality inventories of MMPI format whose *content* is beamed more specifically at the schizotypal deviations in thought, in soft neurology, and body-image aberrations. I hazard the guess that measures of hedonic deficit, to which hardly any psychometric effort has thus far been devoted (because of psychologists' inexcusable ignoring of Rado's seminal contributions), should be assiduously pursued. I have myself constructed a tentative list of inventory items based partly upon the literature but mainly upon my clinical experience with schizotypes. I would not advise anyone to invest much research time trying to construct devices of a psychological sort beamed at the detection of the "interpersonal aversiveness" which is such a dramatic feature of disintegrated schizotypy (but almost equally striking in the decompensated case called pseudo-neurotic), because while it has its qualitatively unique flavor (different from, for example, sociologically based feelings of inferior status, or "garden-variety polygenic social introversion"), I think it unlikely that these subtle phenomenological differences can be satisfactorily tapped by question and answer item material. Difficulty in relating to other people is a ubiquituous feature among mentally aberrated persons. Unless we can tap into the very special quality of the schizotype's deep, pervasive, recalcitrant, and preverbal lack of basic "oral trust," which I doubt we can do with a personality test item (or, for that matter, a Rorschach or TAT), we are going to get too many false positives among nonschizotypal mental patients. I have considerably more faith, on either my own theory or anybody else's, in the improvement of measurement techniques for phenotypic indicators less "psychological," closer to the gene(s). Even in the behavior domain, I should anticipate that psychophysiological measures will do better than personological ones, although I hasten to add that the widespread interest in measures of anxiety seems to me wholly misplaced and, in fact, somewhat naive. Surely *nobody*, on any theory of schizophrenia, supposes that anxiety-proneness is in any way schizospecific? I am puzzled by the direction of research efforts in this field, since there are so many variables we might be looking at that one would expect us to begin by looking at whatever appears, on available clinical and experimental evidence, to have better prior probabilities of ringing the bell. I would think it better strategy to study malocclusion or the tendency to "swallow the wrong way" both clinical correlates of schizotypy by some reports (I agree) than anxiety-proneness. The first two "far-out" guesses have at least a fighting chance of being interesting (as pleiotropic); but the third does not. We should research variables that we have reason for

thinking may be more or less specific to whatever makes schizophrenia behaviorally, prognostically, and *genetically* different from unipolar or bipolar affective psychoses, psychoneuroses, sociopathy, the psychophysiological disorders, and the like. Concentrating on anxiety, whether measured psychometrically or physiologically, when one is interested in the genetics of schizophrenias strikes me as rather like concentrating on fever when one is interested in the genetics of, say, the rheumatoid diseases. But perhaps there is something important going on here that I obtusely fail to understand.

I would look to a refinement and objectification of the "soft neurology" as perhaps the most plausible single area to focus on while remaining in the domain of the exophenotype. Granted the perennial ambiguity of "soft neurology" in the decompensated case, the longitudinal research of Barbara Fish and the ongoing study of Israeli kibbutz children of schizophrenic mothers lend, I think, sufficient quantitative support to the folklore of clinicians (from Kraepelin through Bleuler to Schilder) to justify pursuing this lead. Being a biochemical ignoramus, I shall say nothing here about research possibilities for the endophenotype, except to suggest that on my speculative theory of schizotaxia, single-neuron studies of synaptic parameters might be very profitable, being only one or two steps removed from the postulated "biochemical lesion." Even here, however, the psychogeneticist may still play a critical role, if he can come up with molar behavior indicators having sufficiently high validity for compensated schizotypy. I predict that this will only be possible if "nonpathological" behavior dimensions are treated conjointly via sophisticated "bootstrapped" taxonomic statistics.

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