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Development as a Unifying Concept in Psychiatry*

By LEON EISENBERG

A quotation from Edward Mapother can serve admirably as text for this address: 'In practically all properly investigated cases of insanity, it is found that it is the result of a summation of multiple causes, effective in combination, though inadequate singly. It is this that renders all controversy between extremists of the physiogenic and psychogenic schools so futile' (Lewis, 1969, p 1359). In the same year, 1922, in his Salmon Lecture, Adolf Meyer said: 'The overmechanization of psychiatry . . . (has) led to too much reliance on chemistry and physiology as curealls in mental ills, while psychoanalysis, by laying too much emphasis on the subconscious and sex, has lost sight of the . . . functions of the conscious mind and has . . . disregarded the fact that man is subject to physical . . . biological . . . and social laws' (Meyer, 1922).

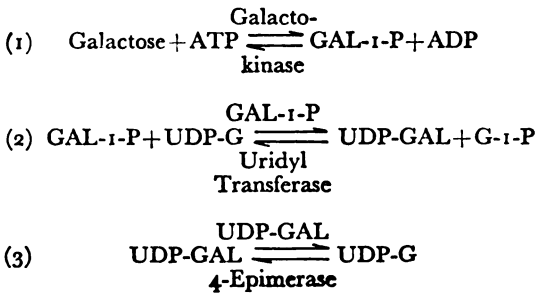
The central thesis of this lecture can be set forth simply enough: the process of development is the crucial link between genetic determinants and environmental variables, between individual psychology and sociology, between Mapother's 'physiogenic and psychogenic' causes 'effective in combination, though inadequate singly'. What remains is to try to persuade you that a developmental approach is a useful way for the clinical investigator to conceptualize the problems he faces in studying and treating maladaptive behaviour. In so doing, I propose to use the term 'development' in a large and metaphorical sense, including not only the roots of behaviour in prior maturation as well as the residual of earlier stimulation, both internal and external, but also the modulation of that behaviour by the social fields of the experienced present (Schneirla, 1957).

* The Fifth Mapother Lecture, delivered at the Institute of Psychiatry, London, 17 November 1976.

From this vantage point, it becomes absurd to dichotomize nature and nurture or to contend that the one or the other is sufficient in itself to account for the phenomena the physician observes either in health or in disease. What is crucial is an understanding of the interactions between the two, interactions that determine the trajectory of development. For most of this century, American psychiatry has disdained the study of heredity as though it were fundamentally antagonistic to a pragmatic national spirit which has emphasized the possibility of improving the human condition. The objection to genetics had had its roots in a fear that the demonstration of an hereditary basis for a trait is equivalent to therapeutic pessimism, a fear, let us acknowledge, that has been reinforced by ill-conceived theories of rigid and unalterable genetic determinism (Eisenberg, 1976). However, in the light of the discoveries of modern molecular biology (Watson, 1976; Jacob, 1973), just the contrary is likely to be true.

The expression of genetic information requires a permissive environment. Consider only the instance of galactosaemia, an autosomal recessive metabolic disorder of infancy which if uncorrected leads to hepatomegaly, failure of development, seizures and untimely death. The immediate mechanism of the disease lies in a deficiency in the enzyme, galactose-1-phosphate uridyl transferase (Fig 1), which results in an inability to convert galactose into glucose, the accumulation of galactose-1-phosphate and galactitol in body fluid and tissues, and the induction, presumably by enzyme inhibition, of widespread biochemical malfunction (Hsia, 1968). Yet the identification of the enzymatic defect by newborn screening and the exclusion of galactose from the diet by eliminating milk and milk products result in a normal growth pattern and a child indistin-

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GAL-1-P accumulates at step (2) because of deficiency in the enzyme

FIG 1

guishable from others except for his dependence on a carefully monitored diet (Fishler *et al*, 1972). By now, more than 150 inborn errors of metabolism have been identified, most of which result in damage to the central nervous system (Brady, 1976). Thus far, only a few are as readily reversible as galactosaemia, phenylketonuria and congenital hypothyroidism; others, like Tay-Sachs disease and Down's syndrome are subject to intrauterine diagnosis and therapeutic abortion, measures, it should be noted, which in most instances enable afflicted families to bear their children safely (National Research Council, 1975). Contrary to the fatalistic myth, the identification of genetically controlled pathways opens up possibilities for decisive medical intervention by environmental modification (as in galactosaemia), by replacement therapy (as in hypothyroidism) or by differentiating defective from normal foetuses in order to enable parental carriers to give birth to healthy offspring (as in Tay-Sachs). But, for my argument, the informative instances are those in which, despite our present inability to repair the enzymatic defect, we can limit and even prevent its expression by modifying the crucial environmental variable with which it interacts.

Attempts at quantitative partition of phenotypic variance into genetic and environmental components require the assumption of linear models, single causes and additive effects, assumptions which ignore the ubiquity of interactions and correlations between genotype and environment (Lewontin, 1974). It is precisely such unwarranted assumptions that invalidate current estimates of the broad 'heritability' of human intelligence (Feldman and Lewontin, 1975). Indeed, when the concept of heritability of intelligence is extended to comparisons between human races, its absurdity is compounded. On the basis of known data for human blood groups, serum proteins and red cell enzymes, Lewontin (1972) has calculated that about 85 per cent of human genetic diversity is attributable to variation between individuals *within* populations and only about 6 per cent of the total is due to variation between races.

The simplifying mathematical convention that additive factors are large in relationship to interactive ones, the convention underlying the use of the analysis of variance in heritability studies, cannot be taken for granted. For a given genotype, a particular environmental variable may have only trivial effects whereas it may be decisive for the expression of a second; this applies to variations in the amount of dietary milk for the phenotypic outcome of the normal versus the galactosaemic genotype. In other instances environmental effects produce a curve shaped like an inverted U with the phenotypic trait maximal in midrange, as in the parabolic relationship between temperature optima and enzyme activity. For two such genotypes which differ in temperature, both genetic and environmental effects will be barely detectable at intermediate temperatures; yet the product of the interaction may be sizeable and even opposite in direction, once we study temperatures displaced to lower and higher values.

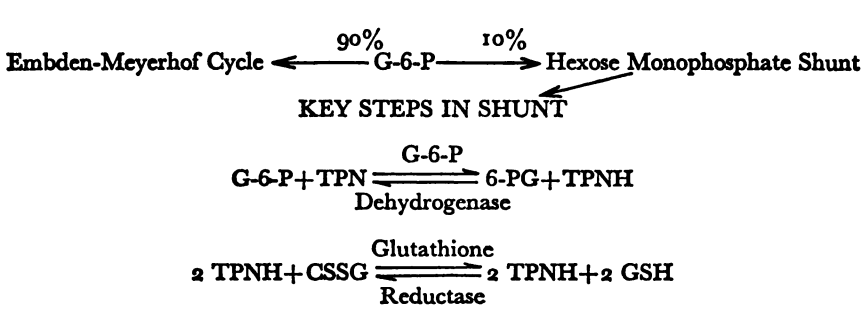
In still another instance, the genotype that is superior in survival value in one environment will be disadvantageous in a second and relatively neutral in a third. Here the prototype is glucose-6-phosphate dehydrogenase (G6PD) deficiency (Fig 2), an X-linked trait of intermediate dominance, with the result that G6PD levels are lowest in the male hemizygote and the female homozygote and intermediate in value in the female heterozygote (Childs *et al*, 1958). Where malaria is endemic, G6PD deficiency confers protection against infection by the plasmodium (Luzzetto *et al*, 1969) by

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lowering the levels of reduced glutathione in the erythrocyte; hence, selective advantage has led to a high prevalence of the gene for G6PD deficiency among groups that live on the malarial coasts of Sardinia in contrast to its rarity among those inhabiting the malaria-free mountainous regions; similarly, sampling of Jewish populations in Europe reveals a prevalence of 1 per cent to 2 per cent whereas rates as high as 58 per cent have been obtained among Jews in Kurdistan (Cavalli-Sforza and Bodmer, 1971). With changes in the prevalence of malaria over time and with the migration of affected populations to new continents, what was a selective evolutionary advantage is changed into vulnerability because G6PD deficient individuals are subject to haemolytic crises if they consume fava beans or ingest oxidant drugs, such as primaquin or phenacetin (Fig 3). If genetically affected individuals are identified and enabled to avoid the offending substances, the trait will be relatively neutral in its effects.

My examples have been chosen precisely because in each case we know enough about the metabolic pathways to pinpoint the genetic defect and the crucial environmental components which jointly constitute 'the summation of multiple causes, effective in combination, though inadequate singly'. For most behavioural phenotypes, we understand only fragments of the developmental sequence. The temptation is great to make the simplifying assumption that effects are additive and that interactions and covariation can safely be ignored. I hope I have persuaded you that the contrary is often the case. I do not suggest that we should abandon analysis of variance as a statistical method in genetic studies of psychiatric disorders; indeed, it provides an important way of testing genetic hypotheses in illnesses that are likely to be multifactorial (in contrast to the cited examples where the major effect of a single gene is predominant). What requires emphasis is the search for interactive as well as additive effects, for heterogeneity as well as homogeneity.

These points are well illustrated in studies of the schizophrenias (Kety, 1974) and the affective psychoses (Slater and Cowie, 1971), in both of which we have strong evidence for familial aggregation but are as yet unable to differentiate monogenic from multifactorial (polygenic) models of genetic transmission (Matthysse and Kidd, 1976; Gershon *et al*, 1975). It would appear likely that the difficulty in teasing out the pattern of inheritance is compounded by the heterogeneity of the disorders included within each of these broad diagnostic categories. For example, Winokur (1976) has advanced the provocative hypothesis that the affective disorders can be divided into bipolar (manic depressive) and two forms of unipolar (depressive) disease. He argues that X-linkage with colour blindness and the Xg^a blood group characterizes bipolar disease, and that familial



In G-6-P-D- deficiency, unavailability of the shunt results in low levels of reduced glutatione (GSH)

FIG 2

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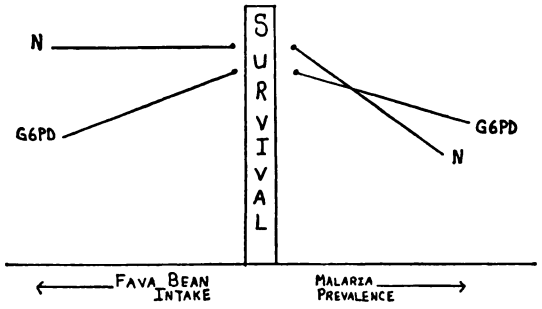


FIG 3.—Genotype environment interaction and differential survival

aggregation patterns are different in the two forms of unipolar disease, 'pure' and 'depression-spectrum'. That the familial transmission in schizophrenia is not explicable by rearing patterns is evident from twin and adoption studies (Wender *et al*, 1974); more surprisingly, children reared by a schizophrenic parent show no higher risk of becoming psychotic than matched children reared apart (Higgins, 1976), despite Rutter's (1966) documentation that the children of sick parents are at greater risk for other psychiatric disorders. The obscurity of the mode of transmission notwithstanding, the evidence for a genetic link directs attention to biochemical abnormalities as a necessary though not a sufficient condition for the appearance of psychosis; what is coded in the genes is protein, hence enzymatic, specificity.

A recent paper by Buchsbaum *et al* (1976) provides an illustration of the ways in which current research can combine clinical investigative and genetic strategies. Platelet monoamine oxidase (MAO) levels have been reported to be low in most studies of patients with chronic schizophrenia and bipolar affective disorders (Murphy *et al*, 1974); moreover, MAO levels are under genetic control (Nies *et al*, 1973). Consequently, several hundred young adult volunteers were recruited for a 'biochemical risk' study. Those in the highest and lowest deciles for platelet MAO values were then contrasted, in order to make the separation as sharp as possible in view of marked overlapping of levels in clinical and normal populations. Low MAO subjects, in contrast to high, reported a significantly higher incidence of personal psychiatric consultation as well as of family history of suicides and suicide attempts. These were, you will recall, ostensibly normal subjects at the time of their enrolment in the study. The extent to which this promising lead will be informative awaits the completion of a longitudinal follow-up. Will the subjects characterized as high-risk and low-risk by this tentative biochemical indicator show a differential incidence of psychosis? If they do, what distinguishes cases from normals among the high-risk group?

Genetic strategies can serve to enhance the search for crucial environmental variables. The fact that the concordance rate for schizophrenia in genetically identical one-egg twins, averaged over a number of studies, is somewhat less than 0·5 (Matthysee and Kidd, 1976) implies that environmental variables play a part in determining the onset of disease in the one twin rather than in the other. It has been customary for some time to assume that those precipitants will be found in psychological (Reiss, 1976) and/or social class (Kohn, 1976) factors, as well they may. But it is equally possible that differential susceptibility to viruses, to dietary substances, to auto-immune phenomena, to birth complications, indeed, to a wide variety of biological as well as psychosocial stimuli may be decisive in the pathogenesis of the psychoses (Kety, 1976). We are only just becoming aware of the extent of human genetic heterogeneity, estimated currently at not less than one-third of gene loci (Harris and Hopkinton, 1972). Such heterogeneity plays a role in vulnerability to disease, whether it be the differential morbidity and mortality linked to the sex chromosomes (Childs, 1965; Verbrugge, 1975; Eisenberg, 1976) or to the histocompatibility antigens (Bach and van Rood, 1976). Trimble and Doughty (1974) calculate that of 100 live-born children 9·4 will have serious genetic diseases or handicaps during their lifetimes. As many as 30 per cent of paediatric hospital admissions are for patients with gene-dependent diseases (Scriver, 1976).

The point to be stressed is that the developmental process begins with the information encoded in the genome but its phenotypic expression is continuously modulated by sequen-

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tial interactions with environmental variables at each stage of development, not excepting circulatory, nutritional and toxic factors during intrauterine life and the obstetrical characteristics of the birth process itself (Eisenberg, 1975). A particularly striking example of the way the phenotype is moulded by stimulation is provided by studies of the visual system.

In the kitten at birth there is a remarkably complex and precise set of interconnections from retina through geniculate body to occipital cortex. Before visual experience, this system responds in highly specific ways to key features of visual patterns, such as edges, orientation and direction of movement (Hubel and Wiesel, 1963). Yet this initial state of function can be permanently disrupted by a relatively brief period of deprivation in infancy; i.e. interference with patterned vision but not with light by placing a translucent cup over one eye for as few as three to four days in the sensitive period during the fourth and fifth weeks of postnatal life (Hubel and Wiesel, 1970). Not only are visual placing and following reactions absent to stimulation of the deprived eye (which appears blind in this respect) but there is atrophy of cells in the lateral geniculate layers receiving projections from it, all of this despite normal pupillary reactions and corneal electroretinograms in that eye. Moreover, the great majority of cells in the occipital cortex are now driven exclusively by the normal eye and no longer respond to the previously deprived one. It is as if the coherent excitation of synaptic junctions by patterned vision on the normal side, while the other is denied organized experience, 'solders in' its wiring preferentially. For, if both eyes are occluded simultaneously, each continues to control cells in the occipital cortex; these animals differ from normal principally in the loss of binocularity (Wiesel and Hubel, 1965). Binocularity depends upon the simultaneous relay of information from both eyes, for if a translucent cup is placed over each eye in turn on alternate days, so that each has a similar amount of visual experience but the two never are open at the same time, binocularity is forfeited. The differential capture of occipital fields by the normal eye is dependent upon the activity of catecholamine neurohormones. If 6-hydroxydopamine is administered in order to deplete forebrain catecholamines before the unilateral occlusion experiment is carried out, the visual cortices of the catecholamine-depleted kittens continue to show a normal number of binocular neurons in the post-occlusion test period (Kasamatsu and Pettigrew, 1976). Thus the outcome of the unilateral deprivation experiment results from the intereactions between the effects of normal visual experience in the one eye and abnormal vision in the other. The main features of the visual wiring system are present at birth, but for them to be maintained and later finely tuned continuous visual experience is required.

In the child, strabismus not corrected before the fifth or sixth year of life results in amblyopia ex anopsia. The severely limited vision in the unused eye cannot be rectified by optical or surgical procedures. Strabismus produced in the kitten by surgical section of extra-ocular muscles results in a sharp reduction in the proportion of binocularly driven units in area 17 (Hubel and Wiesel, 1965). Since surgical strabismus results in loss of binocularity even when the kittens are raised in the dark, it is evident that 'symmetry in the flow of information from the proprioceptive receptors of oculomotor muscles to visual centres is important for maintaining the binocularity of cortical neurons' (Maffei and Bisti, 1976).

It may be objected that these are far too massive environmental insults to provide a relevant paradigm for the dependence of structural and functional integrity on stimulation under more nearly expectable conditions. Yet there is evidence that relatively restricted interference with access to visual experience has telling effects. If young kittens are reared for the first three months of life in a visual environment consisting only of stripes of one orientation (that is, horizontal or vertical), cortical neurons will be most sensitive to stimuli within about 30° of the one to which they were exposed (Spinelli *et al*, 1971). Indeed, even exposure of adult cats to an environment consisting only of vertical stripes for two weeks markedly shifts the functional orientation of the visual cortex, in this case, however, in the direction of *reduced* sensitivity to the adaptation orientation when the

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cat is studied four to twelve hours after the last exposure (Creutzfeldt and Heggelund, 1974). Furthermore, rearing kittens in illumination provided only by strobe lights flashing at eight times per second with a duration of ten microseconds (which results in stationary visual images and the virtual abolition of movement perception) abolishes direction selectivity in cortical neurons, although orientation selectivity is preserved (Cynader and Chernenko, 1976). Rearing in an environment without straight line contours produces highly atypical cortical neurons which respond to small moving spots of light but are virtually insensitive to edges, ordinarily the most effective stimuli (Pettigrew and Freeman, 1973). In sum, these experiments demonstrate the extraordinary plasticity of the organization of occipital cells in response to the characteristics of the rearing environment.

Are these findings relevant to man? In human subjects with astigmatism, no sharp images can be produced outside the meridians of maximum and minimum powers because of errors in the refractive characteristics of the eye. Even precise laser-generated interference fringes that bypass the eye's optics to focus on the retina do not suffice to repair resolution anisotropies, thus strongly suggesting permanent modifications in neural connections in the human adult as the result of abnormal visual experience (Freeman *et al*, 1972). It has even been contended that the normal orientation anisotropy (superior resolution for horizontal and vertical contours) observed in all of us who live in a man-made world may be the result of its visual characteristics, because such anisotropy is not found in Cree Indians living in a more 'natural' environment (Annis and Frost, 1973). However, doubt has been cast on this hypothesis because differences have been found between Chinese and Caucasian subjects, though both are urbanized, so that the findings may reflect ethnic differences arising on a non-environmental basis (Timney and Muir, 1976). The crucial experiment remains to be done; namely, the comparison of Cree Indians who live in a 'carpentered' environment with those living in a 'natural' one.

I now move on to consider psychiatric syndromes in childhood, in which the manifest disorder, to recall Mapother's felicitous phrase, is 'the result of the summation of multiple causes, effective in combination, though inadequate singly'. When disturbed behaviour is encountered in a child with evidence of neurological impairment, the diagnosis of 'brain damage' is commonly regarded as constituting a sufficient cause for the psychiatric disorder. This view persists despite the striking lack of concordance between the psychological and neurological signs and symptoms in children with central nervous system lesions (Eisenberg, 1964); that is, one patient with disabling choreo-athetosis may nonetheless function at a superior intellectual level, whereas a second with relatively mild neurological symptoms may be both retarded and disturbed. Moreover, there is no cluster of symptoms *specific* to brain damage (Shaffer *et al*, 1974); nor does the locus of injury or the age of the child at the time of injury account for the differential prevalence of psychiatric disturbance among a group of such children (Shaffer, cited in Rutter, 1976). Some of the factors that govern the relationship between brain disorder and behavioural competence have been clarified by the epidemiological studies of Professor Rutter and his co-workers. Among children with cerebral palsy and epilepsy, rates for psychiatric disturbance are several times greater than among community controls (Rutter *et al*, 1970a) or physically disabled children (Seidel *et al*, 1975). Yet not all are symptomatic; the risk is greatest for those who also suffer intellectual impairment and who come from disorganized homes (Rutter *et al*, 1970b).

Prospective longitudinal studies provide additional evidence for the thesis that moderate degrees of neurological impairment early in life are not in themselves sufficient to determine later behavioural outcome; rather, they increase the vulnerability to psychiatric disturbance in the presence of other stress factors, of which the most pathogenic are unfavourable home circumstances.

Werner and her colleagues (1971) followed a birth cohort on Kauai, Hawaii, until age 10, with periodic assessments of neurological, psychological and familial characteristics. As in many other studies (Eisenberg and Earls, 1975),

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the intellectual and emotional outcome of the children was strongly correlated with socio-economic status, family stability and parental emotional support for the children. Neurological abnormalities on the one year examination were likely to be associated with poorer outcomes at age 10. However, the neurological findings on the one year examination had *no* predictive power for scholastic aptitude and achievement among the *middle class* children; in contrast, among socially disadvantaged children those with neurological abnormalities in infancy did significantly less well than their peers who had been neurologically normal. It is as if a stimulating and supportive environment enabled the child to compensate for moderate deviations in central nervous system integrity, whereas the stress of an impoverished home led the defects to become manifest (Eisenberg, 1957). Similar findings have been reported in a Minneapolis birth cohort study (Fisch *et al*, 1976) in which three groups of children were compared at age 7, those with superior (120 or over), average (80–119) and low (79 or less) IQ scores. Once again, social class, parental education and favourable home circumstances were strongly associated with superior outcome. Neurological abnormality had been noted with equal frequency (1·2 per cent) among the superior and average children when they were infants but had been present much more frequently (10·4 per cent) among the low IQ group who were also socially disadvantaged. The authors conclude that 'emphasis on improving perinatal care . . . may be no more important than improving the education and socio-economic status of the family' (p 486).

Precisely this has been shown for low birth-weight infants, a population at high risk for developmental abnormalities (Wiener *et al*, 1968; Birch *et al*, 1970). Scarr-Salpatek and Williams (1973) provided an experimental 'enrichment' programme to half of a sample of 30 low birth-weight infants (less than 1,800 grams). The experimentals were given visual, tactile and kinaesthetic stimulation during their six weeks in the newborn nursery; in addition, their mothers were visited weekly for the first year to instruct them on maternal care. At 12 months of age, on the Cattell Infant Scale, the experimentals tested at significantly higher levels than the controls (IQ 95·3 versus 85·7; $P = 0·05$). Similarly, Klaus and Kennell (1976) have shown persisting superiority in development at 42 months for a group of premature infants whose mothers were enabled to care for them in the hospital from birth, when contrasted with a group given standard care in the newborn nursery while separated from their mothers. The enhancement of bonding, the greater maternal self-confidence and responsivity to infant behaviour, and the consequent elaboration of mother-infant reciprocity resulted in a mutually reinforcing process of healthier maturation.

Identical questions of interaction and covariance are posed in attempts to relate nutritional status to neuropsychiatric function. Malnutrition is a problem of overwhelming magnitude in the developing countries of the world (Bengoa, 1974). Protein-calorie deficiency states reflect synergism between infection and malnutrition. Inadequate nutrition lowers humoral and cellular defence mechanisms and increases the rate as well as the severity of infection. Infection increases nutritional demand at the same time that it impairs intake and increases loss through vomiting and diarrhoea; imbalance may be further worsened by traditional 'remedies' for illness which rely on reducing food intake (Birch and Gussow, 1970). Thus, case mortality rates in the first year of life for measles in Africa may be as high as one in ten, four orders of magnitude higher than those in developed countries (Editorial, 1976). In infantile marasmus severe enough to result in death, autopsy shows reduction in brain cell number, amount of lipid per cell, and brain weight, which is reflected in the diminished head circumference of such infants (Winick and Rosso, 1969). But what of less extreme states of malnutrition?

Clinical studies from many developing countries have reported depressed cognitive performance in malnourished children; these same children, however, had also been victimized by other severely adverse social circumstances; thus, the relation between intellectual defect and nutritional status remains a source of controversy (Frisch, 1970). Few enduring effects

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on intellectual aptitude have been detected in a very different group of children who have experienced early malnutrition: those renourished after malnutrition secondary to metabolic disorders such as cystic fibrosis and ileal resection (Valman, 1974; Lloyd-Still *et al*, 1974; Ellis and Hill, 1975). What appears to lead to poor outcome is the concurrence of poor nutrition and poor rearing conditions. This conclusion is borne out by careful study of Jamaican boys who had been in hospital for marasmus or kwashiorkor in the first two years of life. At elementary school age, they were compared with their siblings and with classroom controls; their performance was inferior to both. However, it is equally noteworthy that their siblings did less well than the controls (Hertzig *et al*, 1972). The home circumstances of the index families were characterized by multiple burdens: a more disadvantaged caretaker, poorer and more crowded housing, less intellectual stimulation and less formal schooling, higher mortality rates among siblings, and more isolated families (Richardson, 1974). Although indices of social background, height (as a proxy for nutritional status) and history of malnutrition all correlated with IQ, the largest single component in the variance proved to be social background (Richardson, 1976). However, 'if malnutrition occurs in a context of a poor overall history of physical growth and an unfavourable social background, then the early severe malnutrition has a clear relation to later intellectual functioning' (p 61).

The direct effects of malnutrition on the central nervous system vary with its timing in ontogeny; it strikes differentially at the neurobiological process (neuronal multiplication, glial proliferation, synaptogenesis, myelinization), undergoing the most rapid change during the period when nutrition is interrupted (Dobbing, 1972; Winick *et al*, 1972). Further, the lethargy and apathy that accompany malnutrition reduce the capacity of the infant to attend to its environment and to process information. The altered behaviour of the child in turn impedes the evolution of its relationship with its caretakers and peers and further retards its development. The deficit in stimulus intake (psychological 'starvation') is of course the greater the less the amount and quality of the stimulation provided by the family environment. It is the vector that results from maturational timing, severity and duration of malnutrition and the quality of the current and future social surround that determines the rate and direction of the developmental process. Thus, if we are to intervene effectively in the lives of such children what is required is an ecological approach which emphasizes the simultaneous correction of problems in nutrition, infection, education, family life and general community conditions.

If I have thus far chosen to focus on genetic, neurobiological and nutritional factors, it is in order to emphasize the concept that human disease *always* reflects the outcome of an interaction between human biology and human social organization, a process in which culture occupies a mediating role. Recall that acute infectious diseases, such as measles and poliomyelities, became endemic in human societies only after the technology of agriculture permitted human populations to aggregate in numbers large enough to provide a host reservoir sufficient for disease perpetuation. In Neolithic communities of several hundred, a pathogenic virus introduced from the outside so rapidly kills or immunizes that the virus is no longer able to propagate itself serially (Black, 1975). Culture change created the biological conditions necessary for infectious disease to exert selective evolutionary pressure (Haldane, 1957). To take a contemporary example of the impact of culture on biology, a major component in the recent appalling drought in the Sahel desert margin was the introduction of successful chemoprophylaxis against cattle trypanosomiasis, which led to overgrazing, increased reflectivity of the denuded ground surface and consequent reduction in rainfall (Omerod, 1976).

Such being true of biosocial variables, it will therefore not surprise us to find similar patterns of interconnectedness in the behavioural consequences of psychosocial factors. They are elegantly documented in the research reported from the Children's Department of the Institute of Psychiatry (Rutter *et al*, 1976; Rutter, 1976).

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What is the impact upon the child of separation from his parents? To the developmentalist, the answer is expectable: it depends. It depends upon the reasons for the separation, the condition of the child at the time of separation and the rearing conditions subsequent to the separation. If it results from vacations, family visits, or necessary hospital treatment for illness in the child, there are few or no enduring sequelae. If it is secondary to marital discord, mental illness or criminal behaviour in the parents, disturbance in the child is very likely. Even under these circumstances, whether psychiatric disorder results is a function of whether the next home is a happy one (Rutter, 1972).

Why does one child in the family rather than its brothers or sisters exhibit psychiatric disturbance? Family events interact with the temperamental characteristics of the child, both to make him vulnerable and to select him out as a scapegoat for parental tensions (Graham *et al*, 1973). Is it child and family alone that determine outcome, or do community and schooling make a difference? Clearly, they do. In the comparisons between the Isle of Wight and a London borough, rates were much higher for the urban population (Rutter *et al*, 1975a); differences in school characteristics (pupil and teacher turnover) and in community support systems (availability of adoption) interacted with family and child characteristics in contributing to the differences in rates of disturbance (Rutter *et al*, 1975b). I do not suggest that all of the variance has been explained; far from it, but the Maudsley epidemiological studies point to the answers clinicians need.

Clinical work would be much simpler, and the design of social policy certainly far easier, if the factors determining human development were not so perversely interwoven, but any hope of success in elaborating rational programmes for effective intervention, either at the individual or at the community level, must begin with the clear recognition of the interconnectedness of psychobiological and social variables.

I have one final point to make before I close. This is addressed to the general psychiatrists in the audience who may think themselves happily free of the sticky complexity of behavioural development. Even if, some argue, later behaviour is to a considerable extent the outcome of earlier experience, what is the point of reconstructing that past, since history cannot be changed or relived? We all know patients who, however well they recapture the events of their psychogenesis, continue to perseverate in self-defeating behaviours despite their apparent 'insight'. Indeed, as we look at ourselves no less than our patients, we are tempted to conclude that personality, once 'crystallized', is relatively impervious to change. The search for the 'meaning' of behaviour may be a fascinating intellectual exercise, but the task of the clinician is to change pathology, not simply to account for it.

Change is indeed the charge. But I suggest that we err when we attribute the apparent consistency and continuity in personality to internal psychological structures alone. What determines the similarity between my behaviour last year and what it is likely to be during the next is not nearly so much a matter of that which is 'I' as it is of the social fields of force in which that 'I' moves. That is, having acquired a repertoire of behaviours, I maximize their adaptive utility by seeking out the familiar and avoiding the strange in the social world around me. The apparent consistency in the self is the result, not merely of what has gone before, but of the continuation into the future of the same social forces that have given rise to it. Take any one of us out of familiar circles, strip us of family, friends and social position, and see then whether we remain as much the same as personality theory predicts (Hunt, 1965).

So savage an experiment is beyond medical contemplation. Unfortunately, no such restraints limit despotic governments—or, sadly enough, even indifferent or neglectful societies. Indeed, we need look no further than our own professional experience to find a mundane and all too commonplace 'experiment of nature': the chain of events set into motion by the ways mental illness has been managed.

It is not so long since, in my country, and yours as well, the mentally ill were aggregated in large institutions, denied individuality and dignity, isolated from work and community, and imprisoned in a social world in which

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resource limitations and the dictates of managerial efficiency flattened the cycle of days and weeks into monotony and stereotypy. The diagnosis of psychosis provided a ready 'explanation' for the progressive impoverishment of behaviour that was observed; the large fraction that subsided into chronicity was attributed to the toll mental disease extracted from its victims.

With the rediscovery of the moral treatment of the insane in the United Kingdom, we came to recognize that a major component of the social breakdown syndrome resulted from the institutional environment itself as it acted upon persons particularly vulnerable to its levelling effects because of their psychiatric disability (Eisenberg, 1973). Of course, the new drugs have made an enormous difference, but the change toward a better prognosis anteceded the widespread use of drugs and can only be attributed to the new administrative policies generated by the concepts of social psychiatry. Granted, it continues to be the case that some schizophrenic patients, many fewer than the numbers the asylums generated, continue to require long-stay hospitals despite the improvements in care. But the fact remains that what had been regarded as a product of endogenous disease was the resultant of disease multiplied by the social response to it. The individual differences, the charms, the nuances, even the idiosyncrasies and irritabilities that had distinguished the patients as persons one from another had been washed out, faded away, obliterated till all had become so many automata functioning at the lowest common denominator imposed by institutional thrusts for trouble-free operation. All the years of life that had gone into the formation of a unique human being had been ground out by the force of institutional demands which proved irresistable to all but a few.

This bit of recent history provides compelling evidence for the thesis that human personality is always in the making and never complete. We are what we do. We become as we decide. We are ever defined by the social world in which we move. We exist as we behave, much as the harmonies and dissonances of music inhere in the performance of it and in the ears of its auditors.

Psychiatry is the art and science of human development viewed as a trajectory whose moment to moment directions are determined by the biological uniqueness of the individual, the shaping force of his or her idiosyncratic prior experience, and the expectations implicit in the roles each fulfils within the social group. For all the complexity inherent in development as a concept, the reward is found in its illumination of the creative possibilities in a dynamic process which can be enhanced by removing the restraints upon its evolution.

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