SCHIZOPHRENIC SYNDROME IN CHILDHOOD

The multitude of terms used by psychiatrists to describe serious disturbances in the behaviour and adjustment of children reflects a general uncertainty about their nature and aetiological basis. "Childhood schizophrenia," "infantile autism," "childhood dementia," "symbiotic psychosis syndrome," "atypical development," and "schizophrenic syndrome," or "psychosis in childhood," as well as the disorders associated with the names of Kanner, Bender, Mahler, Weygandt, Heller, and De Sanctis, refer to disorders that are similar to or overlap with one another. This abundance of clinical labels has tended to confuse and complicate rather than advance the process of establishing a rational classification. The reasons for uncertainty are not hard to seek and they lead to the heart of the problems of differential diagnosis. In the well-differentiated personality of the adult the effects exerted by psychotic illness, cerebral damage, and extreme emotional stress may be identified fairly reliably. The relative prominence of intellectual decline, emotional disturbance, the degree of social maladjustment, and the incidence of certain consistent clinical symptoms and signs (such as those characteristic, for example, of the schizophrenic or affective psychoses) vary in the different categories of illness.

The situation is less clear with the unfolding cerebral or mental equipment of the child. Severe emotional disturbance is prone to produce marked intellectual retardation or derangement, while the earliest manifestations of cerebral disease may be those of a behaviour disturbance indistinguishable from the way a child will respond to vicissitude or deprivation. Moreover the relative frequency of brain damage and mental defect on the one hand and psychotic disturbance on the other is the reverse of that which obtains in adult life. Muteness or incapacity for communication increases the difficulties of ascertaining precisely what functions are deranged. For all these reasons the effects of psychosis, brain injury or disease, severe emotional stress, and disabilities such as epilepsy and deafness are far more apt than in the mature individual to blend imperceptibly with one another.

This situation has led many workers[1,2] to question whether "childhood schizophrenia" or "autism" has any claims to being an entity at all. This reflects some misunderstanding of what an entity in psychiatry, or in medicine for that matter, implies, and the purpose and value of defining it. Schizophrenia of adult life is no more of an entity in an aetiological sense than Bright's disease or Parkinsonism. It has become increasingly clear in recent years that psychoses occurring in the course of chronic epilepsy[3] or those sometimes associated with dextroamphetamine intoxication[4] or brain injury,[5] may be almost indistinguishable in their clinical features from schizophrenia unconnected with brain damage. Again, in the schizophrenias of the aged it has recently been shown[6] that lifelong anomalies of personality, social isolation, bereavement, deafness, genetic factors, and, in a minority of cases, cerebral degeneration probably all contribute to causation. The difficulties of differential diagnosis of adult schizophrenia are therefore in many respects similar to those of schizophrenia in childhood: the difference is a matter of degree rather than kind.

Yet the relationship between childhood and adult schizophrenia is far from clear. Although a similar hereditary basis has been claimed for the two disorders by some workers,[7] in the experience of most a family history of schizophrenia is uncommon. It is also rare in the extreme to see schizophrenic illness in adult life which is a recurrence of a childhood psychosis, and there is no agreement whether the final picture of childhood schizophrenia, when traced into the adult years, remains one of retardation and withdrawal[8] or is complicated by the delusions and hallucinations of adult schizophrenia.[9] Though there are certain similarities in the clinical picture between the adult and childhood forms, there is much to be said for the use of a neutral term, such as "childhood psychosis," which permits independent specification of the underlying aetiological factors.[10]

The report[11] in last week's *Journal* of a group of workers under the chairmanship of Dr. Mildred Creak who have been examining case material during the past eighteen months to clarify these issues makes a valuable contribution to the definition of the clinical picture of psychosis in childhood. They emphasize nine features, of which only the first was invariably present: the last was also considered by some to be pathognomonic. These features are: gross impairment of the capacity for emotional relationships, unawareness of personal identity to a degree inappropriate for age, an unaccountable preoccupation with particular objects, sustained and obsessional resistance to any changes in the environment, abnormal perceptual experiences, excessive and seemingly illogical anxiety, failure or regression in speech development, distortion of motility, and, finally, serious intellectual retardation with surviving islets of normal or exceptional abilities. To these may be added evidence of archaic thinking and persistent negativism.

Certain differences from the picture of adult schizophrenia are at once apparent. More relevant here is the relatively greater proportion of cases in

childhood in which cerebral damage contributes to causation. Hence it is even more necessary than in adult cases always to assess the contribution of a wide range of possible aetiological factors (genetic, cerebral, emotional, social, sensory defects, and epilepsy). Yet the evidence suggests that, although overlap is greater, here, too, the organic, psychotic, and neurotic territories are distinguishable. Differentiation between them is important for prognosis and treatment. Notwithstanding the multiplicity of organic syndromes that have been described, the cases in which there is no clue to the underlying aetiology are probably in a majority. An important step in differentiating such a broad functional group from other cases is taken when the alternative possibilities of cerebral damage, encephalitis, deafness or blindness, severe neurotic disturbance, and epilepsy are even considered.

A clearly established period of normal development preceding the oddities of behaviour strongly suggests psychosis rather than mental deficiency, although there are cases of the former in which emotional unresponsiveness and withdrawal are evident from the beginning. Careful neurological investigation and observation of the patient's behaviour with other children and at play will generally yield useful information. In the child with organic damage the deficiencies of cognitive function are more uniform, and, in contrast to the psychotic child, the patient is clearly attempting to compensate for deficiencies in order to master his environment. The psychotic child will, however, often fail to apply abilities which are evidently intact to deal with reality. There is a suggestion that social classes I and II (at the upper end of the scale) are over-represented among the parents of non-organic cases.[12] The presence in the parents of marked coldness, eccentricity, or gross rigidity and obsessionality (particularly stressed by L. Kanner[13] in connexion with infantile autism) tends to be associated with functional illness although many parents prove to be emotionally normal.[14] Extreme anxiety, obsessive ruminations, preoccupations with death, depersonalization, and unreality feelings, in the absence of other features, are probably never schizophrenic, even when they appear to engulf the child's personality, but are analogous with certain severe adult neuroses that may on occasion likewise temporarily assume psychotic features.[15] The E.E.G. is of considerable help, particularly in the separation of cases with the specific features found in epilepsy and inclusion-body encephalitis, and will often provide some aid in the diagnosis of deafness in a very young child. In the hyperkinetic syndrome, first described by F. Kramer and H. Pollnow,[16] the child may be cold, cruel, ruthless, destructive, and difficult to contact emotionally, but the condition is distinct from schizophrenia: about 50 to 60% have epileptic fits or electroencephalographic evidence of focal lesions,[17] and many of the remainder probably have some more subtle cerebral anomaly. The disturbance often becomes attenuated with advancing age and the prognosis is better than in autistic children.

So far as treatment is concerned, in deafness, epilepsy, and certain other cerebral conditions specific remedies may mitigate the organic disease and the behaviour disturbance with it. In the presence of mild cerebral lesions the brain disease merely contributes to, rather than causes, the psychosis, and the prognosis is not necessarily hopeless. In the schizophrenic-like psychosis associated in adults with epilepsy[3] or slight cerebral damage[18] the psychosis may take a favourable course, probably because such individuals are less predisposed genetically than subjects in whom an intact cerebrum provides no protection against becoming schizophrenic. A similar state of affairs may well hold in the case of children, although there have been far too few follow-up studies for any firm opinion to be possible. In the general run of cases the non-appearance or regression of speech is an unfavourable feature.

Physical treatments such as E.C.T. and insulin coma have proved worthless, but phenothiazine derivatives can be useful in controlling restlessness, excitement, and extreme agitation. Whatever the form of treatment, it can work only at several steps removed from the processes that sustain the illness. In the opinion of most psychiatrists these children, with rare exceptions, grow up with personalities that are damaged to varying degrees, and even the 20% recovery rate claimed by R. S. Lourie and his colleagues[19] is considered too sanguine. The value of intensive psychotherapy is clearly limited, but improvement and recovery do occur, possibly in groups awaiting definition, and long-term management should include some attempt to penetrate the barrier that emotionally isolates the child,[12] and to

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[2] Stroh, G., *J. Child Psychol.*, 1960, **1**, 3, 238.
[3] Slater, E., Paper delivered at Maudsley Symposium on Epilepsy and Mental Disorder, 1959, London, Institute of Psychiatry. To be published.
[4] Connell, P. H., *Amphetamine Psychosis*, 1958, London.
[5] Maller, O., in Congress Report, 2nd International Congress for Psychiatry, 1957, Zurich, Vol. 1, p. 102.
[6] Kay, D. W. K., and Roth, M., *J. ment. Sci.*, 1961, **107**, 649.
[7] Kallman, F. J., and Roth, B., *Amer. J. Psychiat.*, 1956, **112**, 599.
[8] Kanner, L., and Eisenberg, L., *Psychopathology of Childhood*, 1955, ed. by Hoch and Zubin, New York.
[9] Bender, L., *Amer. J. Psychiat.*, 1954, **110**, 855.
[10] Creak, M., Congress Report, 2nd International Congress for Psychiatry, 1957, Zurich, Vol. 1, p. 102.
[11] *Brit. med. J.*, 1961, **2**, 889.
[12] Anthony, J., *Brit. J. med. Psychol.*, 1958, **31**, 211.
[13] Kanner, L., *Z. Kinderpsychiat.*, 1958, **25**, 108.
[14] Creak, M., and Ini, S. J., *J. Child Psychol.*, 1960, **1**, **2**, 156.
[15] Roth, M., *J. Neurol. Psychiat.*, 1960, **1**, 293.
[16] Kramer, F., and Pollnow, H., in *Mschr. Psychiat. Neurol.*, 1932, **82**, 1.
[17] Ingram, T. T. S., *J. ment. Sci.*, 1956, **102**, 550.
[18] Krauss, S., Congress Report, 2nd International Congress for Psychiatry, 1957, Zurich, Vol. 2, p. 100.
[19] Lourie, R. S., Pacella, B. L., and Piotrowski, Z. A., *Amer. J. Psychiat.*, 1943, **99**, 542.

help him re-establish his contact with, and differentiation from, the objective world.

To advance inquiries in this field a firmly based classification is urgently needed. The problem need not be insuperable. Diagnostic features such as those defined in the recent report of Dr. Mildred Creak's working party are very valuable, but what is needed next is a generally agreed procedure for their application in the selection of cases. The clinical, psychological, neurological, and electroencephalographical investigation of a carefully selected sample of children should help to determine the relative frequency of the different items and the weighting they ought to receive when diagnosis is being decided. It should also provide more precise knowledge of the different organic and functional syndromes and the degree of overlap between them. With this information available research into causation will start from a better position.

DOSAGE FOR THE NEWBORN

It is a matter of common knowledge that within a short time of the introduction of a new drug, particularly a potent chemotherapeutic agent, reports appear of toxic and sometimes fatal side-effects which, from the initial animal experiments and preliminary clinical trials, come as a surprise. Such reports concerning newborn or premature infants may be less surprising when one considers that the original experiments are likely to have been done on adult animals, not on newborn.

In a recent review of the toxicity of drugs to newborn babies W. L. Nyhan[1] pleads for further studies on the peculiarities of paediatric—and particularly neonatal—pharmacology, and his report certainly substantiates his plea. He suggests that new drugs should be screened on newborn animals before release for giving to the newborn infant and that the drug firms should be required to establish, before marketing, the presence or absence of differential toxicity in the newborn. This would entail extensive clinical trials in the nurseries and wards of maternity hospitals before routine dose schedules were accepted. There are so many possible factors which determine the neonatal response to drugs that simple extrapolation from size (whether by weight or surface area) will not suffice to assess a safe and effective dosage. No formula has yet been described which can be applied to neonatal life, nor is a nomographic method much more satisfactory. These can provide only approximate information, and it may not be accurate enough for any given infant. So far, personal experience has proved the most valuable guide in determining dosage for newborn infants; as Goodman and Gilman[2] say: "The dose for infants should be learned as such and not calculated by formulae."

In addition to differing from the older child or adult in size and surface area the newborn baby, and even more the premature, show remarkable differences in metabolic processes. These materially alter the rate and efficiency of absorption, detoxification, and excretion of drugs, and the dosage needed will vary accordingly. Nyhan cites such factors as inefficient glucuronidation, limited capacity for acetylation, and delayed development of microsomal oxidate systems in the liver. The immaturity of kidney function in premature infants is also important in that it may permit drugs to reach much higher levels in the blood than they would attain in later infancy.

Several reports have drawn particular attention to the possible toxic effects of chloramphenicol, sulphafurazole, and vitamin K, all of which have been, and still are, extensively prescribed in nurseries for the newborn and in units for premature babies. Serious risks attend the use of these preparations routinely and they have all three caused a number of deaths. Chloramphenicol is undoubtedly a valuable, potent, and toxic drug; most doctors respect it and limit its use to certain specific infections in whose treatment its values may be expected to outweigh the possible risks. But, as has been emphasized recently in these columns,[3] the clinical picture of its toxic effects in newborn and premature infants is different. Initial vomiting and reluctance to feed are followed by the development of an ashen-grey cyanosis, hypothermia, and hypotonia; death from peripheral vascular collapse may occur within a few hours. The causative factor seems to be related to the deficiency of glucuronyl transferase, which normally conjugates chloramphenicol. It is therefore of the utmost importance that the dose of chloramphenicol in the newborn should be carefully limited; it should not exceed 25 mg. per lb. body weight (55 mg. per kg.) per day for full-term infants or 12.5 mg. per lb. body weight (27 mg. per kg.) per day for premature infants. Sulphafurazole has special dangers for premature infants, whose powers of sulphonamide acetylation are limited, for it may compete with bilirubin for binding sites on serum albumin and so displace protein-bound bilirubin, thereby leading to hyperbilirubinaemia and kernicterus.[4] W. A. Silverman and colleagues[5] described an "epidemic" of kernicterus in a nursery for premature babies where

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[2] Goodman, L. S., and Gilman, A., *The Pharmacological Basis of Therapeutics*, 1956, 2nd Edition, Macmillan Co., New York.
[3] *Brit. med. J.*, 1961, **1**, 1019.
[4] Odell, G. B., *J. Pediat.*, 1959, **55**, 268.
[5] Silverman, W. A., Anderson, D. H., Blanc, W. A., and Crozier, D. N., *Pediatrics*, 1956, **18**, 614.
[6] Allison, A. C., *Lancet*, 1955, **1**, 669
[7] Hofnagel, D., *New Engl. J. Med.*, 1961, **264**, 168.