STUDIES IN SCHIZOPHRENIA: II. ESTIMATION OF SERUM-CHOLESTEROL.

By H. H. FLEISCHHACKER, M D., and F. N. BULLOCK,
From the Pathological Laboratory, Shenley Hospital, Herts.

[Received 3 March, 1952.]

IN a previous paper (Bullock, Clancey and Fleischhacker, 1951) an attempt was made to separate schizophrenic reaction syndromes, due to diagnosable and often successfully treatable disease of known etiology, from idiopathic or cryptogenic schizophrenia. It was shown that the criteria of idiopathic schizophrenia are—

(1) *Positively :* (a) Mentally, the classical symptoms of inadequacy and inappropriateness : of thought (paralogia), of affect (parapathema), to which one may add of volition (paraboulema), usually accompanied by hallucinations, paranoid ideas, etc.

(b) Physically, a slightly pathological C.S.F., due essentially to an increase of the globulin fraction.

(2) *Negatively :* the absence of generally acknowledged organic disease of the brain, or any physical disease which is known to produce such disorders of the central nervous system or the C.S.F., as mentioned under (1).

It was also suggested in that paper that these criteria, together with an examination of the serum cholesterol, might help to separate true puerperal (endocrine) psychoses, often diagnosed as puerperal schizophrenia, from puerperally precipitated idiopathic or cryptogenic schizophrenias. The true puerperal psychoses appear to be characterized by the absence of true paralogias, but by the presence of mutism or confusion or bewilderment. There is also a long-lasting increase in the serum cholesterol, and what was called a " discordant " C.S.F., viz., a definite increase of total proteins with an outspoken Lange curve, but weak turbidity reactions. The few observations published previously have been subsequently confirmed in a small number of similar cases.* The estimation of serum cholesterol carried out on 22 patients at that time had led to the tentative conclusion that in the absence of obvious endocrine disorder, or change of endocrine function due to known circumstances, including puberty, climacterium, etc., idiopathic schizophrenics have a normal serum cholesterol level. Since then, the number of serum cholesterol estimations on patients clinically diagnosed as schizophrenics has been increased to 94 ; 84 patients were females and 10 were males. These cases were divided into idiopathic and " potentially " schizophrenics.

1. Idiopathic schizophrenics : those who showed clinically the essential signs of disorder of thought, affect, volition, etc. In this group there were 36 such patients, most of them below the age of 40, including 10 males, the serum-cholesterol level being 160 to 210 mgm. per cent. in 29. In 7 patients—5 female and 2 male—it was higher than 225 mgm. per cent. (238—270 mgm. per cent.). All these 7 patients showed unmistakable signs of endocrine involvement (pubertal and other obesity, puerperium, ovarian cysts, hypophyseal eunuchoidism).

2. The rest (58) of the schizophrenics were incompletely examined (from our point of view), and therefore were classified as " potentially schizophrenic." According to the experience of one of us (H. H. F.), about 30 to 40 per cent. of these would not stand our tests of " idiopathic schizophrenia," but would turn out to be schizophrenic reaction syndromes. This group was complicated also by some other factors. Most of these patients were chronic ones, many older than 40 years, and

* Unfortunately, the matter could not be brought to a satisfactory conclusion since Dr. Clancey has left this hospital. It is hoped that he will be able to pursue his researches on this subject and to publish the results, including his attempts to treat such endocrine puerperal psychoses with thyroid and other hormones.

https://doi.org/10.1192/bjp.98.412.466 Published online by Cambridge University Press

quite a number of them had had a prefrontal leucotomy, which operation is sometimes followed by an increase of the cholesterol level. (See also the tables published by Brody and others (1950).) In 27 of these cases the serum cholesterol was normal, and endocrine signs were present definitely in only 2 patients. In 31 patients the cholesterol was higher than normal (up to 300 mgm. per cent.) According to the case papers, only 5 of these latter patients showed definite thought disorder, while in 6 others paralogical thinking might have been present. On the other hand there was unmistakable clinical evidence, in at least 15 patients, of endocrine upset apart from the factors mentioned above. In principle, therefore, the results agree with our first findings, and also with those of Stenberg (1929, survey of literature). On conflicting results see also Eaton and Muntz (1947).

Assuming that in this material cholesterol is essentially an indicator, directly or indirectly, of thyroid function, the results confirm also the findings of Bowman *et al.* (1950), and of Brody and Man (1950). These authors had found, in contrast to some previous investigators, that on the whole, I^{131} uptake, protein-bound serum iodine, B.M.R. and cholesterol are more or less normal in schizophrenia, if one excludes patients whose endocrine and/or vascular system may be disturbed. While, vice versa, we have examined the cholesterol of so-called schizophrenic patients as they came along, and later on found that patients with high cholesterol levels showed, as a rule, signs of endocrine change of function, not connected with schizophrenia proper.

Apart from the 94 patients mentioned above, we examined also the sera of 23 female patients diagnosed as paraphrenia, 22 of whom had a serum cholesterol higher than 250 mgm. per cent. Paraphrenia usually occurs in the second half of the human middle age, when arteriosclerosis, hypertension, the climacterium or involution are either established or imminent. In such circumstances the serum cholesterol is often high, particularly in women, though not necessarily so often (Kountz, 1945; I. H. Page, 1945, own controls), as frequently assumed. Nevertheless, the explanation may be that in paraphrenia such factors are responsible for the increased serum cholesterol. Indeed, if one looks through the physical state of these 23 patients: age, blood pressure, conditions of the arteries, endocrine and vegetative signs, etc., there is scarcely a patient in whom one will not find one or other of these factors, and sometimes even several of them together. From this, one may conclude that the raised cholesterol level is not of any etiological significance, but essentially a concomitant as in cryptogenic schizophrenia.

There is, however, a different aspect of the problem. Paraphrenia, as a subgroup of schizophrenia may be something of a misfit. Kraepelin, although the classification was his, in his later years was not happy about it; neither was E. Bleuler (1918), nor are other authors (Henderson and Gillespie, 1950; FitzGerald, 1951.)

If one goes by the clinical signs of idiopathic schizophrenia (which are those of classical schizophrenia), paraphrenia lacks the most significant ones. The personality is well preserved, the affect is more or less adequate, and thought disturbance, if present at all, is slight. Unfortunately, no results of C.S.F. examinations are available. The main symptoms, on the other hand, paranoid ideas (sometimes grandiose), hallucinations and disturbance of mood are often met with in organic or toxic psychotic diseases. So, paraphrenia, just as schizophrenia, may be a syndrome rather than a nosological entity. What is often (much too often) diagnosed as paraphrenia, symptomatologically very closely resembles the psychoses associated with myxoedema. The psychoses of myxoedema, as Asher (1949) has reminded us recently, are most likely much more common than is generally thought, and although the patient will often look myxoedematous, this is not always the case (in cases of true, and also of secondary myxoedema). It appears highly desirable to diagnose and treat such patients as early and as adequately as possible, as chronicity of the condition, favoured by vascular and other changes occurring with advancing age, may cause irreversible damage to the brain. Asher, most of whose 14 patients were females in the higher age-group (a fact stressed by Simpson, 1949), has treated 9 of them successfully. It is well known (Clerk, 1912; Rice, 1938; Wegelin, 1926) that after the age of 50 or even earlier the thyroid undergoes frequently a marked involution. There is no doubt from our autopsy material that the number of already macroscopically pathological thyroids is rather high in elderly patients, particularly amongst women. The biochemical, supported by morbid anatomical, findings make one think that thyroid disorder may be of some importance in mental diseases other

https://doi.org/10.1192/bjp.98.412.466 Published online by Cambridge University Press

than idiopathic schizophrenia, particularly in the last third of life (see also Annotation, *Brit. Med. J.*, 1949), and incidentally explain, at least partly, why serum cholesterol is often raised in higher age.

SUMMARY.

(1) Further examinations of serum cholesterol of idiopathic and other so-called schizophrenic diseases have shown that, on the whole, cholesterol in idiopathic schizophrenia is abnormal only when clinical evidence of a change of endocrine function is evident. These findings confirm the results of some publications, and may explain contradictions in the literature on this subject, if the concepts of idiopathic schizophrenia and schizophrenic reaction syndromes are appropriately applied.

(2) 22 out of 23 female patients diagnosed as " paraphrenia " had a serum cholesterol level of 250 mgm. per cent. and higher. The diagnostic and possibly therapeutic importance of these findings is shortly discussed.

(3) The importance of differentiating between idiopathic schizophrenia and schizophrenic reaction syndromes is stressed again. Many of the latter psychoses are often more satisfactorily treatable than, for the time being, idiopathic schizophrenia.

REFERENCES.

ANNOTATION, *Brit. Med. J.*, 1949, ii, 587.
ASHER, *ibid.*, 1949, ii, 555.
BLEULER, *Lehrb. d. Psychiatrie*, 1918. Berlin.
BOWMAN, MILLER, DAILEY, SIMON, FRANKEL and LOWE, *Am. J. Psychiat.*, 1950, **106**, 51.
BRODY, MAN and MOORE, *J. Clin. Endocrin.*, 1950, **10**, 716.
Idem and MAN, *Am. J. Psychiat.*, 1950, **107**, 357.
BULLOCK, CLANCEY and FLEISCHHACKER, *J. Ment. Sci.*, 1951, **97**, 197.
CLERK, *Frankf. Z. Pathol.*, 1912, **10**, 1 (as quoted by Rice).
EATON and MUNTZ, *Am. J. Psychiat.*, 1947, **104**, 315.
FITZGERALD, 1951, Meeting of North and Midland Division, R.M.P.A., 26 October, 1951.
HENDERSON and GILLESPIE, *Textbook of Psychiatry*, 1950. London.
KOUNTZ, SONNENBERG, HOFFSTATTER and WOLFF, *Biol. Symposia*, 1945, **11**, 79.
PAGE, *ibid.*, 1945, **11**, 43.
RICE, *Arch. Surg.*, 1938, **36**, 96.
SIMPSON, *Brit. Med. J.*, 1949, ii, 759.
STENBERG, *Acta med. Scand.*, 1929, **21**, 558.
WEGELIN, *Hdb. d. spez. pathol. Anat. and Histol.*, 1926, vol. viii. Berlin.

https://doi.org/10.1192/bjp.98.412.466 Published online by Cambridge University Press