STUDIES IN SCHIZOPHRENIA.

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The diagnosis, aetiology and treatment of schizophrenia are still outstanding among the most important, complicated and least understood problems of psychiatry.

In this paper an attempt is being made to approach the diagnostic problem. The question raised is: Are there criteria to differentiate symptomatic schizophrenic syndromes from "schizophrenia," or better, "idiopathic schizophrenia?" For the purpose of the investigation certain clinical and clinical-pathological criteria have been adopted in order to find out whether there is sufficient correlation between the clinical and laboratory findings to justify the hypothesis that a differential diagnosis between the two conditions, viz. schizophrenic-reaction syndrome and "schizophrenia" (idiopathic schizophrenia) can be made. It was also hoped that clinical and prognostic subgroups might be forthcoming.

The patients investigated were all admitted to this hospital with the diagnosis or differential diagnosis of schizophrenia.

Clinical Criteria.

The clinical diagnosis of schizophrenia was made dependent on the presence to a greater or lesser degree of

1. A disturbance in conceptual thinking, such a disturbance being considered by Kraepelin, Bleuler and Kleist, and more recently stressed by A. Lewis (1946) in this country and by Hanfmann and Kasanin (1942) in U.S.A. to be one of the main characteristics of schizophrenia.
2. An inappropriate and/or inadequate emotional response, this also being considered by most writers to be characteristic of the syndrome.
3. Hallucinations.
4. Absence or diminution of empathy.*

In the early stages of the investigation, ideas of reference, non- or poorly systematized delusions, depersonalization, derealization, alteration in body image, disorders of movement and reflexes were all taken into account, but were later thought to be only of secondary importance.

* *Empathy*. According to the Oxford Dictionary: "the power of projecting one's personality into (and so fully comprehending) the object of contemplation," viz, the patient.

Laboratory Criteria.

According to Kafka and Samson (1928), Neel (1933) and one of us (H. H. F., 1945), the C.S.F.s' of schizophrenics show a slight increase of total protein with a disturbance of the albumin/globulin ratio. This syndrome is absent in normals, neurotics and the true affective psychoses and was, therefore, chosen as the main laboratory characteristic.

All patients also had as a routine urine examination, bacteriology of faeces, Wassermann, blood-sugar estimation, E.S.R. and a total blood count. In a number of the later cases, serum cholesterol estimations and the modified Takata Ucko Test (T.U.T.) were carried out.

Material.

The number of patients reported on is 76, all of them females, admitted between October, 1948, and February, 1950. Sixty-four of them were examined clinically in the way to be described later. In the remaining 12 the clinical examination was less stereotyped, but the results obtained were considered sufficiently clear to warrant their inclusion in this investigation. The laboratory tests were the same in all 76 cases with the exception of blood cholesterol examination and the modified Takata Ucko Test which, as stated before, were only carried out on the later cases. Most of the cases diagnosed as schizophrenics were treated with insulin by one of us (I. C.). In 20 of these cases the C.S.F. was examined both before and after treatment. Twenty-nine of the cases were examined by our psychologist (Miss E. MacDonald). Of these, 6 were examined both before and after treatment.

Technique and Interpretation.

General Remarks.

The first 10 cases were examined without mutual exchange of results between clinician and pathologist, following which a comparison of findings showed a high degree of correlation. The next score of patients were seen clinically by two of us (H. H. F. and I. C.), and the results obtained on the C.S.F. were read by all three of us. Hereafter, with few exceptions, all cases were investigated clinically by I. C., and the C.S.F.s' by H. H. F. and F. B. The clinical laboratory and psychological findings, again with a few exceptions, were not compared until the whole material had been collected.

Clinical Examination.

A general physical and detailed neurological examination was carried out, particular attention being given to disturbances of motility and reflexes.

Mental Examination.

A general psychiatric examination was carried out in all cases. Conceptual thinking was tested by the ability of the patient to define differences and to interpret proverbs. The tests were considered pathological not when the answers were "wrong" but when they were "paralogical." In a

number of cases the collaboration of the patients was so poor that no conclusions could be reached. In such cases the answers were tabulated as doubtful (?) in the accompanying tables. In some, the disturbance was only slight. These are tabulated as (±), and the definite positives are tabulated (+). The history of the case was obtained from the patient, her relatives and friends wherever possible. It was, however, unfortunately necessary in a considerable number of cases to rely on the somewhat scarce data given by relatives on the routine hospital history enquiry form.

The psychological tests given by Miss E. MacDonald were the Bellevue-Wechsler Scale, the Rorschach and Weigl-Goldstein-Scheerer Sorting Test.

Laboratory Tests.

Blood: *Serum cholesterol.*—The technique applied was that given by Panton and Marrack (1947). We have found that the colorimetric readings are facilitated by the use of a Wratten No. 1 (red) filter. The error of the technique on serum is about ± 5 per cent. The normal values of fasting serum according to Panton and Marrack are 160–210 mg. per cent.

M.T.U.T. (*Modified Takata Ucko Test*).—Reagents used: 0·36 per cent. solution of Na_2CO_3 and 0·5 per cent. $HgCl_2$.

Take 10 small test tubes, put 0·9 c.c. of physiological saline into the first, and 0·5 c.c. of it into each of the other tubes. Add 0·1 c.c. of fasting serum to the first tube and make a serial dilution. Add 0·1 c.c. of the Na_2CO_3 solution to each tube, shake gently, add 0·1 c.c. of $HgCl_2$ to each tube and mix well immediately after the addition of the reagent to each tube. Read after 90 minutes against a dark background. The reaction is pathological if there is sedimentation in at least three of the tubes. The reaction may be checked after 18 hours and in pathological cases sedimentation will be found in at least 6 tubes. In contrast to the claims of Bauer (1947), who used the original concentration as given by Takata, this reaction (using Ucko's concentrations, 1935) is not speeded up by the exposure to very low temperatures, but is on the contrary delayed. Heat has a slightly accelerating influence though much less than when C.S.F. is being tested. The reaction is apparently normal in neurotics and emotional disorders when these are not complicated by any physical illness. The pathology of this, and similar reactions in serum (thymol, gold sol, cholesterol flocculation test), is usually ascribed by various authors to disturbances of the globulin/albumin ratio, caused by liver disease. (Literature, see Shattock, 1950). Our own investigations into the significance of this test are still in progress.

C.S.F.—Total protein, Lange reaction, M.T.R. technique and evaluation as described in a previous paper (Fleischhacker, 1945).

Cells.—Technique and evaluation as described before. It would be preferable, however, to take the C.S.F. for the cell count while the lumbar puncture is still in progress.

Pandy Test.—To 1 c.c. of saturated aqueous phenol-solution in a small test-tube add exactly 0·05 c.c. of C.S.F. Mix well by rotating gently. Reaction is read after 15 minutes against the light. With an entirely normal C.S.F. no

turbidity is seen. Turbidity is indicative of an increase of total protein, not of globulins only, as is usually stated. (Bullock and Fleischhacker, 1950.)

Nonne Test.—To 0·5 c.c. of C.S.F. are added 0·5 c.c. of saturated ammonium sulphate solution. Mix quickly. The test is read after 15 minutes against a black background. In the following tables the outcome of the Nonne Test is given in numbers, in accordance with a number of experiments carried out on mercantile pure γ-globulin, as follows :

Very faint trace	3
Faint trace	5
More than faint trace	6 etc. up to
Trace	10

It will be understood that these figures do not exactly represent the true globulin content of the C.S.F., nor is the quotient $\frac{\text{Nonne}}{\text{Total protein}-\text{Nonne}} = \frac{N}{TP-N}$ necessarily equal to the true globulin albumin ratio. It is interesting, however, to mention that the $\frac{N}{TP-N}$ quotient in C.S.F.'s with normal colloidal curves was about 0·14 to 0·16, which corresponds very well with the normal globulin-albumin ratio.

The evaluation and limits of error of the techniques used as seen now on over 1,000 C.S.F.'s are still the same as described previously by one of us (H. H. F. 1945) and a certain slight overlapping of curve types cannot be avoided. This holds particularly good for the finer reading of the Lange colour changes which we find rather difficult to evaluate.

Results.

The results obtained in 48 patients have been tabulated in the accompanying tables. The other 28 cases are being omitted for the following reasons :

Seven idiopathic schizophrenic patients were among the 12 whose examination was not stereotyped, but in whom the results obtained warranted their inclusion in this paper as mentioned earlier. In 21, the clinical and laboratory findings made it evident that the original diagnosis of schizophrenia could not be sustained.

The data based on our findings are in the usual type on the right side of the tables. The data given in italics contained on the left of the table were obtained from others and could not always be checked. We think, however, they are interesting enough to be published although we shall not comment on them with the exception of the puerperal cases later.

Discussion.

Before the results are discussed in detail, it is necessary to say a few words on the evaluation of the findings and the techniques which were employed in the investigation.

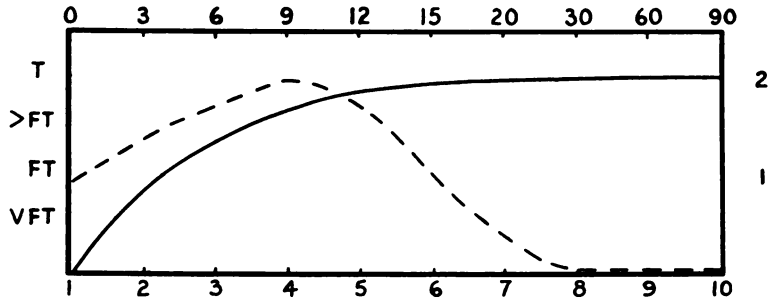

TABLE I.

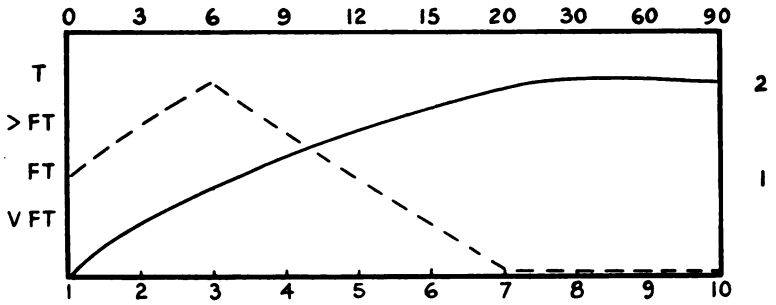

TABLE II.

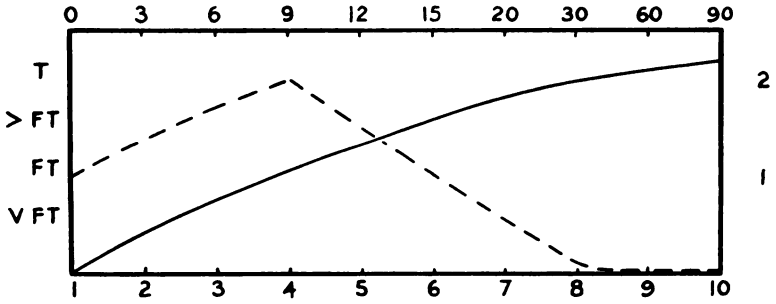

TABLE III.

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TABLE

Name.	Age at present admission.	Hereditary factors.	Constit. factors.	Predisposing factors.	Precipitation of first attack.	Onset of first attack.	Stay in hospital altogether in months.	Disturbance of conceptual thinking.
S. M. J—	17	*Nil known*	Hy ? SEV	I	*I ?*	*Sl.*	4	+
Wi—	28	*P+B*	?? *BC*	*M*	*I? M?*	*Su.*	2	+
Pay—	35	*P ?*	*B ? V*	..	*Tr ? M ?*	*Su.*	4½	+
Cl—	20	*Alc*	*SE*	*IM*	..	*Sl.*	8½	+
Ca—	23	*Alc N*	*S ? EV*	*IM*	*I (Op)*	*Su.*	7	+
Sp—	31	..	*SEV*	*I ?*	..	*Sl.*	12	+
G—	38	*PE*	*SEV*	*Ht IM*	..	..	14	+
M—	17	..	*N* (?)	*I ?*	..	*Su.*	38	+
Bo—	32	*N* (*P?*)	*SE*	*M*	*I ?*	*Sl → Su.*	16	+
V—	28	..	*B ?*	..	..	..	Years	+
H—	24	*P*	*S Epil ?*	*Alc drugs*	..	..	7½	+
Br—	37	*P ?*	*? CEV*	*? Alc I ?*	*? floating kidney M*	*Sl. → Su.*	16	+
Wo—	33	*P*	*SE*	..	*I ? Pp ?*	..	6	+
Pa—	25	*P*	*CE*	*I Ad*	..	*v. sl.*	29	+
L—	29	*P*	*? CE*	*M*	..	..	17½	<+

TABLE

McG—	27	..	*? Ep ? C*	*I Alc Pp*	*M ?*	*Su*	5½	+
Mo—	42	*Ep P Alc*	*C (? S) EV*	..	*Ad ?*	*Sl*	Years	±
Co—	29	*P*	*? C ? BE*	*PA M*	*PA*	*Su*	5	?
Ba—	27	*N*	..	..	*M*	*Su*	2	+
Bo—	18	*P ? N ?*	*S*	*IM*	*M ?*	*Sl*	7½	?
C—	43	..	*C ? E*	*I*	*IM*	*Sl → Su*	Still under treatment	?
D—	31	*P ?*	*SE*	..	*M*	*Sl*	4	+
V—	21	..	*V*	*N*	*?*	*Sl*	4	+
P—	35	*PB ??*	*E ? S*	*M ?*	*Pp ? M ?*	*Sl → Su*	11½	+
F—	30	..	*Hyst ? E*	*I Alc*	*M ? E ?*	*Sl*	12	+
S—	34	*Alc*	*? C Epil*	*I Alc Pp*	*Pp ?*	*Sl*	6	±
McE—	33	..	..	..	*Pp*	*Su*	4½	Confused
Hu—	30	*N*	..	..	*IM ?*	*Su*	Still under treatment	+
Ho—	35	*Nil*	*? C*	*Pp*	*Pp*	*Su*	5½	±

TABLE

P—	40	*P*	*B ? S ?*	*I Alc*	*Pp*	*Su*	2½	±
B—	24	*P*	*S ?*	*M ?*	*? I Pp*	*Su*	Still under treatment	Confused
Ha, D—	31	*Alc*	*N*	*M*	*I*	*Sl*	3	±
D—	18	*N*	*S*	*Alc*	..	*Su*	2½	?
R—	20	..	*B ?*	*M*	..	*Sl ?*	4½	+
S—	17	..	*S (Ep ?)*	*M*	..	*Sl*	Still under treatment	±
Ha, B—	19	*Ep*	*B ? S*	*Ht M*	..	..	3½	?
Sa	18	*P*	*S Epil ? B ?*	*PA*	*? PA*	*Sl → Su*	3½	+
A—	32	*N*	*S*	*I*	*? I Pp ?*	*v. sl*	2½	+
Ba—	23	..	*N*	*E ?*	*M*	*Su*	Still under treatment	Mute
G—	23	..	..	..	*I*	*Sl → Su*	4½	?
T—	30	..	*N*	*Ht Pp*	*I*	*Su*	1½	Confused
H—	36	..	*N*	..	*Pp*	*Su*	1½	,,

TABLE

Wh—	18	..	*SEV (? B)*	*IM*	..	*Sl*	6	?
B—	24	*P*	*Epil E*	*IM*	*M*	*Su*	16	±
S—	19	..	*N ?*	*M Ad*	*H tr M*	*Su*	3½	?
E—	28	..	*B*	*M*	*Pp*	*Su*	4½	Confused
W—	20	*P*	..	..	*Pp*	*Su*	6	Mute
Sp—	21	*Ep ?*	*SBEV ? Epil*	..	..	..	2	+

P = psychosis
Alc = alcoholism
N = neurosis
E = endocrine
Ep = epilepsy
S = schizoid
C = cycloid
PA = pernicious anaemia

I = vegetative
N = normal
Epil = epileptoid
B = backward
Hy = hysterical
I = infection
M = mental

Type of colloidal reaction.

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I.

Emotional reaction.	Hallucinations.	Ease of eliciting hallucinations.	Serum M.T.U.T.	Serum Cholest.	C.S.F. Total protein.	C.S.F. Nonne.	C.S.F. TP TP–N.	C.S.F. Cells 3	Remarks.
+	+	±	3	213	28	10	·55	6	..
−	+	−	..	..	30	10	·5	9	Works but still ill.
±	+	+	2(+1 ?)	260	35	12	·52	4	Second admission (4/12).
−	+	−	..	..	36	12	·5	6	..
+	+	−	..	..	30	10	·5	6	..
−	+ ?	−	2(+1 ?)	336	45	15	·5	3	Unimproved.
±	++	±	3	..	25	8	·47	4	Third admission (7/12). Still in hospital.
+	+	−	..	..	25	8	·47	9	Third admission (13/12).
−	+	−	..	..	23	7	·44	1	Fourth admission (4/12).
−	+	±	..	..	28	8	·4	1	Third admission. Still in hospital.
±	+	+	..	..	35	10	·4	3	Second admission (4/12).
−	+	+	..	..	28	8	·4	4	„ „ (13/12).
−	+	±	..	..	35	10	·4	8	..
− (or +)	+	−	..	..	30	8	·36	5	Second admission (24/12). Still in hospital.
+	+	±	..	..	25	6	·32	2	Second admission (13/12).

II.

−	+	±	..	..	28	8	·4	8	Second admission (3/12).
−	+	±	2(+1 ?)	230	30	8	·36	4	First attack 15. Since then in many hospitals. Present 3/12.
−	+	+	..	..	30	8	·36	4	..
−	+	+	3(+1 ?)	152	30	8	·36	1	Did not finish treatment.
−	+	−	3	..	23	7	·35	1	1st attack few days. 2nd 7/12. Recovered without physical treatment.
−	+	−	1 ?	242	40	10	·3	2	One previous attack ?
±	++	+	3	..	20	5	·3	3	Relapsed later.
−	+	+	4	212	25	6	·32	2	..
−	?	−	..	..	33	8	·32	2	Second admission (9/12).
±	?	−	2(+1 ?)	300	22	5	·3	7	Second attack 9/12—ovarian cyst.
+	++	+	..	..	30	7	·3	1	Second admission.
±	+	+	3	156	22	5	·3	3	..
+	+	±	2(+1 ?)	225	35	8	·3	4	Second admission. Still under treatment.
+	+	+	..	..	38	8	·27	7	..

III.

±	?	..	2	278	55	12	·28	1	Very def. *nil* neurol.
±	?	±	2	150	30	6	·25	4	First admission. 4/12 so far.
±	++	+	3	..	40	8	·25	3	..
±	++	+	4	184	25	5	·25	4	..
+	+	+	..	..	37	7	·23	2	..
−	+ ?	−	2	290	43	8	·23	3	..
−	+	±	2(+1 ?)	217	23	4	·22	1	..
+	+	+	..	..	23	4	·21	2	..
±	+	+	2	300	30	5	·2	2	Very slow onset over years.
±	+ ?	+	3	213	30	5	·2	6	..
+	+	±	..	..	25	4	·2	8	..
+	++	..	3	225	33	5	·18	2	..
+	?	..	2	290	33	5	·18	4	..

IV.

±	?	−	..	..	45	5	·12	2	..
−	+	−	1	288	45	5	·12	6	An organic case (Diss. scler. ?).
+	?	−	2	252	30	4	·15	3	..
±	+	+	2(+2 ?)	288	45	6	·15	2	..
+	?	−	..	..	45	6	·17	2	..
−	+ ?	−	..	..	25	5	·25	10	? Schiz., but very outspoken. Reflex disturbances. Slightly blurred discs.

Ht = head trauma
Ad = adolescence
Tr = trauma
Op = operation
Pp = puerperium
Su = sudden
Sl = slow.

+ distinct
± little outspoken
? doubtful
+ strong
± inadequate
− inadequate and inappropriate

M.T.R. ——— Lange - - - - - -

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It must be stressed that the authors of this paper fully realize that none of the clinical or laboratory findings are in any way *specific*, but that rather the combination of clinical and laboratory findings elicited here are *characteristic* of " schizophrenia."

Paralogical disturbances of thinking and of speech are very often found in patients recovering from organic sensory aphasia. This, of course, was known to Kraepelin and many other writers. Inadequacy and inappropriateness of affect, hallucinations and all the other signs seen in schizophrenia may equally be found in the organic psychoses. Similarly a disturbance in the albumin/globulin ratio in the C.S.F. together with a slight increase of total protein, of cells and pathological deviation of the colloidal reactions may be found in treated G.P.I., occasionally in epileptics, in disseminated sclerosis, in brain tumours, also occasionally following head injuries and very rarely in senile disorders. It is our contention, however, that a clinical picture consisting of a disturbance of thought, a disturbance of emotion, of empathy and most commonly with hallucinations, plus the changes found in the C.S.F. in the absence of other organic disease are the characteristic picture of " schizophrenia."

There are, of course, possibilities of subjective error, partly due to the varying degree of collaboration obtained from the patients which render the interpretation of tests difficult, but these can be overcome by practice. With regard to the paralogias, one of us (H. H. F., 1930) has shown how the margin of error can be narrowed. Similar objections may be raised in respect to the evaluation of the laboratory results. A few points have been dealt with above under Technique. Also, in a previous paper (1945) it was shown that the total C.S.F. syndrome has to be taken into account in order to reach a correct decision. Accordingly, in the majority of the C.S.F.'s examined, the various test results should have been and actually were concordant. In a few others, some of the results, with the techniques used, appeared to contradict each other, usually in that the strength of the Lange reaction corresponded roughly to the increase in total protein while the turbidities of the Nonne and Pandy and M.T.R. were too slight. This discordance has so far commonly been found to occur in patients with raised blood cholesterol.

On the whole, the collaboration between clinician, psychologist and pathologist has worked well and has been of mutual benefit and what is more important, has proved to be of value to our patients.

According to the combined investigation and using our criteria, the patients could be divided into three groups :

A. The 21 cases in which the diagnosis of schizophrenia could not be sustained were as follows :

Involutional melancholia, 2.
Reactive psychoses in high-grade mental defectives, 5.
Toxic infective psychoses and organic disorders of the brain, 14.

Only in two of these cases, one brain tumour and one presenile dementia, might the C.S.F. syndrome have fitted into the type of milder schizophrenia. In the rest of these cases, the C.S.F.'s were normal, or what is usually acknowledged as " organic."

B. The 42 tabulated schizophrenics. There are two subgroups :

1. As represented in Tables I and II.
2. As represented in Table III.

Sub-group 1.—In the material demonstrated in Tables I and II the clinical signs were on the whole very marked, a severe thought disturbance, shallow, inappropriate, inadequate affect, loss of empathy and hallucinations about which the patient was very reticent. The C.S.F. showed a very strong increase of globulins and the M.T.R. rose to its peak within 15–20 minutes or less. There are, however, differences in the intensity of clinical and biochemical reactions between Tables I and II which may be significant in that for the patients in Table II the length of stay in hospital is less and the percentage of remissions is appreciably greater than in Table I.

Sub-group 2.—The patients in Table III presented a difference in accentuation. These patients are more obviously hallucinated, their emotional response is usually inappropriate but has greater depth, empathy is present and, finally, the thought disorder is usually difficult to elicit. (Tabulating the results makes it possibly difficult to convey adequately an idea of this difference between the sub-groups.) The C.S.F. shows, on the whole, that the increase in total protein is due to a relatively greater increase than in Sub-group 1, in the albumin fraction. The M.T.R. accordingly rises more slowly, taking from 60 to at least 90 minutes to reach its peak.

All patients of this sub-group are first admissions, consequently having a better prognosis but, unless treated, a number might have drifted into chronicity.

C. In this group, consisting of 6 patients, we were unable to make an adequate diagnosis as they did not fit either clinically or clinico-pathologically into the schizophrenic group. It is interesting to note that on the whole, the T.P. in the C.S.F.'s of these patients is higher than those of Group B. The globulins are only slightly increased and the M.T.R. ascends slowly in a straight line.

Miscellaneous Remarks.

Twenty-two serum cholesterol examinations and 26 M.T.U.T.'s only were carried out. It is interesting to note that abnormal cholesterol values were found in patients with some endocrine disturbance (dysplastic adolescents, puerperals, climacterics, two ovarian cysts). In these cases the M.T.U.T. was often normal. It was also normal in one puerperal case with a subnormal cholesterol.

The findings of the C.S.F.'s before and after insulin treatment are, as it has been described by other writers, only slightly different. They appear to run more or less parallel with the clinical course. Three cases may be worth while mentioning : In one of these three cases, while the pathological and psychological laboratories showed a deterioration of the patient's condition after treatment, the patient was very much improved clinically. Another case, a puerperal who showed clinical improvement after insulin while the C.S.F.

was worse, relapsed soon after her discharge. A third patient whose C.S.F. was worse after treatment, remained in hospital for more than a year.

These simple techniques that can be used in any hospital or laboratory have helped us to sort out 21 cases from the 76 loosely diagnosed as schizophrenics, thus enabling us to establish their true diagnoses with obvious benefit to these patients. Beyond this diagnostic value these findings have apparently a prognostic significance, as is shown by the length of stay in hospital in the tables, those in Table III having a better prognosis.

Will these methods enable us to differentiate further any schizophrenic sub-groups ?

The small groups of puerperal cases may allow us to approach this problem. There were 10 patients in groups B and C in whom the psychosis began very soon after delivery.

The principal possible connections between puerperium and psychotic reaction in these cases are as follows :

(1) The psychosis is a true puerperal psychosis of schizophrenic colouring.

(2) The psychosis is a true "schizophrenia" precipitated by the puerperium.

The material is tabulated as follows :

TABLE V.—*Puerperal Psychoses.*

Name.	Disturbance of conceptual thinking.	Emotional reaction.	Hallucinations.	C.S.F.				Serum	
				Total protein.	$\frac{N}{TP-N}$	Cells $\frac{}{3}$	Reaction type.	Cholesterol.	M.T.U.T.
E—	Confused	±	+	45	·15	2	D	288	2 (+2v. sl.)
W—	Mute	±	+	45	·17	3	D		
H—	Confused	+	+	33	·18	4	D	290	2
P—	±	±	?	55	·28	1	D?	278	2
S—	±	+	++	27	·3	4	D?		
A—	+	±	+	30	·2	2	D?	300	2
B—	+	+	?	30	·25	4	C	150	2
Ho—	+	+	±	38	·27	8	C		
McF.—	Confused	±→+	+	22	·3	3	C	156	3
Pe—	+	—	?	33	·32	8	C		

Although it was clear in these 10 cases that the puerperium had a definite connection with the psychosis, it was not very clear in any of these patients whether a psychosis had existed before delivery, which means that we have to rely on the facts of the clinical and laboratory examinations. According to the school of Kleist, schizophrenia should not be diagnosed unless there is an outspoken disturbance of thought with paralogias. From this point of view it will be noticed that thought disorder was not very outspoken in any of the five patients in the upper half of the table, in three of these the C.S.F. results were discordant (D), three of the cholesterols high + no M.T.U.T. was definitely pathologic. In the lower half of the table four patients showed definite conceptual disturbance and in three of these the C.S.F. findings were concordant (C), and only one cholesterol was high.

In three C.S.F.'s no decision as to con- or discordance could be made.

Summary and Conclusions.

1. An attempt has been made by close co-operation between clinical and laboratory workers and, in a number of cases, the psychologist, to correlate and classify their findings in cases at first loosely diagnosed as " schizophrenia " and so to define more clearly the basic clinical and clinico-pathological signs of " idiopathic schizophrenia " and to eliminate schizophrenic-reaction syndromes.

2. The case material consists of 76 cases admitted to this hospital between October, 1948, and February, 1950.

3. The clinical diagnosis of " idiopathic schizophrenia " was made dependent on the presence to a greater or lesser degree of :

(*a*) A disturbance of conceptual thinking.
(*b*) A disturbance of affect.
(*c*) Hallucinations.
(*d*) Absence or diminution of empathy.

The laboratory diagnosis was based on the finding of an increase in total protein with a disturbance of the albumin globulin ratio in the C.S.F.

The cases fell into the following groups and sub-groups :

A. In 21 cases the diagnosis of schizophrenia could not be sustained. The patients were diagnosed as suffering from involutional melancholia, psychotic reactions in feeble-minded people, toxic and infectious states or organic diseases of the brain.

B. Forty-nine cases were " idiopathic schizophrenics." Forty-two of these were tabulated and fell into two groups.

Sub-group I—Tables I and II.

This sub-group was characterized by a severe disturbance of conceptual thinking, shallow inappropriate affect, absence of empathy and hallucinations that were difficult to elicit. The C.S.F. showed a very strong increase of globulins and the M.T.R. rose to its peak within 15–20 minutes. Prognosis on the whole was bad.

Sub-group II—Table III.

These patients were more obviously hallucinated, their emotional response was usually inappropriate but had greater depth. Empathy was present and finally, the thought disorder was difficult to elicit. The C.S.F. showed, on the whole, that the increase in total protein was due to a greater increase in the albumin fraction than in the cases of sub-group I. The M.T.R. accordingly rose more slowly, taking from 60 to at least 90 minutes to reach its peak. Prognosis on the whole was good.

C. A group of 6 unclassified patients.

Conclusions.

The clinical and clinico-pathological criteria used in this investigation proved of definite diagnostic value in the differentiation of schizophrenic-

reaction-syndromes from idiopathic schizophrenia; they also revealed the existence of clinical and prognostic sub-groups amongst idiopathic schizophrenics.

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