(after 4 to 5 hours on duty) as compared with the first reading, and then a fall at the time of leaving duty (7.30 a.m.) to a level near the first reading or slightly below it.

Three other male nurses and one female nurse who visited different wards during the night showed a slight decrease in the S.P. at midnight.

The following table affords a comparison between the average systolic and diastolic pressures of male nurses and those of patients (in improved states) suffering from certain forms of insanity:

	S.P.	D.P.	Average age.
Day male nurses . .	124·8	85·9	37·8
Night male nurses . .	127·5	87·4	37·6
Delusional insanity . .	128·2	89·1	47·0
Melancholia . . .	121	83·8	42·7
Manic-depressive insanity .	127·1	77·4	42·2

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The Hæmoclastic Crisis in Mental Defectives. (From the Laboratory of the Rampton State Institution.) By W. Rees Thomas, M.D., M.R.C.P., D.P.M., Medical Superintendent, Rampton State Institution; and W. J. Lascelles, M.B., B.Ch., D.P.M.,* Assistant Medical Officer, Cane Hill Mental Hospital, Coulsdon, Surrey.

The ingestion of a pint of milk by a normal fasting individual is followed by certain blood changes, the most important of which are an increase in the leucocyte count and a slight rise of blood-pressure. In the condition known as anaphylaxis, or protein shock, the general symptoms are accompanied by a fall in the number of

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blood leucocytes, a reversal of the differential count, and a lowering of the blood-pressure.

Dr. Robertson, working at the Maudsley Hospital, found a leucopenia accompanied by the other changes which constitute the hæmoclastic crisis after ingestion of milk by a fasting subject in 94% of patients suffering from dementia præcox, in 85% of melancholias, in 75% of chronic manias, and in over 60% of early psychotic and neurotic cases. If these results are confirmed the hæmoclastic crisis should become an important diagnostic and prognostic factor in early psychotic disorders.

Our study of 300 unselected mental defectives at the Rampton State Institution was begun in the hope of offering some proof as to the existence of mental characteristics which were common to them and to those suffering from ordinary psychoses. The considerable number of cases in which a positive reaction was obtained offers evidence of at least one common factor. The tests were carried out between 9 a.m. and midday, the conditions on all occasions being similar. In a large number of cases the test was repeated several times in order to satisfy ourselves as to the uniformity of the results obtained. Excepting 10 patients who at the first test gave indeterminate results, there was on no occasion any variation in the character of the curve although the intensity of the reaction was not always constant. After repeated tests and after an interval of two months, 6 of the 10 indeterminates reacted by a leucopenia, 3 by a slight leucocytosis, while 1 remained persistently indeterminate. This last case was grouped with the positives.

Of 300 cases examined, 163 gave a relative leucopenia (positive reaction) and 127 gave a leucocytosis (negative reaction). A leucocytosis was accompanied by no change or a slight rise in the sphygmomanometer readings. Of the 163 positive cases, 127 (78% showed a slight fall, 30 (18·4%) no change, and 6 (3·6%) a slight rise of systolic blood-pressure. The maximal fall was 10 mm. of mercury, but the systolic and diastolic pressures at the 40-minute period were commonly only 2 mm. below the initial figure. Films were taken and a differential blood-count was carried out in 68 positive cases, the comparison being made between the initial blood-film and that taken at the point of observed maximal leucopenia. The changes consisted of an absolute and relative decrease in the polynuclear leucocytes, a tendency to an absolute and relative increase of the mononuclears, and a relative increase with an absolute decrease of the lymphocytes. In a few cases the lymphocyte change was great enough to produce an absolute increase. Although eosinophiles and transitional cells were not counted, it should be

noted that a tendency to an increase in the eosinophiles was observed.

The following results are taken at random from the series. In Table I are given the results in 6 positive cases, and in Table II the results in 6 negative cases.

TABLE I.

No.	Initial count.	20 min.	40 min.	60 min.	First B.P.	B.P. at 40 min.	Polymorphs.	Mono-nuclears.	Lympho-cytes.
1	9,400	6,400	6,000	7,400	130/82	128/80	79% : 68%	3% : 5%	18% : 27%
2	8,000	6,800	5,400	11,800	106/64	102/60	68% : 61%	4% : 4%	28% : 35%
3	9,800	4,000	5,600	8,800	128/82	122/80	70% : 62%	7% : 8%	23% : 30%
4	9,200	5,000	7,400	9,000	120/72	118/70	63% : 59%	6% : 7%	31% : 34%
5	6,400	4,400	3,600	7,000	124/78	120/74	70% : 59%	1% : 2%	29% : 39%
6	5,200	4,400	5,000	6,200	122/78	120/74	70% : 65%	5% : 4%	25% : 31%

TABLE II.

No.	Initial count.	20 min.	40 min.	60 min.	B.P. at 1st.	B.P. at 40 min.
1	10,200	12,800	13,000	11,000	130/82	134/84
2	9,400	12,000	13,800	10,000	146/94	150/100
3	7,400	12,600	8,200	11,200	130/80	132/86
4	6,200	8,400	8,800	6,200	120/78	124/80
5	6,800	7,600	9,200	7,000	142/90	142/90
6	8,600	10,800	9,000	8,000	126/78	130/84

A physical examination of each patient was made with the object of discovering some factor which might account for the occurrence of an abnormal reaction to milk. Of 15 patients suffering from morbus cordis without loss of compensation 8 were positive and 7 negative. In one case each of rheumatoid arthritis and congenital syphilis a positive reaction was obtained. One patient suffering from blood syphilis, and who had been given neo-salvarsan two months previously, reacted normally. Of 4 cases of hemiplegia and paresis, 2 were positive and 2 negative; in no case was the affection of recent origin. Nephritis was found to be present in 2 cases, one of whom gave a positive reaction. Chronic gastritis occurring in 6 patients was in each case associated with leucopenia (positive reaction). Four cases suffering from the sequelæ of encephalitis lethargica were examined, 3 being positive and 1 negative. Thirty-one epileptics were included in the series, 17 of whom (55%) showed a typical hæmoclastic crisis, the other 14 (45%) being negative. Thus a positive reaction is not in all cases associated

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with true epilepsy, and the test cannot therefore be used to differentiate essential epilepsy from conditions which simulate it.

It is noted that while Wilson obtained a positive reaction in 18 out of 19 epileptics, only 50% of those examined by Tudoran gave an abnormal reaction, and Feinblatt obtained hæmoclasis in 2 of only 3 cases recorded by him.

The influence of mental age, as determined by mental tests, on the character of the reaction to milk was examined in 158 cases. The results are shown below:

Mental age.	Positive reaction.	Negative reaction.	Total.
7 and under	23	21	44
8	16	16	32
9	20	24	44
10 and over	19	19	38
Totals	78	80	158

There appears to be no special tendency towards an abnormal reaction at any particular mental age.

Another classification of our 300 cases was made on the basis of mental condition. In a previous paper one of us has pointed out the occurrence of mental disorders in defectives as a factor in anti-social conduct, and that psychoses and psychoneuroses commonly occur in high-grade defectives of dangerous and violent propensities. Of the 300 cases in our series, 200 were considered to be of the psychotic type. It is noteworthy that 63% of the psychopathic patients showed a leucopenia following the ingestion of milk. Their further classification is given in the following table:

Type of mental disorder.	Positive.		Negative.		Totals.
	No.	Per cent.	No.	Per cent.	
Dementia præcox	66	74	23	26	89
Manic-depressive psychosis	18	60	12	40	30
Delusional and persecutory types	16	60	11	40	27
Confusional states	17	49	18	51	35
Dementia, secondary	9	56	7	44	16
Anxiety states	1	33	2	66	3
Totals	127		73		200

The results as tabulated suggest that certain factors have an important influence on the production of hæmoclasis. The frequent association of chronic gastritis with liver insufficiency

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will account for the uniformly positive results given in these cases. On the other hand, the mental state of the patient appears to be significant. The psychotic types of defectives tend to give an inversion of the normal formula, so that when mental disorder supervenes on mental deficiency, there is a corresponding increased tendency towards a positive reaction. In this respect there is a measure of agreement with the results obtained by Dr. Robertson, at the Maudsley Hospital, with early psychotics. In both cases the difficulty of definite and differential diagnosis is very great, but on the whole the results indicate that the hæmoclastic crisis test may be a valuable aid to diagnosis providing it is used solely in confirmation of clinical findings.

The classification by mental ages shows that increasing degrees of mental defect are not associated with an increase in the proportion of positive reactions.

It is obvious that a mental disorder arising at an early age, especially when of the dementia præcox type, will tend to produce early dementia with consequent lowering of the intelligence level. Thus, psychotics tend to become demented, and on test will show an intelligence quotient far below that of the pre-psychotic period. If it can be said with Dr. Robertson that the hæmoclastic crisis is closely associated with mental disorder—and, indeed, many of our own results show this—the even proportion of positive reactions at all mental ages demonstrates that the tendency to psychoses is greater at the higher mental levels. If this is true, it would appear to disprove the widespread belief that psychoses are more common at the lower mental age-levels.

In the 4 cases suffering from sequelæ of encephalitis lethargica the period subsequent to the attack was 9 years, 6 years, 5 years and 2 years respectively. The first case (9 years after his attack) was negative and the others positive. No physical condition of the intestinal tract suggesting hepatic dysfunction was discovered in any of them. One of the positive cases still shows a marked Parkinsonian syndrome with cranial nerve involvement, inversion of sleep-rhythm and alteration of the cardio-respiratory ratio. In 10 cases of post-encephalitic complications Xavier found the test negative in 4, slightly positive (or the normal reaction retarded) in 4, and clearly positive in 2 cases. Of these 2, 1 concerned a man who had tabes dorsalis in addition to encephalitis, and who had undergone treatment with neo-salvarsan. It has been frequently noted that injections of neo-salvarsan have been followed by a positive hæmoclastic crisis, probably because arsenical preparations cause hepatic lesions which are demonstrable by means of Widal's test. In this particular case a further test was carried

out after an interval of 3 weeks without treatment, with a negative result (leucocytosis). The other case concerned a pregnant woman, and the pregnancy itself may be assumed to have caused hepatic insufficiency, thus accounting for the positive reaction.

In the cases which yielded weakly positive results the reaction was attributed to the previous intravenous injections of cerebro-spinal fluid. There was no proof that the hæmoclasis was due to the encephalitis. Xavier concluded that no demonstrable relation exists between the liver and the striate body in these cases, and that the parallel involvement of a portion of the brain and the liver, such as occurs in Wilson's lenticular degeneration, cannot be shown. In our own cases, apart from the fact of a previous attack of encephalitis, with consequent moral degeneration and transient and indefinite signs of mental disorder, no reason for the inversion of the normal blood formula can be suggested unless it be due to functional or organic changes in the central nervous or vaso-motor systems.

During our experiments it was noticed that initial counts taken later in the morning were usually higher than those taken an hour and a half earlier, but it was found that the absolute value of the leucocyte count did not in any way affect the character or intensity of the blood reaction. Counts were, however, made to determine the variations occurring in fasting patients over the period during which our tests were normally carried out—from 9 a.m. to 12 midday. In 10 fasting patients, whose reactions had been previously ascertained, and of whom 5 were positive and 5 negative, blood was taken every 20 minutes for 2 hours and the leucocytes counted. It should, perhaps, be added that their normal dining hour was 12 midday.

In each case a slow but steady relative increase of the blood-leucocytes occurred. This leucocytosis occurring in the absence of any digestive reaction has been found by many workers, and probably accounts for some of the adverse opinions on the value of Widal's test. But as in our own cases the variation did not include leucopenia, and did not in any way affect the character of the reaction to milk, we cannot agree that the hæmoclastic crisis is of no value. To our mind it rather tends to show that the changes occurring in a normal fasting subject are always profoundly modified by the ingestion of protein. We also cannot agree with the statements of other workers that there is no variation in the leucocytic curve over 1 hour—the time required to carry out the ordinary Widal test.

The hunger curve, at least during the 2 hours preceding a meal, shows a definite leucocytic rise, but we find that the character of

the reaction to milk is not altered by the position in the curve at the moment of the initial count. It is, however, extremely important that no interval be allowed between the initial count and the administration of the test-meal. We have found a constant leucopenia occur in a patient whose initial counts have shown as great a variation as 75%.

In order to determine whether the leucopenia following ingestion of milk in positive cases was merely a peripheral reaction, parallel counts were made with flowing blood taken from the median basilic vein and from the finger capillaries. Blood from the vein was taken with a wide-bored needle. Initial counts were made at 30- and 60-minute intervals. A leucopenia in the capillary blood was always accompanied by a corresponding change in the leucocytes of the venous blood and the parallel changes were maintained during 1 hour. Examples are given below.

Comparison between Venous and Capillary Counts after Milk in 2 Positive Cases.

No.	Initial count.		30 min.		60 min.	
	Venous.	Capillary.	Venous.	Capillary.	Venous.	Capillary.
1	5,000	4,800	3,600	4,600	8,200	7,600
2	7,000	6,400	6,200	5,400	9,000	9,600

The hypodermic injection of 2 minims of a 1 : 1000 solution of adrenalin chloride prior to the ingestion of milk reversed the reaction in positive cases, a leucopenia being converted into a leucocytosis. It seemed probable that this reaction was the result of changes in the peripheral blood-vessels, due to the action of adrenalin on their muscular structure. Parallel venous and capillary counts were made in 6 people who had previously given a positive reaction. The capillary leucocytosis which occurred after the test-meal was accompanied by a venous leucocytosis, the time of maximal intensity of the reaction being the same in most cases. A few sample results are given below:

No.	Initial count.		20 min.		40 min.		60 min.	
	Venous.	Capillary.	Venous.	Capillary.	Venous.	Capillary.	Venous.	Capillary
1	7,200	7,600	8,000	13,600	8,600	8,400	8,000	8,600
2	5,200	7,400	11,800	12,200	8,800	9,800	6,000	8,200

It is therefore probable that the effect of adrenalin is not purely peripheral. It is, however, true that local heat, cold and pressure do produce alterations in the leucocytic count, probably due to peripheral vascular effects. In negative cases adrenalin does not alter the character of the milk curve. Thus a patient reacting to milk with a leucocytosis will also give an increased white cell-count after adrenalin and milk.

The modifying effect on the blood reaction of thyroid gland extract was next determined in 5 subjects who had previously given a positive hæmoclastic crisis. 30 gr. of dried thyroid extract were given daily for 3 days, after which the tests were carried out. In each case a reversal of reaction occurred, a leucopenia being replaced by a leucocytosis. The effect of atropine and adrenalin on the hunger curve was investigated in 10 patients. Both adrenalin (mij) and atropine sulphate (gr. $\frac{1}{100}$) cause a leucocytosis, the latter being somewhat irregular in character. With both drugs, however, the blood curves at the end of 1 hour appeared to take on the character of the normal hunger curve, this being maintained up to the end of the second hour. In all three the initial count was much lower than the final one.

There is a very extensive literature on the subject of hæmoclasis, and although the results obtained by different authors show great variation, it seems that there is a balance of opinion in favour of the occurrence of a hæmoclastic crisis in hepatic or associated disorders, and also in cases where there is evidence of emotional disturbance and vagotonia or psychic disorder. It is possible that we are dealing with two different functions, one referring to the failure of the liver to prevent the products of digestion, especially of protein digestion, from entering the general circulation, and the other due to the disturbing effect on vaso-motor balance of the act of digestion, and being in the nature of an anaphylactic shock either of central nervous or vasomotor origin. It is quite possible that the chemical products of a cerebral infection or of actual cellular degeneration may be accompanied by the pouring into the blood-stream of obnoxious protein products which sensitize the system and so prepare the ground for anaphylactic phenomena.

Conclusions.[1]

A. *General.*

1. The almost constant numerical and differential blood changes and the uniformity of results in the same patient show that the hæmoclastic crisis is a real blood change and is not accidental.

2. In the present state of our knowledge it may be said that the test can be used in confirmation of the clinical diagnosis, but is not sufficiently constant to justify its adoption as a separate diagnostic test.

3. The leucocytic count during two hours of physiological rest is not constant, but tends to show a gradual rise, which has, however, no influence on the character of the reaction.

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4. It is evident that reference to liver function does not afford an explanation of the blood phenomena in our series. The reaction is a general one and is not confined to the capillaries.

5. The effect of the administration of adrenalin and thyroid was to cause a reversal of the action with milk in cases which previously gave a marked leucopenia. No such reversal occurred with these drugs in cases which had given a leucocytosis after milk. Atropine caused a leucocytosis 10 minutes after injection in 10 patients who previously gave an abnormal reaction to milk. This leucocytosis quickly fell to normal, and the remainder of the curve over 2 hours followed fairly closely the normal hunger curve.

B. *Mental Defectives and Hæmoclasis.*

1. In a series of 300 mental defectives of dangerous and violent propensities a typical hæmoclastic crisis occurred in 163 cases (54%). The degree of mental defect does not appear to influence the result, the number of positive cases being about the same at all mental age-levels. In patients showing mental disorder (200) supervening on mental deficiency the correlation was higher in dementia præcox (74%), manic-depressive psychosis (60%), delusional and persecutory types (60%). Six cases of chronic gastritis in the series were positive. In 4 patients who had suffered from encephalitis lethargica 3 gave a positive hæmoclastic crisis and 1 was negative. Of 31 epileptics, 17, or 55%, gave a positive reaction.

2. In 3 cases of a psychopathic type with a marked anxiety component, only one gave a positive hæmoclastic crisis. This suggests that anxiety states do not necessarily cause a reversal of the blood formula after ingestion of milk.

3. It is probable that psychic disorder is accompanied by a reversal of the normal reaction to milk, and that this is quite independent of the proteopexic function of the liver.

(1) For the literature on this subject the reader is referred to papers by Robertson in numbers of this Journal for July, 1925, and July, 1926.

A Biochemical Study of the Blood and Urine in Mental Disorders.

By B. Reid, M.B., Ch.B., Assistant Medical Officer, Whittingham County Mental Hospital.

This work has been undertaken with the object of disclosing metabolic deviations which might aid in the ætiology or diagnosis of the psychoses, especially in cases of dementia præcox, epilepsy, melancholia and secondary dementia.

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