MILD DEPRESSIVE PSYCHOSIS

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In a recent paper upon the health of the doctor, Hope Gosse (1942) gave a table showing the relative frequency of various conditions which had been the cause of sickness of more than seven days' duration in a large group of doctors. The diagnosis "anxiety state" appeared fifth on this list, being more frequent, for example, than appendicitis, peptic ulcer, or cardiovascular disease. Gosse did not claim that this was especially a doctor's disease, so that similar findings might be expected from many other groups of people. The context of his table suggests that the term "anxiety state" was used to cover a wide range of psychiatric conditions not amounting to insanity. His findings agree with the clinical observations of others that functional nervous disorders of this type account for a very large annual wastage through sickness. Indeed, the incidence may be even higher than that stated, since it is notorious that physical diagnostic labels tend to be used in preference to psychological ones wherever possible.

Among the cases thus loosely designated would undoubtedly be found a number of different types. The Cassel Hospital, which was founded to provide treatment for such functional nervous disorders, can furnish from its records evidence of what these types are and which of them are preponderant. A study of these records shows that the majority of cases are grouped under three diagnostic headings. In 1938, for example, out of 137 total admissions there were 45 cases of depression, 35 of anxiety neurosis, and 22 of hysteria. Under all other diagnostic headings together there were 35 cases. Depression was thus the commonest, and it was also the most painful and, owing to suicidal risk, the most dangerous condition requiring hospital treatment.

Lewis (1938) has defined a depression as follows: "Any person who is unhappy and ill with his unhappiness may properly be said to be in a state of depression." In this phrase he has caught the essence of the condition—the symptoms presented by the patient are dependent upon the disorder of mood, which is fundamental. It may be misleading in one sense, however, in that the patient does not invariably complain of his unhappiness but often only of the symptoms consequent upon it. A depression may be said to be psychotic in character, and hence to belong to the group under discussion, when it occurs in the absence of any discoverable psychological trauma, becomes disproportionate to the trauma, or persists unduly when the trauma has ceased to operate.

The treatment of the common functional nervous disorders, including mild psychotic depression, was admirably laid down by T. A. Ross (1937). He dealt most fully with the anxiety neurosis and the hysterical reaction, and his methods still form the basis of the most successful and widely used therapy. Towards depression, however, he was more cautious in his attitude, holding that treatment could increase the comfort of the patient but could not radically affect the course of the illness. Lewis (1934), at the conclusion of his masterly historical review of the subject, expressed similar views:

"There has been very little written in this review as to therapeutics. Notable as have been the changes in the general care of the insane, there is little to be said about the particular treatment of depressive states. To hinder suicide, to prevent irritation, and to provide for nutrition, sleep, or rest and in due course occupation and interests have long been the objects of judicious treatment, conscious that of the factors potent to heal time is more important than any kind of interference so far attempted."

The position to-day is widely different. The introduction of shock therapy for the treatment of depression has produced a revolution in psychiatric therapy which is still not sufficiently

appreciated. In most cases this treatment is capable of cutting short the attack within the space of three or four weeks. It is of outstanding value in the mild non-certifiable types of depression which are so often encountered in clinical practice and in the case material of the Cassel Hospital. Remission rates for all types of depression quoted by various authors—e.g., Hemphill (1942) and Sands and Sargent (1942)—are very high. It must of course be remembered that these cases usually recover spontaneously in the end, but the time and misery saved by effective treatment are very great.

This being so, the early recognition of the mild depressive reaction becomes of the utmost importance, more especially since it appears to be true that the earlier the treatment is begun the more rapidly the remission occurs. Clinical experience in this hospital has led us to the conclusion that in very many cases recognition comes, if at all, much too late. We have therefore felt it advisable to set forth a description of the mild depressive reaction as it has come to our observation, in the hope that it may assist others to detect it.

Survey of 100 Consecutive Cases

It may at first sight appear to be a curious procedure to present a picture of an illness including only so-called mild examples. Our justification is that we have found that these are precisely the cases which present the greatest difficulty and occur with the greatest frequency in general practice. The personality is well preserved, delusions are absent, and the practitioner who has learned to recognize severe examples of the manic-depressive psychosis may fail altogether to recognize these cases for what they really are. It is as if the physician who has observed a severe streptococcal bronchopneumonia should fail to appreciate that a streptococcal sore throat is also a respiratory infection which may require similar treatment. All of our cases were mild ones in the sense that they were not certifiable or acutely suicidal, and they were able to live in the relatively open environment of the Cassel Hospital. In the sense of degree of incapacity produced by the illness they were not in most cases mild at all.

Our survey covers 100 consecutive cases of mild psychotic depression admitted to this hospital between 1939 and 1942. Our aim has been to present so far as is possible a review of the typical history, symptomatology, and characteristic features of the illness in order to facilitate its recognition by the busy practitioner who has little time for psychiatric niceties.

Diagnosis on Admission

It may be of interest to record the diagnoses with which these patients were sent to hospital. The majority were referred by general practitioners or non-psychiatric consultants, a minority by psychiatrists. A diagnosis of depression was made in 25% of cases; 32% were classed as anxiety neurosis, 14% as neurasthenia or psychasthenia; in 15% no diagnosis was proffered. In the other 13% a heterogeneous series of diagnoses were made, including hysteria 4%, schizophrenia 3%, phobia, obsessional neurosis, etc.

Had we any right to assume that in these cases our diagnosis was the correct one? There can be no hard-and-fast criteria in psychiatry, no infallible signs to guide one to the proper diagnosis. On the other hand we had several advantages over our colleagues who referred the cases to us: we were able to study them for a considerable period in detail, we had them under observation for 24 hours of the day, and we received daily reports from a trained nursing staff. Moreover, when there was doubt about the diagnosis the ultimate grouping depended upon the combined opinion of at least three psychiatrists. We believe that, given the same opportunity for observation, our fellow psychiatrists would have reached the same conclusion as ourselves in nearly every case. The problem of differential diagnosis will be discussed later.

Sex, Age, Occupation

Of our patients 56 were males, 44 were females. There is no evidence from these figures of any sex predisposition, a fact which is confirmed by others (e.g., Rennie, 1942). Age distribution is shown in Table I. There is no special occupational bias: employment covers the whole range of occupation usually met with at the hospital. It is, however, noteworthy that with few exceptions all these patients were usefully employed before

their illness and were often living particularly full and productive lives. This fact would be less often observed in a similar group of anxiety neuroses or hysterical reactions. Ross has emphasized this point.

TABLE I.—100 Cases of Depression. Age on Admission and at First Attack

Age	On Admission			First Attack		
	Males	Females	Total	Males	Females	Total
Under 20 ..	2	1	3	13	5	18
20-29 ..	4	9	13	11	15	26
30-39 ..	12	11	23	14	9	23
40-49 ..	11	12	23	6	11	17
50-59 ..	19	7	26	8	1	11
60 ..	8	4	12	4	1	5
Totals ..	56	44	100	56	44	100

Symptomatology

In Table II are shown the leading complaints of our patients at the time of admission. It will be noted that only 58% actually complained of feeling depressed. Almost all of them subsequently admitted such feelings in response to definite

TABLE II.—100 Cases of Depression. Frequency of Occurrence of Leading Symptoms

	Males	Females	Total
Physical symptoms ..	40	38	78
Depression ..	38	20	58
Fear, anxiety, agitation ..	30	17	47
Feeling of inadequacy ..	26	19	45
Feeling of guilt or unworthiness ..	9	10	19
Perplexity or unreality ..	—	10	10
Suicidal thoughts ..	4	4	8

leading questions, but we are here concerned with the spontaneous observations of the patients themselves. Physical symptoms figured among the leading complaints in 78% of cases. There was a variety of such complaints, ranging from insomnia, fatigue, headache, loss of appetite, constipation, palpitation, to all kinds of strange feelings—i.e., tension in the spine, peculiar feelings in the skin, tightness in the head, etc. Only 10 of these patients presented a single physical symptom; in all other cases complaints were made of a number of physical symptoms.

Next in frequency came a group of complaints of "fear," "anxiety," "agitation," etc. The most common fear was of becoming insane; other fears were of death, of cancer, of meeting people, etc. Nearly half of the patients complained of a feeling of inadequacy, expressed in various ways—e.g., incompetence, the mind not working as it formerly did, inability to carry on with duties properly, etc. Feelings of guilt and unworthiness—of not being good enough for one's family, of having committed terrible mistakes, etc.—occurred in 19%. Feelings of unreality or perplexity were found in 10%: it is interesting to observe that these patients were all women. Suicidal thoughts were mentioned in only 8% of cases, but, as with the complaint of depression, many more had experienced such ideas than mentioned them at the first interview.

Absence of hallucinations, delusions, etc., is to be explained by the nature of the group of cases we are here studying.

Previous Personality

A study of the previous personality of our patients reveals some interesting observations. Though the descriptions were recorded by a number of different observers working largely independently, three groups of cases emerge quite clearly. The first and largest contains 44 patients, all of whom were described in terms stating or implying overconscientiousness and a tendency to perfectionism in all their actions. Of these, 12 were also possessed of great drive, and were as a rule definite leaders in their own sphere; 7 were also described as timid and fearful, and these were on the whole overwhelmed by their own conscientiousness. The second group contains 13 patients whose normal personality was gloomy and pessimistic; in addition they were more or less hypochondriacal. In contrast to these two groups was a third, totalling 11 cases, in which the personality was described as cheerful, "outgoing," and either placid or active. It is worth noting at this point that out of a total of 9 manic attacks in the life histories of the

whole series 7 (each single attacks) occurred in this small group. These were in fact evidently the true manic-depressives, whose physique and temperament have been described by Kretschmer (1936). Unfortunately we have not sufficiently reliable data on the physique of these patients.

The rest of our series was a heterogeneous one including 8 whose previous personality was frankly inadequate, 5 unstable psychopaths, 2 paranoiacs, and 17 in whom no special features were noted.

Precipitating Factors

Precipitating factors, mainly of psychological but to a small extent of physical or mixed origin, were found in 82% of cases. These figures correspond closely with Rennie's observations. Psychological factors were represented by conditions or events which would place a special strain upon the individual. In Table III distinction has been drawn between acute psycho-

TABLE III.—100 Cases of Depression. Precipitating Factors

Chronic stress* alone ..	38
Plus acute stress ..	10
Plus physical disease ..	14
Acute stress alone ..	11
Plus physical disease ..	4
Physical disease alone ..	5
Total with precipitating factors ..	82
„ without known precipitating factors ..	18
Total ..	100

* "Stress" = psychological stress.

logical stress or trauma—in our cases mainly the death of a parent or marriage partner—and chronic psychological stress, which seems to play a more important part, being present in 62 cases. The commonest sources of such stress were business and professional worries and marital difficulties.

Physical disease, either alone or in connexion with acute or chronic psychological stress, appeared in 23 cases. Of these 7 had focal sepsis in teeth, tonsils, or sinuses, 9 had had influenza, and two presented degenerative cardiovascular disease. There were no examples of frank endocrine disorder, though involuntary factors were thought to be present in 5 cases.

The war as a source of chronic stress (i.e., aggravation of business or personal worries, anxiety and loss of sleep due to air raids) played an indirect part in 26 cases. In 2 cases it appeared to be directly responsible through the patients' personal experience of an air-raid disaster.

History of Previous Attacks of Depression

Out of the 100 cases 51 had had one or more previous attacks of depression before their admission to hospital. The figures are necessarily approximate, since one often had to rely upon the descriptions given by patients or their relatives. The age at onset of all first attacks is shown in the second part of Table I. The peak occurs in the 20-29 age group. A surprisingly large number of first attacks happened at or before the age of 20. With one doubtful exception all these occurred after puberty. Of the 61 patients over the age of 40 admitted to hospital 33 had had previous attacks. This figure corresponds closely with clinical experience, and it may be said with confidence that of all patients over 40 seen in an attack of depression at least half may be expected to have had one or more previous attacks.

Family History

Findings concerning family history are shown in Table IV. They are based upon 83 cases, since in 17 no record of the

TABLE IV.—100 Cases of Depression. Analysis of Family Histories

Recorded histories	83	
With abnormality	62	
Without „	21	
Disorder	Total Cases Recorded in 87 Histories	Rate per 100 Family Histories
Depression	13	15.7
Suicide	14	16.9
In mental hospital	18	21.7
Neurotic, unstable, etc.	44	53.0

family history was found. Records concerned first- and second-degree relatives, with the addition of data about first cousins

in two cases. For convenience the number of abnormal individuals per 100 family histories is presented in column 2 of the table. It will be observed that the number of relatives who have had a serious attack of depression, had been in a mental hospital, or had committed suicide is such as to give a combined rate of 54.3 per 100 family histories. This figure may convey some idea of the degree of taint in the family histories of cases of depression and of the frequency with which positive findings may be anticipated.

Differential Diagnosis

We are now in a position to build up the picture of a typical case of mild depression as it may be met with in clinical practice. Among the commonest positive features are the following:

The patient may be of either sex and any age past puberty. In three-quarters of the cases one of the leading complaints will be of physical symptoms, nearly always multitudinous and often rather unusual. In approximately half the cases there will be a complaint of depression, anxiety, or feelings of inadequacy, often of all these things. In half the cases the patient will have been of a conscientious perfectionist nature—very often before his illness a successful individual, though occasionally overwhelmed by his own conscientiousness. Three-quarters of the cases will show definite precipitating factors of a psychological kind. Chronic stress will be found much more frequently than acute disaster. About a quarter of the cases will present physical precipitating factors; among these, sepsis and influenza are worthy of note. Half the patients over 40 years of age will have had a similar attack in the past. The family histories will frequently include one or more relatives who have had an attack of depression, have been in a mental hospital, or have committed suicide.

In addition to these positive findings there are certain others which are very characteristic of the depressive attack but less easy to present in statistical form. There is often a tendency towards a diurnal rhythm: the patient is worse in the morning and better in the afternoon or evening. Insomnia is common; the patient can usually get off to sleep promptly, but awakes very early. Loss of weight, amenorrhoea, and lack of sexual feeling are also frequent. The weight curve is usually a reliable guide to the progress of the attack. Lastly, the depressed patient tends to have a special attitude towards himself and his symptoms. He feels so unworthy that he almost apologizes for taking up the doctor's time. This is in marked contrast to the neurotic patient, who generally revels in his own symptoms and expects the physician to be as interested in them as he is himself.

The above positive findings, taken singly, will not furnish much evidence of the nature of the attack, but where several are found in one case (and their frequency is such that more than one is likely to be found in each case of depression) they provide strong pointers to the correct diagnosis. Since, however, no mere mathematical sum of clinical facts is sufficient in itself to enable one to arrive at a diagnosis it is necessary to add certain observations of a more general character.

Anxiety neurosis was the diagnosis most frequently made before admission. Indeed, complaints of anxiety, agitation, and fear were often so prominent as to mask the underlying state of depression. The genuine anxiety neurosis tends to be of two types—an acute form in which each individual attack of anxiety develops abruptly, lasts for a few minutes or a few hours, and then dies away; and a more chronic form, often termed neurasthenia, in which smouldering symptoms of anxiety are almost constantly present. In both types psychodynamic factors can always be found which have an immediate cause-and-effect relationship to the anxiety symptoms. In the acute type the situation in which the attack occurs, or some association which that situation arouses, is usually pregnant with meaning for the patient and provides the clue to his repressed fears. In the chronic type there may be a more diffuse and complex cause for the symptoms, based upon faulty mental habits, with unhealthy attitudes towards himself, excessive timidity, etc. In both types depression occurs as well as anxiety, but it also is dependent upon situational factors—in contrast to the mood of a true depressive psychosis, which is far less affected by environmental changes.

In the history of a typical anxiety neurosis the symptoms will be found to have a gradual progressive evolution in the life history of the patient. The neuroses have been termed by

Gillespie (1942) "disorders of social relationships," and this phrase illuminates most aptly their essential distinction from psychotic depression, which is an illness occurring as a more definite and circumscribed entity in the life history of an individual who at other times may appear relatively well adjusted.

The differential diagnosis from schizophrenia is usually evident from the bizarre nature of the symptoms in this condition and the previously shut-in nature of the schizophrenic personality. Difficulty chiefly arises at the two opposite poles of adult life—in adolescence and at the involutional period, when depression often assumes an unusual character. Discussion of these problems, however, belongs to the psychiatric textbooks.

It is necessary to bear in mind that depression produces a lowering of the whole psychic efficiency of the individual, so that, for example, obsessional symptoms may make their appearance. When such symptoms occur in attack form it is always wise to consider the possibility of an underlying depression.

Course and Treatment

It is difficult to predict the probable duration of an untreated attack of depression. A few cases clear up very quickly, lasting only a few days or a few weeks. The majority last for several months, a few very much longer. In the present series the longest duration was 7 years, and there were one or two others with a duration of 3 or 4 years.

Without shock therapy remission is generally a gradual process. The weight begins to improve, appetite to return, insomnia to lessen. There are often brief spells of cheerfulness to break the gloom, which seems by contrast all the worse. Indeed, it is sometimes then that suicidal risk is greatest, particularly as the power of decision is returning to the mind. Occasionally there is a sudden abrupt remission in some quite incongruous situation. Occasionally also there may be a swing over to a state of elation and excitement. Minor hypomanic episodes are fairly common, but they are usually transient and easy to handle. More severe examples are rare in this group, as may be inferred from the fact that there was a history of only 9 manic attacks during the previous life of all these patients. The misery which these patients experience during their illness has in the past only served to emphasize the inability of the physician to provide any specific remedy. General measures as emphasized by Ross and by Lewis have played their part as in many other conditions, but recovery, when it has occurred, has often been ascribed by the patient to some quite fortuitous circumstances.

There can be little doubt in the minds of those who have observed any considerable series of results that convulsion therapy provides the means, so long sought, of cutting short the attack of depression. The theoretical basis for the treatment is almost non-existent. It was introduced by von Meduna for the treatment of schizophrenia. Experience suggests that it is in fact not the treatment of choice for schizophrenia, but that it should be reserved mainly for depression. Cardiazol was at first used to induce a convulsion; but it is unpleasant for the patient, and the risk of fractures during treatment is considerable. Electric-shock therapy, credit for the introduction of which to this country must be shared between Fleming, Golla, and Grey Walter (1939) and Shepley and McGregor (1939), is rapidly superseding it. This method is without unpleasantness save for the transient disturbance of memory, and the risks are very slight. At this hospital, for example, about 400 convulsions have been induced during the past 12 months without serious misadventure. The majority of mild depressions, even those of several years' duration, are relieved by 3 to 8 convulsions, administered twice weekly. In many cases the improvement after two treatments is dramatic in the extreme.

In suitable cases treatment can be undertaken in the out-patient department or consulting-room. However, there is one point that must not be overlooked: treatment is not finished when the attack of depression has been overcome. The majority of cases have had some important psychological precipitating factor. It is necessary to attempt to deal with this factor, lest relapse occur speedily. This may require quite extensive psychotherapy or, more commonly, an attempt to

instil into the patient's mind certain principles of mental hygiene which he had previously ignored. The importance of the constitutional factor must not be forgotten; but this should only emphasize the need for the patient to live within the limits of his capacity. There is no evidence that convulsion therapy has any power to prevent the recurrence of depression in the future. Experience over many years has, however, taught us that mental hygiene, sensibly applied, can greatly influence the probability of relapse.

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ABNORMAL AGGLUTINATION REACTIONS OF A STRAIN OF *LEPTOSPIRA ICTEROHAEMORRHAGIAE*

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Proof of the diagnosis of Weil's disease (spirochaetal jaundice) depends in most instances on serological investigation. It is often impossible to differentiate this condition, on clinical grounds alone, from infective hepatitis (catarrhal jaundice), and only on rare occasions are leptospira seen in the blood or isolated by culture or guinea-pig inoculation during the first few days of the disease. Most commonly, Weil's disease is suspected because the patient, by vocation or chance, is brought into contact with rats (e.g., working in sewers, damp mines, fish-markets; immersion in canals or stagnant pools). Confirmation is obtained from the blood count, which in Weil's disease shows a polymorphonuclear leucocytosis; and proof is furnished by the presence in the serum of increasing amounts of antibody to *Leptospira icterohaemorrhagiae*.

The agglutination test is generally used to detect the presence of antibodies, and the specificity of the reaction has been well established, although care is needed in the choice of strain, preparation of antigenic suspension, and interpretation of results (Brown and Broom, 1939). In our case, for routine tests we chose, after a considerable amount of experimental work, a strain of *L. icterohaemorrhagiae* (Jackson) which we isolated in 1934 from a London sewer-worker suffering from Weil's disease. Cultures of this strain, grown in Fletcher's rabbit-serum-broth medium and formalinized to 0.2%, were used for eight years. This strain proved satisfactory throughout that period as judged by the correlation between the agglutination results and the clinical histories, blood pictures, and (in positive cases) the occasional isolation of leptospira from the blood or urine of patients.

Recent Abnormal Reactions

During the autumn of 1942, however, the sera of 34 cases of jaundice admitted to the Cambridge Hospital, Aldershot, were found to agglutinate this strain of *L. icterohaemorrhagiae* although there was nothing in the history of these patients to suggest that they were suffering from Weil's disease. In addition, differential blood counts were either normal or showed a relative mononuclear increase, as occurs in infective hepatitis, instead of the polymorphonuclear leucocytosis characteristic of leptospirosis. Nevertheless, these sera produced a true agglutination of *L. icterohaemorrhagiae* (Jackson). The agglutinated clumps, examined by dark-field illumination with a 1/12-in. objective, proved to consist of leptospira, thus

differing from the false agglutination referred to by Brown and Broom (1939). During the course of the disease in these patients the agglutination titre of the serum rose to a limited extent (titres of 1/300 were not unusual) and then disappeared completely in a few weeks. In true Weil's disease the titre commonly reaches 1/10,000 to 1/30,000, and remains demonstrable, though at a lower level, for years after recovery.

The occurrence of a positive agglutination and the rise in titre during the disease suggested the possibility of atypical Weil's disease. Centrifuged deposits from the urine of patients between the fifteenth and twenty-third days of disease were examined microscopically by dark-field illumination, and were scarified into guinea-pigs by Lieut.-Col. N. T. Whitehead, R.A.M.C. All precautions were of course taken to examine as fresh urine as possible; and alkalis were administered to the patients to render the urine slightly alkaline. Blood taken from patients during the first ten days of the disease was also inoculated into guinea-pigs. In no case were leptospira seen and no guinea-pig became infected.

Protection Tests

The serum from cases of Weil's disease will normally protect guinea-pigs against infection by a virulent strain of leptospira. Pooled serum from six of the Aldershot cases was therefore injected intraperitoneally into guinea-pigs, each animal receiving a single dose of 5 c.cm., 2.5 c.cm., or 1 c.cm. The same doses of known anti-leptospira serum were given to another series of guinea-pigs. All the animals, and also controls which had received no serum, were inoculated with 0.5 c.cm. of a virulent culture of *L. icterohaemorrhagiae* (W.P.R.L. strain). The temperature of each animal was taken and recorded daily.

The results of this experiment were unusually clear-cut for a protection test. The anti-leptospira serum protected all the animals, none of which showed even a rise of temperature. The control guinea-pigs and all those which had received the pooled Aldershot serum showed the accustomed signs of leptospirosis in guinea-pigs—namely, temperatures mounting to 106° F. followed by a sudden fall to subnormal, and terminated by death between the fifth and seventh days. Post mortem the appearances were typical, and leptospira were seen in microscopical preparations from the livers.

Further Tests

Additional serological tests were carried out with other strains of *L. icterohaemorrhagiae*—namely, one human strain (Coppard) and two rat strains (Wild Rat and W.P.R.L.), all of which agglutinate well with anti-leptospira sera. The sera under investigation failed to agglutinate these strains. In addition, the adhesion test described by Brown and Davis (1927) was applied to these sera. The same strain (Jackson) which gave the spurious original agglutination results was used, but as a living, not a formalinized, culture. The adhesion test was consistently negative with these sera. These serological tests were carried out in duplicate, independently, in London and Aldershot, and only insignificant quantitative differences were obtained by the two workers.

It is apparent, therefore, that formalinized suspensions of this particular strain have become unduly sensitive to sera of certain cases of jaundice other than Weil's disease. The effect is not caused by the presence of bile in the serum reducing interfacial tension, because serum from a number of cases, including twelve of arspenamine jaundice, produced no agglutination.

It seemed possible, therefore, that the result might be due to an altered protein ratio of the serum. We had intended to carry out protein-fractionation of all sera, but unfortunately pressure of other work rendered this impossible. However, to test this point with serum the protein ratio of which was known to be altered, blood from 25 patients suffering from various diseases which produce a high red-cell sedimentation rate was kindly supplied to us by Dr. J. M. Alston. Only one serum agglutinated *L. icterohaemorrhagiae* (Jackson); the others were all negative. The positive serum was from a child with a rheumatic condition; but after a few days in hospital he was removed by his parents and lost sight of.

There was no suggestion, therefore, that the protein changes which produce high E.S.R. are responsible for the agglutination.