

Conclusions

After 10 days of fairly intensive study I came to the following conclusions.

That the end-product in both Britain and Denmark—the picture of the welfare state as it is seen by the elderly, and as it is translated for the elderly—is very similar. Denmark has one tremendous advantage in that it provides what Sir Keith Joseph and others so much look forward to in Britain—co-ordination of policy and co-ordination of performance—due to the existence of a Ministry of Social Affairs, with departments of social affairs in the municipalities. I was so impressed by this and, in contrast, so confused by the traditional muddling through in Britain, that when all the pieces have been fitted in and the complete design appears it is surprising to find that old people here are in most respects as well cared for as the elderly in Denmark.

A further advantage to Denmark is that the smaller population can be much more easily organized. But the Danish machinery is so geared that it could cope with any number without impairing efficiency.

In both countries the basic policy is that care should be in the home for as long as possible and that when home care breaks down the alternative provided by the State should be set in an environment which includes all age-groups.

Both countries have, to my mind, set off on the wrong foot in arriving at their objective (or perhaps it would be more truthful to say that both countries had already set off on the wrong foot before they realized their objective) by building "hotels" or "towns" for the elderly which are expensive to run and, no matter how efficient and dedicated the staff, inevitably transfer old people from the security of their own homes to a one-age-group environment; from the seclusion to which they are accustomed to the publicity of "bedrooms" (or wards) which they are expected to share with strangers; to community feeding and a boarding-school atmosphere—all at the age at which they are least able to adapt themselves to change. (I am not the only family doctor, I am sure, who has seen such patients turn their faces to the wall rather than attempt to cope with this type of community existence.)

We have fallen more deeply into this pit than the Danes, for though the "Old People's Town" provides us with the best (or worst) example of this one-age-group existence, yet even here the independent have their own private apartments until such time as they come to need constant care and supervision. Whereas in our "hotels," provided with television, lawns, writing-rooms, and the minimum of rules and regulations, not a trace can be found of the original home atmosphere from which the elderly inmate has been torn.

Moreover, Denmark is ahead of us in the measures taken to retain the elderly in their own homes: subsidizing flat or house rentals; supplementing allowances in privately owned nursing-homes; giving "unofficial" help to relatives, and so on. They have the handicap of too many small houses and an inadequately matured health-visitor service.

I should like to see a proportion of all new houses built in this country set aside for the elderly, who should be made more financially secure by having their pensions adjusted according to the cost-of-living index—as in Denmark.

In both countries there is a need for more trained geriatric nurses and social workers, and there is a vital need for night care—without which care in the home inevitably breaks down sooner or later.

In short, though the end-result to the elderly may be the same in both countries, the Danes have more reason to be proud of their organization than we have, and we have much to learn from them.

I called on the Secretary of the Danish Medical Association (Dr. Fenger), the Ministry of Social Security, the National Health Service (Department of Health), the principal of a social school (Mr. Watt Boolsen), the Director of Social Security for Aarhus (Mr. Orla Jensen), the Chief Medical Officer for Copenhagen (Dr. Inge Jespersen), a distinguished general practitioner whose particular interest is in rehabilitation (Dr. F. E. Backer, to whom I am particularly grateful for his detailed description of the Danish National Health Service), the Medical Director and the Matron of the Old People's Town in Copenhagen (Dr. Lünd and Miss Ib-Hanson), and others. I was generously entertained by Dr. Hübner, the chairman of Messrs. Lundbeck & Co. I took every possible opportunity to speak to "ordinary" men and women whom I met on particular occasions, so that I could get the views of the "man in the street" on the welfare state in which he lived.

Finally, I must record my very sincere gratitude to the British Embassy for the tremendous help given to me in arranging my programme, and for the entertainment given to those whom I visited; to the Secretary of the British Medical Association (Dr. D. P. Stevenson) for so kindly warning Denmark of my impending visit; to the College of General Practitioners for allowing me to represent them during my tour; to the Danish Institute; and to the British Council.

REFERENCES

- Blacker, C. P. (1959). *Mentally Infirm People Over Sixty-five*. London.
Boucher, C. A. (1957). *Rep. publ. Hlth med. Subj.*, No. 98.

SUBACUTE BACTERIAL ENDOCARDITIS

BY

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This investigation began with a review of blood cultures in subacute bacterial endocarditis (S.B.E.) to determine the frequency with which the first cultures were positive. If the early cultures were usually positive it might be possible to recommend beginning antibiotic treatment before the results of culture were known.

In addition to the results of blood culture, we report some of the clinical features and the treatment of all cases of S.B.E. admitted to the United Bristol Hospitals during a period of eight and a half years. Five patients had been thought to have S.B.E., with persistently negative blood cultures, and their cases are considered in detail.

Plan of Study

The results of every blood culture performed between January 1, 1950, and July 31, 1958, were scrutinized and the hospital clinical records were studied of all patients in whom the diagnosis of S.B.E. had been made. Those with positive blood cultures are described in the first part of the paper. The second part deals with patients whose blood cultures were negative. As every blood culture has been recorded we feel that we have

discovered every case of S.B.E. that occurred during the period of the study.

Two patients who did not have blood cultures taken before treatment was started and one who was first treated in another hospital and was admitted here in relapse have been omitted.

Patients with Positive Blood Cultures

There were 60 patients with evidence of arterial embolism and at least one positive culture: 11 of them had two attacks and one had three. Six who were observed in their second attack had had their first before 1950, and records of their earlier blood cultures were not available. Thus our study covered 67 bacteriologically proved attacks of S.B.E.

Blood Culture.—5 ml. of blood was added to each of two bottles, one containing 300 ml. of heart-infusion broth and the other 300 ml. of a modification of Brewer's (1940) thioglycollate broth. Usually, also, 1 ml. of blood was taken into sterile citrate solution to which nutrient agar was added and a plate poured as soon as possible. The risk of contamination was minimized by the clinical pathologists themselves performing the venepuncture and by avoiding frequent subculture during incubation. The cultures were examined daily by an experienced technician who made smears and put up subcultures when visible growth appeared or, if not, after 12 to 14 days' incubation. Penicillinase was incorporated in the medium when necessary.

Results

A positive culture was obtained from the first specimen in 63 of the 67 attacks. The first culture made from two of the remaining four attacks was invalidated by contamination, and from each of these the second blood culture was positive. The other two failures were from patients who had recently received penicillin (see below).

Excluding the two recently treated patients, a total of 166 blood cultures were made from 65 attacks; 164 were positive and two were spoiled by contamination.

The infecting organism in 58 of the 67 attacks was a *Streptococcus viridans*, and in all but two it was sensitive to penicillin (minimum inhibiting concentration between 0.01 and 0.04 unit/ml.). One penicillin-resistant *Str. viridans* (M.I.C., 0.5 unit/ml.) was isolated from the blood of a patient who had been taking 120 mg. of phenoxymethylpenicillin by mouth three times a day for the previous 18 months, to prevent the recurrence of acute rheumatism.

The organisms responsible for the other nine attacks were: *Staphylococcus aureus*, three attacks; *Staph. albus*, three attacks; *Str. pneumoniae*, *Str. faecalis*, and a diphtheroid (*Corynebacterium hofmannii*), once each. The aetiological role of the diphtheroid was very well substantiated, with six positive blood cultures. In this group only the *Str. faecalis* was resistant to penicillin.

There were no mixed infections.

Second and Third Attacks.—Eleven patients were known to have second attacks and one a third. All seemed to be new infections rather than recurrences. Two of the 11 patients who had formerly had streptococcal infections became infected again—one with *Staph. aureus*, the other with a diphtheroid bacillus.

Effect of Fever on Blood Culture.—It is common clinical practice to take blood for culture at the height of the fever. If, however, the bacteraemia is constant, as our findings suggest, the cultures should be positive

at all times. This has been our experience. Though most patients were febrile every day until treatment was started, in 22 instances the temperature charts showed no fever on days when positive blood cultures were obtained. One patient with three positive cultures was afebrile throughout his illness.

Effect of Penicillin on the Blood Culture

Two patients whose first cultures were negative had received penicillin earlier. One had been treated with 1.5 mega units daily for eight days, and the first culture, two days after stopping treatment, was negative. The next, five days later, was positive.

The other patient had signs of mitral- and aortic-valve disease and a chest infection. Her doctor had given her an injection of 600,000 units of procaine penicillin immediately before sending her to hospital. A blood culture taken on admission was sterile. Further treatment consisted of 1 mega unit of penicillin daily for four days, followed by chlortetracycline orally for eight days, and then an injection of 1.5 mega units of benzathine penicillin with the object of preventing a further attack of acute rheumatism. Blood cultures were taken 9, 16, 25, and 31 days after this injection. The first three were sterile, but the last yielded a penicillin-sensitive *Str. viridans*. Despite intensive penicillin therapy the patient died, and S.B.E. was found at necropsy. This experience suggests that when a patient with rheumatic or congenital heart disease develops any febrile illness which may require prolonged treatment blood cultures should first be taken.

During penicillin treatment of S.B.E. caused by a sensitive organism the blood usually remains sterile. Of 66 cultures taken from bacteriologically proved cases after treatment had begun, only one was positive. These cultures were requested because of continuing or recurring fever despite treatment. The fever could usually be attributed to the shedding of emboli rather than to the persistence of bacteraemia. If the infecting organism was initially sensitive to penicillin, attempts to isolate it from the blood during treatment are almost certain to be in vain, even when penicillinase is used. A negative culture under these circumstances gives no assurance that the antibiotic is successfully destroying the organisms in the depths of the vegetations. The laboratory should not be burdened with requests for blood cultures during treatment unless there is reason to believe that the sensitivity of the organism has changed; and this is a rare occurrence.

Sources of the Infecting Organisms

Ten patients gave a history of recent tooth extraction without penicillin cover, in one case before each of two attacks. It is clear, therefore, that despite the fact that danger of extracting teeth without antibiotic cover had been recognized for many years, the risk was not infrequently taken, and contributed appreciably to the incidence of bacterial endocarditis.

One patient with a *Staph. aureus* endocarditis had had a boil on the hand shortly beforehand. The one *Str. faecalis* infection resulted from the dilatation of a urethral stricture.

The Underlying Lesion

Chronic rheumatic heart disease was thought to be the underlying lesion in 40 of the 60 patients. Of these 40, 21 had the signs of mitral-valve disease only, aortic incompetence alone was found in 1, and in 18 there was evidence of damage to both valves.

A further eight patients had aortic-valve disease of uncertain causation. One came to necropsy, and no evidence of rheumatism was found. All but one had aortic systolic murmurs.

There were 12 patients with congenital heart disease, including four with ventricular septal defects, three with pulmonary stenosis, and two with coarctation of the aorta.

Treatment

Treatment consisted of 2 mega units of penicillin daily, injected intramuscularly in four- or six-hourly doses for six weeks.

One infection by a *Str. viridans* resistant to 0.6 units of penicillin per ml., was treated successfully with 16 mega units of penicillin daily, in three-hourly doses, and with erythromycin as well by mouth. Another, with a streptococcus resistant to 0.5 unit/ml., recovered after treatment with 20 mega units of penicillin daily, sometimes with six-hourly injections and sometimes by continuous intravenous drip, together with 1 g. of streptomycin twice a day, and probenecid.

Prognosis in First Year

Treatment was given for 67 attacks. There were five deaths during treatment, of which one was in a second attack.

Of the 62 patients who left hospital 57 (85%) survived for one year or more. This is a higher proportion of one-year survivors than in Dormer's (1958) series of 51 patients, of whom 30 (59%) survived. The two groups were similar in age and sex distribution and in average duration of symptoms before starting treatment. However, all of the present cases were treated after 1950, when the results and recommendations of the M.R.C.'s Penicillin Trial Committee were known (Christie, 1949), whereas Dormer's series began in 1945, and it may be presumed that his earlier cases received treatment that would now be regarded as inadequate.

The unfavourable prognosis of infection of the aortic valve is illustrated in this series. Ten of the 14 patients known to have died in the first year or later had aortic-valve disease either alone (5) or in combination with a mitral lesion (5). Only 2 of the 21 patients with mitral-valve disease alone are known to have died. The two other deaths were in patients with congenital heart disease.

Patients with Negative Blood Cultures

The results of every blood culture taken in the hospital between January 1, 1950, and July 31, 1958, were reviewed in order to ensure that no possible case of S.B.E. was overlooked. Apart from the bacteriologically positive cases already described, the diagnosis had been suspected strongly enough for three or more blood cultures to be taken from 60 other patients. Their case records showed that 56 were given no antibiotics, and, of these, one died in hospital with evidence of S.B.E. revealed at necropsy (Case 1, see below). The other untreated patients left hospital, and most were observed for long enough to exclude the diagnosis of S.B.E. There remained four patients who were given full courses of penicillin, despite negative blood cultures, and they, together with the untreated patient who came to necropsy, were the only likely examples of bacteriologically negative S.B.E. which we could discover, and are described in detail.

Case 1

A man of 40 had had chorea at the age of 7, and was subsequently rejected for military service. When 35 he was referred to hospital with a complaint of giddiness, and was found to have mitral incompetence and aortic stenosis and incompetence. Three years later he again complained of giddiness and other symptoms that were attributed to Ménière's disease, and for this he was treated with 6 g. of streptomycin injected daily for eight days. He returned home to develop in the next nine months increasing lethargy, loss of weight, shivering attacks, and profuse nocturnal sweats. He was readmitted to hospital with heart failure. Gross clubbing of the fingers and splenomegaly developed, and a splinter haemorrhage occurred under one nail. There was a low-grade fever, and a few petechiae appeared on the sole of the right foot. During the course of 13 days eight blood cultures were taken, but all were sterile. He developed pulmonary oedema and died before antibiotics could be given.

At necropsy, Dr. D. H. Johnson found that the mitral-valve cusps were thickened and fibrosed, and the aortic valve was severely stenosed. There were small vegetations on the mitral valve. At the base of the aorta there was a large area of ulceration which appeared to be an infected aneurysm. On microscopy of sections stained by Gram's method, however, no organism could be seen, nor could any be demonstrated by aerobic or anaerobic culture. The wall of the aneurysm was covered with fibrin and granulation tissue, invaded by a few polymorphs. The appearances suggested a healing infection.

Comment.—This case could well be an example of the bacteriologically negative S.B.E. described by Libman (1913). Alternatively, the streptomycin given nine months before death could conceivably have destroyed the organisms. Evans *et al.* (1959) have shown that *Rickettsia burneti* can cause infective carditis with negative blood cultures. This possibility, unknown to us at the time, has not been excluded.

Case 2

A man of 28 presented with haematuria, oedema of the ankles, and hypertension; a diagnosis of acute glomerulonephritis was made. His oedema and haematuria disappeared, but on his discharge from hospital the urine still contained albumin and occasionally red cells, and the E.S.R. was raised.

Four years later he was readmitted, again with haematuria, hypertension, and an apical systolic murmur. There was an irregular fever. The diagnosis of S.B.E. was considered, and was thought to be confirmed when a small number of petechiae appeared on the fingers at intervals of a few days. Seven blood cultures were taken, but all were sterile. Treatment with penicillin, 2 mega units daily, was given for six days and then stopped. In the next 14 days eight more blood cultures were taken; all remained sterile except for two bottles, from one of which a yeast was isolated, and from the other a micrococcus. Penicillin therapy was begun again and continued for six weeks in doses of 1 mega unit every three hours, together with probenecid. There was no very striking response to treatment, but the fever gradually subsided, and no more petechiae were seen. The E.S.R. remained high, and since leaving hospital the patient has continued to show evidence of chronic glomerulonephritis. On reviewing the case, the only finding that cannot be explained on the basis of glomerulonephritis alone was the occurrence of petechiae.

Case 3

A housewife of 30 had had rheumatic heart disease from the age of 6 years. In the five weeks before admission to hospital she had noticed increasing breathlessness, swelling of the ankles, pain in the chest, and haemoptysis. There was considerable enlargement of the heart with signs of a severe mitral-valve lesion, and a low-grade fever. The urine contained albumin and red cells. Petechiae were thought

to be present in small numbers on the trunk. There was early finger-clubbing. Three blood cultures were taken; all remained sterile. In spite of negative cultures a full course of penicillin was given. After treatment she had pains in the knees, hands, and elbows, and a high E.S.R. These features were thought to be due to a recurrence of acute rheumatism. On discharge from hospital the E.S.R. remained high.

Case 4

A man of 40 developed a cough and shortness of breath which kept him away from work for a week. He returned to work but felt ill and tired and began to sweat at night. He was admitted to hospital six weeks after his symptoms began. He was pale, and had many carious teeth. The heart was enlarged and there was a systolic thrill over the aortic area and an aortic diastolic murmur. The pulse was collapsing in type. There were no petechiae, no finger-clubbing, and no fever while in hospital. The blood Wassermann and Kahn reactions were strongly positive. A small haemorrhage appeared in one optic fundus, and this, together with the presence of scanty red cells in the urine deposit, was taken as evidence of emboli. Ten blood cultures were taken, but all were negative. He was treated with penicillin for six weeks and his symptoms improved. He died at home five years later.

Comment.—The findings in this case were probably the result of syphilitic aortitis. There was little to suggest S.B.E., but because of the evidence of emboli it was thought wisest to give a full course of penicillin.

Case 5

A 46-year-old policeman had three attacks of sudden breathlessness accompanied by haemoptysis. He was admitted to hospital for blood cultures to be taken. In addition to the signs of mitral stenosis and aortic stenosis and incompetence, there was obvious finger-clubbing. No embolic phenomena were discovered. For three days he ran a fever between 99.4 and 100.2° F. (37.4 and 37.9° C.). The E.S.R. was persistently raised. A few petechiae appeared on the shoulders and others appeared a few days later. On one occasion the spleen was thought to be palpable. The urine was normal. Five blood cultures were sterile. He was treated with penicillin for six weeks with little change in his general condition. The E.S.R. remained high. At the time of his discharge from hospital it was thought that he probably had not had bacterial endocarditis. He remained ill and breathless, and died of heart failure six months after finishing his penicillin treatment. At necropsy, performed by Dr. E. J. Harries, no signs of bacterial vegetations were found on the stenotic mitral and aortic valves. There were multiple pulmonary infarcts, some recent, some of longer standing.

Comment.—The clinical diagnosis of S.B.E. in Cases 2–5 was made on the basis of a heart murmur with one or more of the following: fever, splenomegaly, petechiae, haematuria, clubbing of the fingers, and a high E.S.R. However, any of these may occur in the absence of bacterial infection, and we observed one patient who showed all these features but did not have S.B.E.

Case 6

This patient, a man of 58, was admitted to hospital with fever and breathlessness. There were signs of chronic rheumatic heart disease with aortic stenosis and incompetence. Gross clubbing of the fingers was present. The spleen was palpable. Retinoscopy revealed a small haemorrhage in the retina, and he developed a sudden pain in the left calf which was diagnosed as being due to embolism of a calf vessel. The dorsalis pedis pulse was absent; E.S.R. 65 mm. Pus cells and Gram-negative bacilli were found in the urine. Six blood cultures were sterile. He was given a sulphonamide for five days for his urinary infection but no other chemotherapy. He was discharged home, but was readmitted four months later with left

ventricular failure and died. Necropsy revealed evidence of rheumatism of the mitral and aortic valves, but no vegetations were found.

Discussion

Before any antibiotics are given, blood cultures should be taken from every patient who might have S.B.E., otherwise the correct treatment may be dangerously delayed. In many cases of S.B.E. a delay of a few days is permissible, but when treatment is required urgently the question arises of how many blood cultures should be taken to ensure the recovery of the organism. Once enough cultures are incubating, treatment may be safely begun. Our experience suggests that, except in those cases whose cultures are always negative, a positive culture can be obtained on nearly every occasion. All the 164 blood cultures taken without contamination from 65 bacteriologically proved untreated cases of S.B.E. were positive. Thus it appears that three cultures, if necessary taken on the same day, should normally be sufficient, even though one be contaminated. The constancy of the bacteraemia suggests that it is not essential to wait for the temperature to rise above normal before taking blood from a patient who is temporarily afebrile. But if antibiotics have already been given there can be no certainty how soon the organism will be isolated.

Several writers have found that the bacteraemia in some cases of S.B.E. is not constantly demonstrable. Cates and Christie (1951) reported that, of 83 cases, positive cultures were obtained in 68 at the first attempt, in 7 at the second, in 7 at the third, and in 1 at the fourth. Newman, Torres, and Guck (1954) found that, of 32 untreated patients, 24 gave constantly positive cultures, while in 8 the positive cultures were intermittent. Belli and Waisbren (1956) found the first culture to be negative in 23 of 74 untreated patients, all of whom gave positive cultures later. On the other hand, Dormer (1958) reported that 44 out of 48 proved cases gave positive cultures at the first attempt. He does not state whether the failures were due to contaminants. Thus the results reported by Dormer are essentially similar to ours, and point to the constancy of bacteraemia in S.B.E.

The problem of the patient with clinical evidence of S.B.E. but with negative blood cultures is peculiarly difficult. Such cases fall mainly into two groups. The first was described by Libman (1913), who reported 22 patients, of whom 16 came to necropsy. Most had had one or two negative blood cultures in life, and post-mortem examination of the vegetations revealed no organisms. Five features were prominent in the clinical picture—anaemia, brown pigmentation of the face, renal disease, splenomegaly, and phenomena due to detached vegetations. Libman suggested that the heart lesion was healing and had gone into a bacteria-free stage. Libman and Friedberg (1948) described further cases with large vegetations containing no organisms, and stated their belief that healing commonly occurs to some extent in untreated S.B.E.

The second group of bacteriologically negative cases are those with no demonstrable bacteraemia but with bacteria in vegetations at necropsy. Keefer (1937) described 15 such cases. There was nothing to distinguish individual cases from those with positive blood cultures, and at necropsy the vegetations in the two types were identical. Keefer suggested that the negative cultures were due to high levels of bactericidal antibodies.

The description of endocarditis in Q fever (Evans *et al.*, 1959) shows the importance of looking for evidence of infection by microbes other than bacteria.

Our difficulty in finding convincing cases of bacteriologically negative S.B.E. in a period of eight and a half years was surprising. In the M.R.C. series (Cates and Christie, 1951) there were 408 cases proved by blood culture and 34 others, from six centres, with negative cultures. The clinical features of those 34 strongly suggested bacterial infection, and vegetations were found on the heart valves of all 15 who came to necropsy. Other published series include the following proportions of cases in which no positive blood culture was obtained: Newman *et al.* (1954), 33%; Wedgwood (1955), 10%; Dormer (1958), 23%. Friedberg (1950) states that blood cultures may be persistently negative in 10–30% of cases. In our series there was one patient (Case 1) who resembled those described by Libman (1913). Here, unfortunately, the picture was confused by the fact that he had earlier had a course of streptomycin. There were four others, with negative blood cultures, who conceivably may have had S.B.E.; in only two of them was the diagnosis considered likely, and in neither was it made with confidence.

Unless the technique of blood culture is satisfactory, a diagnosis of bacteriologically negative S.B.E. must be especially doubtful. The occurrence of cases with intermittently positive blood cultures should suggest a review of technique. Our method with large volumes of medium have been satisfactory, but smaller volumes of liquid broth (Stokes, 1955) should be as good. It is essential to use anaerobic as well as aerobic medium. The use of the two bottles of broth, as well as a plate culture, simplifies the distinction between significant organisms and contaminants. Skill in venepuncture, a careful aseptic technique at the bedside, and daily scrutiny of the cultures during incubation are important.

Any patient who is considered on clinical grounds to have S.B.E. must be given antibiotic treatment, even when a thorough bacteriological investigation fails to confirm the diagnosis. But before the diagnosis is finally accepted all the alternatives should be considered, especially if the response to treatment is inconclusive. Our difficulty in finding convincing examples of bacteriologically negative S.B.E. leads us to suggest that the condition is rarer than has been supposed.

Summary

Sixty-seven attacks of subacute bacterial endocarditis confirmed by positive blood culture are recorded. Brief reference is made to the clinical features, treatment, and progress in the first year after treatment. The bacteraemia was constant. The only sterile cultures were obtained from two patients who had previously had penicillin administered. Two further cultures were spoiled by contaminants. Provided no antibiotic has been given three blood cultures should suffice to isolate the infecting organism, and treatment can be begun before the results of the culture have been reported.

Only five possible examples of S.B.E. with persistently negative blood cultures were found. One died before any penicillin was given. There were no organisms in the vegetations found at necropsy. The four others were treated with a full course of penicillin and recovered: in two the diagnosis was doubtful and in two signs of embolism were unconvincing.

It is thought that S.B.E. with persistently negative blood culture is less common than has been supposed.

We are grateful to the physicians who allowed us to study their patients. Special thanks are due to Professor C. Bruce Perry, Dr. D. H. Davies, and Dr. J. E. Cates for their constructive criticism, and to Mr. L. J. Waller for technical help.

REFERENCES

- Belli, J., and Waisbren, B. A. (1956). *Amer. J. med. Sci.*, **232**, 284.
 Brewer, J. H. (1940). *J. Amer. med. Ass.*, **115**, 598.
 Cates, J. E., and Christie, R. V. (1951). *Quart. J. Med.*, **20**, 93.
 Christie, R. V. (1949). *Brit. med. J.*, **2**, 950.
 Dormer, A. E. (1958). *Ibid.*, **1**, 63.
 Evans, A. D., Powell, D. E. B., and Burrell, C. D. (1959). *Lancet*, **1**, 864.
 Friedberg, C. K. (1950). *Med. Clin. N. Amer.*, **34**, 769.
 Keefer, C. S. (1937). *Ann. intern. Med.*, **11**, 714.
 Libman, E. (1913). *Amer. J. med. Sci.*, **146**, 625.
 — and Friedberg, C. K. (1948). *Subacute Bacterial Endocarditis*, 2nd ed. Oxford Univ. Press, New York.
 Newman, W., Torres, J. M., and Guck, J. K. (1954). *Amer. J. Med.*, **16**, 535.
 Stokes, E. J. (1955). *Clinical Bacteriology*. Arnold, London.
 Wedgwood, J. (1955). *Lancet*, **2**, 1058.

REED-STERNBERG CELLS IN THE PERIPHERAL BLOOD AND BONE-MARROW IN HODGKIN'S DISEASE

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Hodgkin's disease is, as a rule, associated with enlargement of lymph nodes which are either palpable or ascertainable by radiography. Splenomegaly is often found. The reticulum of the bone-marrow can also participate in the pathological process, and the involvement of the sternal marrow is then revealed by a circumscribed tenderness of the sternum and sometimes also by presternal oedema. There may or may not be accompanying constitutional symptoms and signs.

In the so-called abdominal form, in which one or several of the deep-lying abdominal lymph-node groups are the only ones to be enlarged to any extent, the diagnosis may on occasion be entirely unsuspected clinically.

Two cases of this latter type are reported: both presented as pyrexia of unknown origin with a macrocytic anaemia, leucopenia, and thrombocytopenia. In neither of the patients were the superficial and mediastinal lymph nodes enlarged, nor was the spleen palpable. In the first case, thought to be a perforated peptic ulcer, the diagnosis was revealed by the finding of Reed-Sternberg cells in the peripheral blood films; in the second, an obscure macrocytic anaemia, the pathognomonic cells were identified in the marrow aspiration material.

Case 1

A 58-year-old labourer was admitted to hospital on February 21, 1956, with a history of abdominal tenderness and colic of one week's duration. He had apparently collapsed at work six weeks previously. He had lost weight and vomited the day before and on the day of his admission.

He was running a temperature of 103° F. (39.4° C.) (Fig. 1) and looked pale and emaciated; B.P. 90/70. There were