THE FINDING OF BACT. ALKALIGENES ON BLOOD CULTURE

Its significance in 17 unselected cases

By HAROLD E. VICKERS, M.D.

Consultant Pathologist, Walton Hospital, Liverpool 9

Bact. alkaligenes is a normal intestinal inhabitant (Topley and Wilson, 1946) which can infect most sites in the human body, from many of which it is isolated from time to time on routine bacteriology (see reviews by Weinstein and Wasserman, 1951, and Librach, 1954). There are reliable accounts of its association with, and probably causing, typhoid-like ('parenteric') fevers, but its presence in the blood is usually disregarded. For example, Hall and Garvan as recently as 1949, claiming to be the first to record the condition in Australia, emphasized: '*Bact. faecalis alkaligenes* is not infrequently grown from the blood of patients in a prolonged febrile illness, but it is usually discarded as a contaminant.' In the same year Banerjee and Sankar (1949), describing 27 cases of blood stream infection in Calcutta, commented similarly: 'We had no idea it was such a common infection.' Many authors writing since the discovery of the organism in faeces in 1896 appear worried by the fact that it only occasionally causes serious disease and attempt with varying degrees of success to define a specific clinical picture. An understandable emphasis on the serious aspects of the condition loses sight of a more general conception in which mild or insignificant clinical responses are usual and a state of mind which recognizes only serious diseases erroneously dismisses them as examples of 'contamination.' Seventeen cases are now described, ten of them from this country (in which recorded cases are rare), and their significance is discussed.

Material

The organism was isolated in the course of routine blood cultures, without special preparations or techniques, and was recognized as a motile coliform and gram-negative bacillus of varying appearance which failed to produce acid or gas from the usual carbohydrates. The first seven cases occurred in a European military hospital of 350 beds in Karachi, over a period of 18 months

some years ago, and the remainder in an English civilian general hospital of over 1,000 beds during the last six years. All cases encountered during these periods are included and their case histories have been summarized.

Cases

CASE 1. Male serviceman with four weeks' pyrexia (see chart). Admitted on second day of swinging pyrexia of 102 to 103°F., which began two days after T.A.B. inoculation and swung at various levels for the subsequent twenty-seven days. Day 4: Blood culture sterile, spleen enlarged on percussion and liver one finger breadth enlarged. Day 6: No malarial parasites seen in blood. W.B.C., neutrophils 3,600, lymphocytes 3,600, monocytes 300/cu. mm. Day 7: Rose spots suspected on abdomen, not confirmed later. Day 10: *Bact. alkaligenes* isolated from blood. Day 18: *Bact. alkaligenes* isolated again from blood. Day 23: W.B.C., neutrophils 2,500, lymphocytes 2,700, monocytes 700, eosinophils 100/cu. mm. No shigellae or salmonellae organisms were isolated from the stools on days 2, 5 or 9.

CASE 2. Male serviceman with seven-day fever (see chart). Admitted on second day of headache, rigors and muscular weakness. No diarrhoea, but was regarded as 'clinical dysentery.' Day 3: No malarial parasites found in blood (twice). W.B.C., neutrophils 3,700, lymphocytes 1,300, monocytes 350, Turk cells 50/cu. mm. Day 5: *Bact. alkaligenes* isolated from blood. Day 6: No malarial parasites found in blood. Day 17: Patient's serum agglutinated a suspension of *Bact. alkaligenes* to a titre of between 1/200-400. No spleen or liver felt at any time.

CASE 3. Male serviceman with six-day fever (see chart). Admitted as acute bacillary dysentery, which was confirmed by sigmoidoscopy on day 6. Was apyrexial until day 12. Day 14: Severe frontal headache. Day 15: *Bact. alkaligenes* isolated from blood. Day 17: W.B.C., neutrophils

CASE 1

CASE 2

CASE 3

4,100, lymphocytes 1,400, monocytes 150, eosinophils 100, Turk cells 50/cu. mm. Day 26: No detectable agglutination by patient's serum of a

suspension of *Bact. alkaligenes*. No spleen or liver felt at any time.

CASE 4. Male serviceman with dysentery. Admitted on fifth day of diarrhoea, with temperature 102°F., which resolved two days later. Day 6: *Bact. alkaligenes* isolated from blood. Stool culture grew no shigellae or salmonellae. Day 13: Sigmoidoscopy showed 'resolving bacillary dysentery.' No spleen or liver felt at any time.

CASE 5. Wife of serviceman; infective hepatitis. Yellow fever inoculation three days previous to admission. Backache and fever the following day. Temperature 102°F. on admission, rising to 103°F. the same evening and resolving slowly to normal by day 9. Day 9: *Bact. alkaligenes* isolated from blood. No shigellae or salmonellae isolated from stools. Day 10: W.B.C., neutrophils 2,700, lymphocytes 1,900, monocytes 300, eosinophils 100/cu. mm. No spleen or liver palpable. Day 11: 'Now obviously infective hepatitis.' Further course uneventful.

CASE 6

CASE 6. Male serviceman with infective hepatitis (the author) (see chart). Admitted at onset of symptoms with temperature 100.8°F. Day 2: *Bact. alkaligenes* isolated from blood. W.B.C., neutrophils 2,800, lymphocytes 1,900, monocytes 200, eosinophils 100/cu. mm. Day 5: Fouchet's test on urine positive, and infective hepatitis diagnosed provisionally. Day 8: Diffuse maculopapular rash over trunk, spleen not palpable, liver two finger breadths enlarged. Day 9: *Bact. alkaligenes* isolated again from blood. Serum bilirubin 9 mg./100 ml. Day 10: Patient's serum agglutinated suspension of autogenous *Bact. alkaligenes* at a dilution of 1/160. Day 12: No shigellae, salmonellae or *Bact. alkaligenes* isolated from stools. Day 13: Rash now gone. Day 17: Serum bilirubin 11.5 mg./100 ml. Subsequent

course uneventful, except that serum agglutination of autogenous *Bact. alkaligenes* was 1/80 six weeks after onset of illness, when liver was one finger breadth enlarged. No palpable spleen at any time.

CASE 7. Male serviceman. *Bact. alkaligenes* isolated from blood during four weeks' stay in hospital. No details available.

CASE 8. Female aged 24 with acute rheumatism. *Bact. alkaligenes* isolated from blood on sixth day of attack. Total W.B.C. on same day 4,800/cu. mm. No fever at any time.

CASE 9

CASE 9. Male aged 45 (see chart). Known to have had mitral stenosis for three years and was admitted feeling 'off colour,' with a swinging sub-normal temperature of 96 to 98°F., congestive cardiac failure and possible bacterial endocarditis. Blood culture was sterile six days after admission, but grew *Bact. alkaligenes* three days later. Slight pyrexia three days afterwards.

CASE 10. Female aged 44. Old mitral stenosis, with three weeks' history of congestive cardiac failure and possible hypostatic pneumonia. *Bact. alkaligenes* isolated from blood on day following admission. Liver very enlarged. Died shortly afterwards. No post-mortem examination.

CASE 11. Female aged 44. Old mitral valvulotomy for mitral stenosis. Admitted for unaccountable fainting attacks. Temperature constantly 97°F. throughout stay in hospital. Four days after admission blood culture grew *Bact. alkaligenes*. Patient took own discharge three days later.

CASE 12. Female aged 16. Old aortic stenosis and regurgitation with previous admissions and three sterile blood cultures one year previously. Admitted now as being 'off colour.' *Bact. alkaligenes* isolated from blood on second day after admission. No pyrexia noted and long subsequent course uneventful.

CASE 13

CASE 13. Male aged 39. Old mitral stenosis with myocarditis of obscure origin (see chart). Two blood cultures sterile in the week preceding present episode. Now right pleural effusion of recent onset, with temperature 101°F., falling to normal by five days later. *Bact. alkaligenes* was isolated from blood after two days of normal temperature, followed after two further days by rising pyrexia. This lasted four days and was succeeded by a deep venous thrombosis of calf, with normal temperature for two days. A further pyrexia on seven days ensued, this time with sterile blood culture. Subsequent course uneventful.

CASE 14. Female aged 29. Old mitral stenosis and aortic regurgitation admitted in acute left ventricular failure. During an episode of profuse apyrexial sweating and signs of left ventricular failure, two out of three blood cultures spread over four days grew *Bact. alkaligenes*.

CASE 15. Male aged 80. Leukaemia, congestive cardiac failure, purulent conjunctivitis and long-standing bronchitis (see chart). Temperature

CASE 15

102°F. on admission, normal two days later. Day 4: *Bact. alkaligenes* isolated from blood. Day 6: Temperature 'spike' 99.6°F. Total W.B.C. 26,000. Film: 'probably leukaemia.'

CASE 16. Female aged 30. Had *B. coli* pyelitis for six weeks. Five weeks previous to admission *Bact. alkaligenes* had been isolated from sputum. Now admitted with temperature 102.6°F. and total W.B.C. 9,000/cu. mm. Day 5: Temperature 99.6°F. in morning. Blood culture grew *Bact. alkaligenes*. Temperature 97.6°F. the same evening and remained normal. Day 7: Urine purulent, not cultured. Further course uneventful.

CASE 17. Female aged 34. A long previous and subsequent history of pyrexia and symptoms of unknown origin, possibly periarteritis nodosa. Presented at various times with miscarriages, *B. coli* pyelitis, polyposis of bladder, endometritis and localizing spinal symptoms of obscure origin. *Bact. alkaligenes* was isolated from the blood on three separate occasions over a single period of one week, coinciding with an attack of *B. coli* pyelitis and purulent endometritis. Total W.B.C. 5,000/cu. mm. on last occasion.

Discussion

The isolation of *Bact. alkaligenes* from the blood is the only common finding in these cases. They can be conveniently grouped into three.

Group 1. Four cases (1, 2, 3 and 6) in which the bacillaemia probably caused a significant clinical response. In case 1 the bacillaemia can reasonably be accepted as the sole cause of the condition. In case 2 the clinical diagnosis was indefinite, being resolved into 'dysentery sine diarrhoea.' *Bact. alkaligenes* septicaemia is a more convincing alternative diagnosis. Case 3 was an acute but apyrexial bacillary dysentery which was well on towards recovery by the twelfth day when a *Bact. alkaligenes* bacillaemia heralded a five-day fever, otherwise unexplained. Case 6 was known to be suffering from infective hepatitis, but the diffuse rash over the trunk on the eighth day was that of enteric fever. The isolation of *Bact. alkaligenes* from the blood on the second and ninth days, during or just previous to rises in temperature, suggests, with the rash, that the pyrexia was due as much, if not more, to an enteric type of reaction to the *Bact. alkaligenes* in the blood rather than the infective hepatitis. There is a well-recognized association between infective hepatitis and enteric fever, as there is between dysentery and *Bact. alkaligenes* septicaemia.

Group 2. Five cases in which there might be an association, not necessarily causative, between the bacillaemia and the clinical state (8, 9, 11, 12 and 14). Anderson (1933) reported two cases resembling acute rheumatism with *Bact. alkaligenes*

in the blood and the present case 8 is included for that reason. In case 9 a slight pyrexia followed a positive blood culture, but three days later, while in case 11 the positive blood culture was the only positive finding associated with unaccountable fainting attacks; it is the only positive finding in case 12. Case 14, also case 9, showed the bacillaemia occurring in otherwise uncomplicated congestive cardiac failure. This group of cases merges with the next.

Group 3. The remaining cases, in which there was either no reaction at all, or an indefinite association between the bacillaemia and the clinical condition (4, 5, 7, 10, 13, 15, 16 and 17).

The predominance of mitral stenosis with congestive cardiac failure (five cases out of the ten arising in this country), plus one of aortic valvular disease, is notable, but is a reflection of the clinical awareness of bacterial endocarditis as a complication of cardiac valvular disease. It is probably by far the commonest indication for blood culture in this country and if this were done equally frequently on all hospital patients the predominance would materially alter. Cases 1 to 7 were investigated under entirely different circumstances, in which enteric fever was endemic and blood was cultured correspondingly frequently.

Among the reliable accounts of enteric-like conditions associated with blood stream infection by *Bact. alkaligenes*, Ravenal (1921) instances a fatal case indistinguishable from typhoid except by the isolation of *Bact. alkaligenes* at post-mortem. Other accounts also include strong circumstantial evidence that blood stream infection can be associated with significant or serious disease. The present cases of Group 1 are claimed to be examples of this association. Those in Group 2 show a much less definite association and the bacillaemia is definitely secondary to another diagnosis, but they may well illustrate a transitional stage between those of the first group and those in Group 3, in which there is an inconclusive or definitely insignificant relationship.

In no case can *Bact. alkaligenes* be considered a contaminant. If the contamination is cutaneous, *Bact. alkaligenes* is not a cutaneous organism. If it is faecal, *B. coli*, *Ps. pyocyaneus*, *B. proteus* and paracolon type organisms would be met individually as frequently as *Bact. alkaligenes* and collectively far more frequently. If it is air-borne, the organisms encountered would be miscellaneous cocci or *Subtilis* type organisms. No untoward contamination of cultures with these or other organisms occurred during the periods in question; *Bact. alkaligenes* was isolated from the blood sporadically and from isolated cases. If *Bact. alkaligenes* is postulated as a contaminant, it is necessary to describe a hitherto unrecognized

cause of the contamination and one in which this organism plays a special role. It is much more likely that it has a host relationship which is specific among normal intestinal organisms, and which enables it alone to invade the blood stream in sufficient numbers and over a long enough period to be detected moderately frequently by random blood culture. It is reasonable to assume that this invasion is facilitated by insults to the reticulo-endothelial system, such as T.A.B. inoculation (case 1), the virus of infective hepatitis (case 6), which was combined with yellow fever inoculation in case 5, and perhaps the results of cardiac failure (cases 9 to 15). Damage to the bowel wall (cases 3 and 4) due to dysentery is another possibility, but it remains to stress that these postulated causes are far more frequent than the condition they are called on to explain.

Conclusion

The incidence of *Bact. alkaligenes* bacillaemia is much greater than is commonly realized. The organism is not a contaminant of blood cultures.

Occasionally capable of causing serious disease, it is usually a secondary invader and often innocuous, but in a given case one is not justified in assuming that it will necessarily have no adverse clinical effects.

Summary

Seventeen unselected cases are described in which *Bact. alkaligenes* was isolated from the blood. The clinical significance of this series of cases is discussed and conclusions are drawn.

I am grateful to my clinical colleagues in all cases for the clinical details.

BIBLIOGRAPHY

- ANDERSON, W. K. (1933), *Practitioner*, **131**, 102.
 BANERJEE, J. B., and SARKER, J. K. (1949), *Indian med. Gaz.*, **84**, 384.
 HALL, G., and GARVAN, J. (1949), *Med. J. Aust.*, **2**, 681.
 LIBRACH, I. M. (1954), *Postgrad. med. J.*, **30**, 424.
 RAVENAL, M. P. (1921), *J. Amer. med. Ass.*, **76**, 720.
 TOPLEY and WILSON (1946), 'Principles of Bacteriology and Immunity,' third edition, p. 902.
 WEINSTEIN, L., and WASSERMAN, E. (1951), *New Engl. J. Med.*, **244**, 662.

NOTICE OF SPECIAL INTEREST TO SUBSCRIBERS:

'WHY NOT HAVE YOUR COPIES OF THIS JOURNAL BOUND INTO YEARLY VOLUMES?'

You can have your twelve monthly issues fully bound in dark green pin head cloth, lettered in gilt on spine with name of Journal, Volume Number and year, complete with index at front, for 22s. 6d. post free. A limited number of out of print journals are available to bind into volumes and make your library complete. Price on application giving details of issues required to complete back volumes.

THE FELLOWSHIP OF POSTGRADUATE MEDICINE
 60 PORTLAND PLACE, LONDON, W.1

**WHY NOT
 HAVE YOUR
 JOURNALS
 BOUND?**

copyright.

Bibliography continued from page 483—H. Ellis, M.Ch., F.R.C.S.

- GRIFFITHS, D. LI. (1940), *Brit. J. Surg.*, **28**, 239.
 GRIFFITHS, D. LI. (1948), *J. Bone J Surg.*, **30b**, 280.
 HARMAN, J. W. (1947), *Amer. J. Path.*, **23**, 551.
 HORN, J. S., and SEVITT, S. (1951), *J. Bone J Surg.*, **33b**, 348.
 HORWITZ, T. (1940), *Arch. Surg. (Chicago)*, **41**, 945.
 HUGHES, C. W. (1954), *Surg. Gynec. Obstet.*, **99**, 91.
 JONES, S. G., and COTTON, F. J. (1935), *J. Bone J Surg.*, **17**, 659.
 KINMONTH, J. B. (1952), *Brit. med. J.*, **1**, 59.
 LAPEYRE, N. C., and CARABALONA, P. (1952), *Lyon Chir.*, **47**, 419.
 LEARMONTH, J. R. (1943), *Proc. roy. Soc. Med.*, **36**, 515.
 LE GROS CLARK, W. E. (1945), *Lancet*, **1**, 17.
 LINDER, J. M., and HARLEY, J. H. (1953), *Surgery*, **34**, 51.
 MACAUSLAND, W. R., GARTLAND, J. J., and HALLOCK, H. (1953), *J. Bone J Surg.*, **35a**, 604.
 MACFARLANE, J. A. (1942), *Ibid.*, **24**, 739.
 MEYERDING, H. W. (1930), *J. Amer. med. Ass.*, **94**, 394.
 MIDDLETON, D. S. (1930), *Brit. J. Surg.*, **18**, 188.
 MILLER, D. S., MARKIN, L., and GROSSMANN, E. (1952), *Amer. J. Surg.*, **84**, 317.
 MURPHY, J. B. (1914), *J. Amer. med. Ass.*, **63**, 1,249.
 MUSTARD, W. T., and SIMMONS, E. H. (1953), *J. Bone J Surg.*, **35b**, 437.
 PARKES, A. R. (1945), *Brit. J. Surg.*, **32**, 403.
 PHALEN, G. S. (1948), *Ann. Surg.*, **127**, 112.
 RICHE, V., AUSSILLOUX, J., and GINESTIE, J. (1939), *Presse med.*, **47**, 1,173.
 SALEMBIER, Y. (1954), *Lyon Chir.*, **49**, 620.
 SEDDON, H. J. (1956), *J. Bone J Surg.*, **38b**, 152.
 SIMMONS, E. H. (1956), *Arch. Surg. (Chicago)*, **73**, 625.
 SIRBU, A. B., MURPHY, M. J., and WHITE, A. S. (1944), *Calif. west. Med.*, **60**, 53.
 SPENCER, F. C., and GREWE, R. V. (1955), *Ann. Surg.*, **141**, 304.
 STANFORD, S. (1944), *Lancet*, **1**, 462.
 THOMSON, S. A., and MAHONEY, L. J. (1951), *J. Bone J Surg.*, **33b**, 336.
 WATSON-JONES, R. (1952), *Fractures and Joint Injuries*, 4th edition, **1**, 116.
 WILSON, W. C. (1932), *Brit. J. Surg.*, **20**, 393.