COMMENT

It is clearly recognized that intravenous thrombosis may occur at many different sites in the body, and that to afford a degree of protection against its development and extension, and the risk of pulmonary embolism, total body anticoagulation is indicated. However, such anticoagulation may be precluded by circumstances. Regional anticoagulation of blood in a limb where there is a strong presumption of a deep vein thrombosis certainly offers no insurance against the process developing in the opposite limb, in pelvic or other veins. However, if physiotherapy, adequate hydration, and other measures are used to combat the development of thrombosis elsewhere, local anticoagulation in a limb with evidence of deep vein thrombosis may offer the patient some added protection. It is obvious that the method described does not anticoagulate blood in muscle veins, where thrombosis so often begins, but its propagation in intermuscular veins may be prevented. Whether this procedure will find a place in patient care remains to be seen.

B. N. CATCHPOLE, M.D., CH.M., F.R.C.S., F.R.A.C.S.,
Professor of Surgery, University of Western Australia,
Royal Perth Hospital, Perth, Western Australia.

Toxoplasmosis and Myocarditis

Brit. med. J., 1968, **4**, 559–560

The clinical and pathological features of toxoplasmosis have been well described by Siim (1956). The diagnosis of toxoplasmosis should always be considered in a patient with features of glandular fever but a negative Paul–Bunnell test, and the finding of lymphadenopathy together with an abnormal electrocardiogram (E.C.G.) should suggest, among other conditions, the possibility of toxoplasmosis. In the case described below the diagnosis was supported by serological testing and isolation of toxoplasma from an enlarged lymph node.

CASE REPORT

The patient, a woman aged 21, was first seen in June 1966 in the casualty department. For two weeks she had been vaguely unwell and had complained of some pain on the left side of her neck. She was presumed to have cervical adenitis, but failed to respond to a short course of tetracycline. She was later seen in the outpatient department and found to have a tender, enlarged lymph node on the left side of her neck. Her throat was normal and there was no other lymphadenopathy. The spleen was not palpable. Frequent ventricular ectopic beats were noted (see Fig. 1). The blood pressure was 110/60 mm. Hg. A clinical diagnosis of toxoplasmosis with myocarditis was made, and this was confirmed by subsequent investigations.

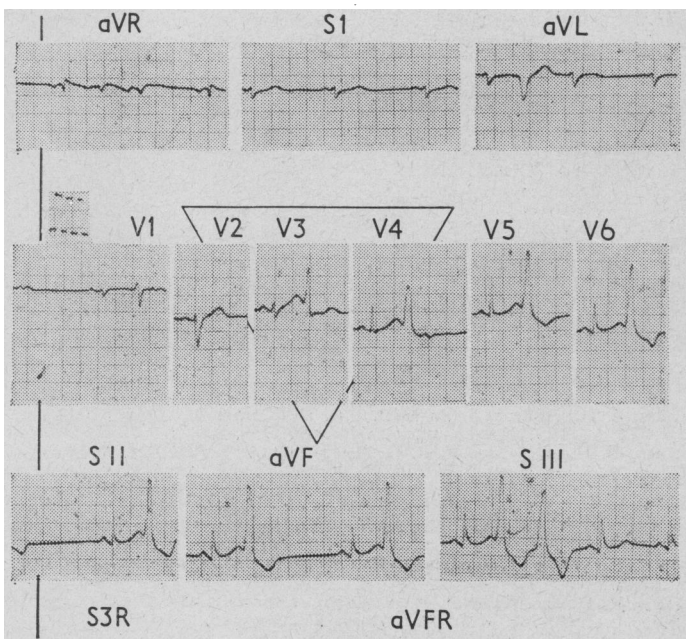

FIG. 1.—E.C.G. showing frequent coupled beats.

Investigations.—Hb 13.6 g./100 ml (93%); W.B.C. 6,000/cu. mm. (neutrophil polymorphs 58%, lymphocytes 32%, monocytes 10%). A very occasional atypical lymphocyte was noted. Westergren E.S.R. 2 mm./hour. Paul–Bunnell test was negative. The patient's serum failed to agglutinate sheep red cells even in the lowest dilution (1:10). Wassermann reaction was negative. Midstream specimen of urine was normal. A chest radiograph was normal. Toxoplasma serology is given in the Table.

Toxoplasma Serology

Date	7/7/66	21/7/66	6/10/66	27/10/66	26/1/67	12/8/67
Dye test titre	1/1,024	1/2,000	1/32	1/512	1/256	1/32

Lymph Node Biopsy (20 July).—Approximately half of the lymph node was received measuring 1.5 by 1.2 by 1.2 cm. The cut surface had a white appearance. On section intense reactive changes were seen with a mild periadenitis. The lymphoid follicles showed germinal centres with phagocytic cells containing nuclear debris. The pulp showed reticular hyperplasia with focal collections of pale histiocytes (Fig. 2) and many plasma cells. The sinuses were filled

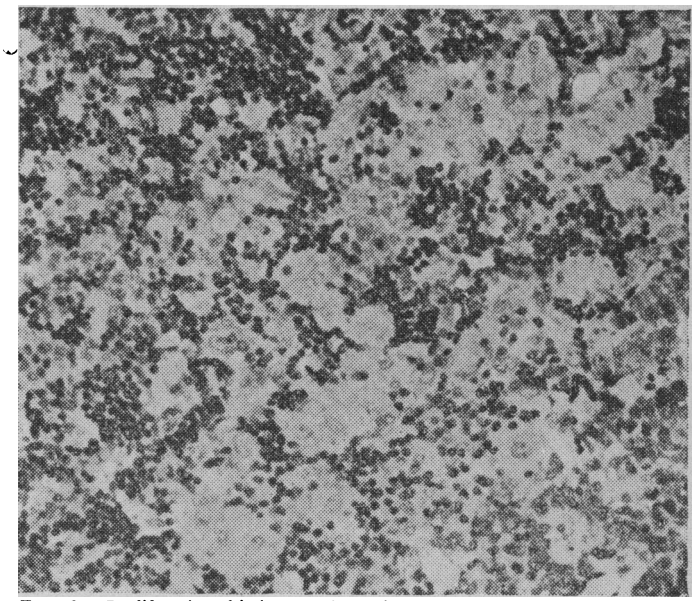

FIG. 2.—Proliferating histiocytes in pulp of lymph node. (H. and E. ×200.)

with proliferating lymphocytes and monocytoid cells. Examination of multiple sections showed no toxoplasma cysts, but the changes are similar to those described by Stansfeld (1961). A diagnosis of toxoplasmic lymphadenitis was made.

Isolation of Toxoplasma.—The other half of the lymph node was emulsified with saline containing penicillin 100 units and streptomycin 10 μg./ml. and inoculated intraperitoneally into five mice (Beverley, 1960). All the mice remained well throughout the observation period. Seven weeks later two of them were killed

and search for toxoplasma cysts in emulsions of the brains was negative. The emulsions were pooled and passed into two further mice, which on later examination were found to be infected with cysts. The other three of the original mice were killed and examined for cysts 10 weeks after inoculation. Two of the three were found to have typical cysts (Fig. 3). No cysts were found in the third one. Some of the mice were killed at seven weeks in an attempt to confirm the diagnosis as early as possible. These were negative on direct examination, but further passage proved that at least one of them was infected. By delaying examination of some of the mice for a further three weeks a parasitological diagnosis was made 10 weeks after the biopsy; that is earlier than would have been the case had all the mice been killed at seven weeks, found to be negative at that time, but proved to be positive by further passage.

Clinical Course.—The patient continued to complain of tiredness and low-grade fever and was admitted to hospital on 29 September. She failed to respond to treatment with pyrimethamine (Daraprim) 25 mg. b.d. and sulphadiazine 1 g. six-hourly. Pyrimethamine in excessive dosage can cause a megaloblastic anaemia (Drew, 1962). In our patient occasional macrocytes were seen in the peripheral blood, and treatment with pyrimethamine was therefore stopped. The appearance of the peripheral film returned to normal on oral folic acid. She was later given propranolol hydrochloride (Inderal) 10 mg. q.d.s. for six days, but this failed to reduce the number of ventricular ectopic beats. She was subsequently treated with prolonged rest and some sedation, and was finally discharged on 8 December. She has continued to remain well, but when last seen, on 19 March 1968, still had frequent coupled beats.

FIG. 3.—Toxoplasma in cystic stage as seen in saline emulsion of mouse brain (×1,250). Note the cyst membrane and the contained toxoplasma closely packed together. The crescentic shape of some of them can be appreciated while others are seen obliquely or in end view.

DISCUSSION

The first case of toxoplasmosis in the human was described by Janku (1923), and Wolf *et al.* (1939) showed that toxoplasmosis could cause congenital encephalomyelitis. Kean and Grocott (1945) first described toxoplasmosis-like cysts in the myocardium, and a number of cases of myocardial toxoplasmosis have now been described. Thus Adams (1962) noted fluctuating S–T changes in a boy aged 15 with a glandular type of toxoplasmosis. The organism was finally isolated from an axillary lymph node. Myocardial toxoplasmosis has also been observed in a young female laboratory worker handling infective material (Bengtsson, 1950). During the course of her illness she complained of weakness, shortness of breath, constricting chest pain, and angor animi. Serial E.C.G.s showed T-wave abnormalities. Myocarditis has also been reported in patients with the acute febrile exanthematous type of toxoplasmosis (Pinkerton and Henderson, 1941; Kass *et al.*, 1952). More recently toxoplasma have been isolated from the heart of a man aged 30 who had severe myocarditis, heart failure, and left bundle-branch block (Potts and Williams, 1956). Myocardial toxoplasmosis should also be considered in all obscure cases of myocarditis and unexplained cardiac hypertrophy (Paulley *et al.*, 1956).

It has been suggested by Mohr and Hoenig (1954) that pseudocysts in heart muscle do not necessarily disturb cardiac function. However, rupture of pseudocysts will result in an intense inflammatory reaction. These workers injected toxoplasma into golden hamsters and found that the animals which developed acute myocarditis also had E.C.G. changes. On the other hand, the presence of isolated pseudocysts in the myocardium with no cellular reaction gave rise to no E.C.G. abnormalities. Unpublished observations also suggest that myocardial lesions can also be produced experimentally in the mouse (Henry and Beverley, 1968).

Our patient failed to respond to specific treatment. The reason for this is that drugs affect the parasites but will have no effect on the damage they have caused. In this connexion it should be noted that the dye test titre of 1:32 on 6 October was much lower than the previous one on 21 July and lower than the titre on 27 October. This apparent anomaly may well be due to the chemotherapy given from 8 September to 16 October. Such treatment, whether combined with steroids or not, will cause a fall of titre (sometimes to below the level of detection) to be followed, on stopping treatment, by a quick rise of titre (Nutt and Beverley, 1963). Though the specific drugs are parasiticidal to the free forms, they also act by preventing multiplication of encysted forms (Beverley, 1958). It is inviting to think that during treatment antigen formation is curtailed, thereby limiting antibody production. On stopping treatment the surviving parasites proliferate and form more antigen, which stimulates antibody production.

The source of infection in our patient remains unknown. Her family had all been well, and there was no history of illness in their dog. The long-term prognosis of glandular toxoplasmosis is usually good. However, in our patient ventricular ectopic beats were still present 21 months after the onset of her illness. Prolonged follow-up will therefore be necessary.

Our thanks are due to Dr. C. E. Davies, who kindly allowed us to publish this case, and to Dr. T. E. Gumpert for translating some of the German literature.

D. P. MULLAN,* M.A., M.B., M.R.C.P.,
Consultant Physician to Salisbury Group of Hospitals.

L. HENRY, M.D., M.R.C.P., M.C.PATH.,
Senior Lecturer in Pathology and Honorary Consultant, United Sheffield Hospitals.

J. K. A. BEVERLEY, M.D., B.SC., M.C.PATH.,
Reader in Medical Microbiology, University of Sheffield.

* Requests for reprints to Dr. D. P. Mullan, Salisbury General Infirmary, Wiltshire.

REFERENCES

Adams, J. L. (1962). *N.Z. med. J.*, **61**, 20.
Bengtsson, E. (1950). *Cardiologia (Basel)*, **17**, 289.
Beverley, J. K. A. (1958). *Trans. ophthal. Soc. (U.K.)*, **78**, 109.
Beverley, J. K. A. (1960). In *Recent Advances in Clinical Pathology*, series III, edited by S. C. Dyke, p. 44. London.
Drew, W. R. M. (1962). In K. MacLean's *Medical Treatment*, 2nd ed., p. 594. London.
Henry, L., and Beverley, J. K. A. (1968). Unpublished observations.
Janku, J. (1923). *Čas. Lék. čes.*, **62**, 1021.
Kass, E. H., Andrus, S. B., Adams, R. D., Turner, F. C., and Feldman, H. A. (1952). *Arch. intern. Med.*, **89**, 759.
Kean, B. H., and Grocott, R. G. (1945). *Amer. J. Path.*, **21**, 467.
Mohr, W., and Hoenig, W. (1954). *Kreisl.-Forsch.*, **43**, 641.
Nutt, A. B., and Beverley, J. K. A. (1963). *Trans. ophthal. Soc. Aust.*, **23**, 35.
Paulley, J. W., Jones, R., Green, W. P. D., and Kane, E. P. (1956). *Brit. Heart J.*, **18**, 55.
Pinkerton, H., and Henderson, R. G. (1941). *J. Amer. med. Ass.*, **116**, 807.
Potts, R. E., and Williams, A. A. (1956). *Lancet*, **1**, 483.
Siim, J. C. (1956). *Ann. N.Y. Acad. Sci.*, **64**, 185.
Stansfeld, A. G. (1961). *J. clin. Path.*, **14**, 565.
Wolf, A., Cowen, D., and Paige, B. (1939). *Science*, **89**, 226.