part of her illness the patient was preparing for her wedding and her symptoms of malaise, fatigue, and dizziness were not unreasonably attributed to anxiety over this event. But immediately before admission her behaviour was very odd and was thought to signify a psychiatric disturbance until she became frankly stuporous. Though headache is generally regarded as the major presenting symptom of cryptococcal meningitis,[4 5] several workers have emphasized the frequency of mental changes and some cases of frank psychosis have been reported.[6 7]

The other point we wish to emphasize relates to laboratory diagnosis. Changes in the normal constituents of the C.S.F. are variable and repeated attempts to show the organism by culture or India ink mount may be fruitless; this is especially true in patients with chronic meningitis.[8 9] The only abnormality on initial C.S.F. examination in this patient was a mild pleocytosis, which had returned to normal by the second examination when brain function was severely disturbed. At both examinations routine search for yeasts using India ink preparations was unrewarding and cultures were likewise negative. The diagnosis was made on the basis of a positive latex test for cryptococcal antigen in serum and it was only on the third examination that cryptococci were seen in the C.S.F.

Hence, serodiagnostic tests should be performed in all patients in whom the possibility of cryptococcal infection is considered. Tests for the detection of anticryptococcal antibodies are not entirely satisfactory[10] and greater specificity has been shown for the polysaccharide antigen in the latex agglutination[11 13] and complement fixation tests.[14 16] Wolf *et al.*[17] have recently shown successful results with an immunofluorescence test that uses the patient's serum antibody and the patient's cryptococcal organisms as the antigen. Nevertheless, the greatest diagnostic yield results from a search for both antigen and antibody simultaneously in serum and C.S.F.[11 12 14 15] Thus, Kaufman and Blumer[13] made a presumptive diagnosis of cryptococcal infection in 92% of 66 patients in whom the diagnosis was ultimately confirmed by culturing the organism.

Most studies show that the presence of cryptococcal antigen in serum or C.S.F. is sufficiently reliable evidence of active infection to warrant treatment.[9 13 15] Diminution of antigen titre and the subsequent appearance of anticryptococcal antibodies during treatment indicate a favourable prognosis; but persistent or raised antigen titres may reflect continuing infection.[16] The only disadvantage is that processing the serological tests takes some time. Nevertheless, these tests are invaluable in cases in which the disease is suspected clinically but organisms are not demonstrable in the C.S.F.

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References

1 Partridge, B. M., and Winner, H. I., *Lancet*, 1965, **1**, 1060.
2 Epidemiology, *British Medical Journal*, 1974, **1**, 252.
3 Diamond, R. D., and Bennett, J. E., *Annals of Internal Medicine*, 1974, **80**, 176.
4 Butler, W. T., *et al.*, *New England Journal of Medicine*, 1964, **270**, 59.
5 Edwards, V. E., Sutherland, J. M., and Tyrer, J. H., *Journal of Neurology, Neurosurgery and Psychiatry*, 1970, **33**, 415.
6 Cox, L. B., and Tolhurst, J. C., *Human Torulosis*, Australia, Melbourne University Press, 1946.
7 Fetter, B. F., Klintworth, G. K., and Hendry, W. S., *Mycoses of the Central Nervous System*, Baltimore, William and Wilkins, 1967.
8 Emmons, C. W., Binford, C. H., and Utz, J. P., *Medical Mycology*, Philadelphia, Lea and Febiger, 1970.
9 Goodman, J. S., Kaufman, L., and Koenig, M. G., *New England Journal of Medicine*, 1971, **285**, 434.
10 Seeliger, H. P. R., *Systemic Mycoses*, London, Churchill, 1968.
11 Bloomfield, J., Gonlon, M. A., and Elmendorf, D. F., *Proceedings of the Society for Experimental Medicine*, 1963, **114**, 64.
12 Gordon, M. A., and Vedder, D. K., *Journal of the American Medical Association*, 1966, **197** 131.
13 Kaufman, L., and Blumer, S., *Applied Microbiology*, 1968, **16**, 1907.
14 Neill, J. M., Sugg, J. Y., and McCauley, D. W., *Proceedings of the Society for Experimental Biology and Medicine*, 1954, 77, 775.
15 Bindschadler, D. D., and Bennett, J. E., *Annals of Internal Medicine*, 1968, **69**, 45.
16 Walter, J. E., and Jones, R. D., *American Review of Respiratory Diseases*, 1968, **97**, 275.
17 Wolf, P., Russell, B., and Jacobs, P., *Journal of the American Medical Association*, 1973, **226**, 1009.

SHORT REPORTS

Bacterial Endocarditis after Insertion of Intrauterine Contraceptive Device

Bacterial endocarditis developed in a young woman soon after the insertion of an intrauterine contraceptive device (I.U.D.). It is suggested that the two events may be related.

Case Report

A 24-year-old schoolteacher of previous good health was admitted to the North Middlesex Hospital with pyrexia of unknown origin. Six weeks previously an I.U.D. (Gravigard; Searle and Co. Ltd.) had been inserted, and at the time the cervix appeared normal. Two weeks later she developed a persistent offensive yellow vaginal discharge. Two weeks before admission she had suffered attacks of shivering and joint pains. She appeared ill and was feverish. Though three splinter haemorrhages were found the heart appeared to be normal. Vaginal examination showed a profuse green discharge arising from the cervix. The adnexa were tender. The I.U.D. was removed and a cervical swab taken which later grew *Streptococcus viridans*, *Staphylococcus albus*, and a diphtheroid. A penicillin-sensitive *Str. viridans* was isolated from blood cultures four days after admission. At that time an early diastolic murmur was heard, endocarditis was diagnosed and treatment with parenteral penicillin was started (10 MU daily).

During six weeks of treatment she developed cardiomegaly and orthopnoea. Cardiac catheterization showed severe aortic incompetence. The left ventricular end-diastolic pressure was 27 mm Hg. Left ventriculography showed greatly impaired contractility, the ejection fraction measuring 49%. An aneurysm of the left sinus of valsalva was seen. Four weeks after penicillin was stopped the aortic valve was replaced under cardiopulmonary bypass at St. Bartholomew's Hospital. The aortic valve was bicuspid, with fusion of the left and right coronary cusps. An aneurysm 2 by 1 cm was found just above the origin of the left coronary cusp. The mitral subvalvar apparatus, inspected through the aortic root, appeared normal. The aortic valve was excised and replaced with a No. 9 Starr-Edwards Silastic ball valve. Bypass was discontinued but the heart required intensive inotropic support, and despite counterpulsation with a balloon pump the patient's condition deteriorated. She died 30 hours after returning from the theatre.

Discussion

Clinically this patient developed an intrauterine infection associated with the insertion of the I.U.D. Since a mixed growth was obtained from the cervical swab, and since *Str. viridans* is a vaginal commensal, there is only suggestive evidence that endocarditis was caused by inserting the device four weeks before the development of symptoms. The swab, however, was taken from the cervix rather than the vagina. The culture of *Str. viridans* from the cervix was discarded before it was realized that the patient had endocarditis; thus a comparison of the organism with the streptococcus isolated by blood culture was not possible.

Though intrauterine infection after the insertion of an I.U.D. is thought to be rare in Britain,[1] investigators in the U.S.A. have reported an incidence of 2·5% in the first year.[2] There has been one previous report of endocarditis after the insertion of a Lippes I.U.D.[3] The timing of surgical intervention in patients with bacterial endo-

carditis is difficult. Ideally, active infection should be eradicated first; the tissues hold sutures better and the hazard of infecting the valve replacement is decreased. Uncontrollable heart failure may require urgent surgery before completion of a full antibiotic course; however, early mortality rates approach 30%.[4]

We wish to draw attention to the possible risk of I.U.D. insertion causing endocarditis, which in our case resulted in the death of a young, previously asymptomatic patient. Endocarditis still has a mortality of some 30%.[5] We therefore suggest that I.U.D. insertion in patients at risk from endocarditis should be covered by antibiotics. Because of the Gram-negative organisms in the vagina a broad-spectrum antibiotic such as ampicillin should be used.

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[1] Newton, J., *et al.*, *British Medical Journal*, 1974, **3**, 447.
[2] Meerer, C. I., *New England Journal of Medicine*, 1969, **280**, 1058.
[3] Cobbs, C. G., *Annals of Internal Medicine*, 1973, **78**, 451.
[4] Wilson, L., *et al.*, *Archives of Surgery*, 1971, **101**, 756.
[5] Hayward, G. W., *British Medical Journal*, 1973, **2**, 706.

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Hyper-transaminasemia with Heparin Therapy

Many side effects seen with heparin therapy have been related to the coagulation system. Biological effects on intercellular enzymes,[1] bone electrolytes, antidiuretic hormone, and aldosterone,[2] however, have been noted. Recently we have noted a rise of serum transaminase levels beginning during heparin treatment. Since transaminase determinations are important in the differential diagnosis of myocardial infarction, liver disease, and pulmonary emboli, rises that might be caused by drugs are very important.

Patients, Methods, and Results

Transaminase levels were recorded before, during, and after heparin therapy in 14 inpatients. All patients received 10 000 units of heparin intravenously every six hours for a period of 10 to 21 days. Blood samples for the enzyme determination were taken from 60 to 90 minutes after the morning injection of intravenous heparin. Serum levels of GOT and GPT were estimated by the SMA 12/60 method, (normal levels with this method are 20 to 40 units for GOT and 20 to 45 units for GPT.) In 10 out of 14 patients the serum transaminase levels rose during heparin treatment (see table). These were definitely abnormal after heparin therapy started with the GPT being higher than the GOT and both falling to normal when treatment ended. The possiblity that heparin interfered with the SMA 12/60 determination of serum transaminases was excluded by performing the determination on paired blood samples from normal controls, to one of which heparin was added after blood was withdrawn. No difference was noted between these two samples.

Discussion

Serum transaminases rose in 10 out of 14 patients receiving intravenous heparin for their underlying disease. This rise was unrelated to dose or to the duration of therapy and in no patients were other diseases discovered that could explain this. It is not clear why this happens. Vavgornik[3] noted the rise in other serum enzymes, such as aldolase, sorbitol dehydrogenase, and leucine aminopeptidase in patients undergoing chronic hemodialysis with heparinization. No change in the GOT and GPT levels before and after dialysis were noted, but the levels during treatment were not tested.

The clinical importance of the rise in serum enzymes during heparin therapy is obvious. Heparin therapy is frequently given for thromboembolic phenomena, and the diagnosis of pulmonary infarction, hepatic damage, and myocardial infarction in these patients is important. The determination of transaminase levels is an established aid in the differential diagnosis of these conditions. The cause of this enzyme rise is not evident, and further studies must be carried out to determine this.

[1] Coon, W. W., and Willis, P. W., *Clinical Pharmacology*, 1966, **7**, 379.
[2] Lamirande, G. D., Weber, G., and Camtero, A., *American Journal of Physiology*, 1956, **184**, 415.
[3] Vavgornik, V. J., *Wiener klinische Wochenschrift*, 1974, **86**, 583.

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Calcium Polystyrene Sulphonate: An Unusual Cause of Inhalation Pneumonia

Calcium and sodium polystyrene sulphonate are two potassium absorbing resins administered orally or by retention enema for treatment of hyperkalaemia. Histologically sodium polystyrene sulphonate has been seen on the surface of sections of gastric mucosa.[1] We report here an unusual case of pneumonia associated with the inhalation of the calcium resin.

Case Report

An elderly man was admitted to hospital with a brief history of severe chest pain and shortness of breath. Clinical and electrocardiographical examination showed left ventricular failure, pericarditis, and an acute myocardial infarction. The next day heart block occurred, and the patient underwent cardiac catheterization for maintenance by a pacemaker. Persistent hypotension was treated with intravenous isoprenaline. Oliguria failed to respond to large doses of frusemide and subsequent hyperkalaemia was treated with oral calcium polystyrene sulphonate (Calcium Resonium). Three days after admission the patient had a cardiac arrest and died.

Diagnosis and Maximum Enzyme Level

Age (Years)	Diagnosis	Maximal GOT Level	Maximal GPT Level	Day of Maximum Rise	Duration of Rise (Days)
29	Deep Thrombophlebitis	65	40	5	10
53	Cerebral Emboli	75	110	9	13
24	Deep Thrombophlebitis	70	155	9	13
32	Deep Thrombophlebitis	95	235	7	15
24	Deep Thrombophlebitis	70	120	9	9
33	Deep Thrombophlebitis and Pulmonary Emboli	90	120	12	21
50	Deep Thrombophlebitis	60	60	3	7
46	Pulmonary Emboli	70	135	7	15
33	Deep Thrombophlebitis	85	170	15	17
69	Pulmonary Emboli	70	100	3	13