patients the haemoglobin was below 50%, the lowest reading being 32%. Macrocytosis was present in all, and the bone marrow showed marked depression of haematopoiesis in three cases.

In Cases 1 and 2 the bone-marrow picture suggested aplastic anaemia, although, as is not unusual, aleukaemic lymphatic leukaemia was difficult to eliminate by marrow aspiration alone. Persistent reticulocytosis and a leuco-erythroblastic anaemia in the absence of myeloid metaplasia indicated that some marrow function remained. A possible explanation for the leuco-erythroblastic anaemia may have been infiltration of the bone marrow by the tuberculous process. Chapman and Whorton's series, however, indicated that a leuco-erythroblastic picture was rare, while miliary spread to the bone marrow was a common finding. In Case 3 the bone marrow was normal, and the absence of splenomegaly contraindicated a hypersplenic mechanism as the cause of the cytopenia. Case 4 was remarkable in that, although clinically showing many haematological features similar to those of the other cases, post-mortem examination showed that it differed in that widespread visceral infiltration with lymphoid cells was present, indicative of a co-existing lymphatic leukaemia. Although lymphatic leukaemoid reactions have been reported (Gardner and Mettler, 1949) to be associated with miliary tuberculosis, the presence together of leukaemia and generalized tuberculosis must be extremely rare. Forkner (1938) has reviewed this subject. Of much interest was the fact that the patient's previous history was one of good health and there was no suggestion of previous tuberculosis. A possible explanation for the dual findings may have been the presence of a latent focus of tuberculosis which was exacerbated by the developing leukaemia, with resulting widespread dissemination.

From the clinical standpoint the cases presented were primarily problems in diagnosis, of which the cardinal feature was the presence of marked haematological changes, together with pyrexia and progressive weight loss. In only one instance was a definite diagnosis reached before death (Case 2), following the appearance and biopsy of an enlarged lymph node in the neck. Case 1 showed no clinical evidence of tuberculosis at any time during the course of the disease, while routine investigations for tuberculosis in Case 3 were negative, although latterly the x-ray findings of the chest were suggestive. A clinical diagnosis of aleukaemic lymphatic leukaemia was made in Case 4, and it was not until necropsy that the enlarged lymph nodes and spleen, in life considered to be due solely to leukaemic infiltration, were found also to be the seat of extensive tuberculous disease.

In view of the present chemotherapeutic agents available for the treatment of tuberculosis it is essential that an early diagnosis be made. As in the above cases, in the presence of pancytopenia with or without depression of the blood-forming elements in the bone marrow, together with pyrexia and loss in weight, and in the absence of any other causative factor, tuberculosis should be considered. The presence of lymphadenopathy demands a biopsy in order to differentiate from Hodgkin's disease, or lymphosarcoma, and aleukaemic lymphatic leukaemia. In addition to routine diagnostic procedures, the bone marrow should be examined for the presence of miliary tubercles either following trephine biopsy or by the technique described by Schleicher (1946). Culture of blood obtained by bone-marrow aspiration, together with guinea-pig inoculation, should also be carried out in an attempt to demonstrate the presence of tuberculous disease.

Summary

Four cases of disseminated tuberculosis are described associated with pancytopenia and macrocytosis. The bone marrow in one was normal, but in three cases a profound depression of the blood-forming elements in the bone marrow, with a preponderance of lymphocytes, was present. In two a leuco-erythroblastic anaemia was

observed, and aleukaemic lymphatic leukaemia together with generalized tuberculous disease was observed at necropsy in one instance.

The difficulties entailed in diagnosis are described and suggestions made regarding the procedure likely to prove helpful in similar cases.

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CARDIAC ARREST UNDER ANAESTHESIA DURING INDUCTION OF LABOUR WITH "PITOCIN" DRIP

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The intravenous use of the oxytocic principle of the pituitary seems now to be established practice in obstetrics, and successful results are causing it to be more widely used. A recent fatality, which appeared to result directly from the administration of a continuous intravenous "pitocin" (oxytocin) drip, is recorded to draw attention to the fact that there are circumstances in which the practice is not free from danger.

Case Report

A 4-para aged 41, who was two weeks past her expected date of delivery, was admitted to hospital because of painless vaginal bleeding. The blood loss was estimated at about half a pint (285 ml.).

There was no abnormality of the heart or lungs, the blood pressure was 130/60, and the urine was free from albumin. The vertex was presenting and the head was high. A provisional diagnosis of placenta praevia was made, and it was thought advisable to examine her under anaesthesia, with full preparation to proceed to caesarean section if this should seem necessary. Blood was cross-matched for the patient. She was given an injection of atropine, 0.65 mg., one hour before the time fixed for operation.

Because the preliminary examination would necessarily delay the delivery of the foetus should caesarean section be undertaken it was thought best to avoid thiopentone altogether and to use only cyclopropane and oxygen in a closed circuit. Induction was smooth and uneventful, and within five minutes it was possible for the obstetrician to begin his examination. At the same time an intravenous drip of 5% glucose-saline was set up.

Examination showed the cervix to be two fingerbreadths dilated, with the membranes bulging through. On further examination to feel the position of the placenta the membranes were ruptured accidentally. The lower edge of the separated placenta was felt about 1 in. (2.5 cm.) above the edge of the cervix, situated anteriorly. This examination provoked brisk bleeding, which was quickly controlled by fundal pressure and pushing the head of the foetus into the pelvic brim. In view of the fact that the bleeding was controlled in this way it was decided that caesarean section was unnecessary, as labour could be induced immediately by the use of a pitocin drip. Since we were aware of possible danger from the combination of "pituirrin" and cyclopropane the administration was delayed while the anaesthetist washed away the cyclopropane with a rapid flow of nitrous oxide and oxygen, the haemorrhage being meanwhile controlled by fundal pressure.

After five minutes the face-mask was removed, the patient showed signs of returning consciousness, and word was given for the addition of 30 units of pitocin to the fluid remaining in the 1,000-ml. saline bottle. Within a minute or two of the start of the flow of the pitocin the patient became cyanosed; the intravenous drip was immediately stopped, and the lungs were inflated with oxygen, but without improvement, and it was evident that the heart had stopped though respiration was still present. An injection of 10 ml. of 1% procaine was immediately given into the left ventricle, followed by 0.5 ml. of adrenaline, while the surgeon opened the abdomen and diaphragm to massage the heart. Strenuous efforts at resuscitation were continued for 75 minutes before being finally abandoned.

One point of interest is that, although the characteristic wormlike contractions of ventricular fibrillation were felt, some spontaneous cardiac contractions did later occur in response to massage; these were, however, weak and ineffective and were not long maintained. An attempt was made to estimate from the fluid level in the saline bottle how much pitocin had actually reached the patient, but uncertainty regarding the exact level of the saline at the time of adding the pitocin made calculation impossible.

Post-mortem examination confirmed the obstetrical findings, and showed in addition some terminal oedema and congestion of the lungs. The only significant finding was atheroma of the coronary arteries excessive for the patient's age.

Comment

Although the condition of "pituirrin shock" has been known for many years it does not seem to be widely accepted in this country that the administration of pituirrin in combination with anaesthesia (particularly cyclopropane) has any special dangers. In America, however, numerous reports of serious effects on the respiratory system—bronchospasm and increased secretion (Burstein, 1941; Greene, 1942)—and on the cardiovascular system—hypotension and arrhythmias (Adelman and Lennon, 1941; Burstein, 1941; Belinkoff, 1944)—have caused the recognition of "cyclopropane-pituirrin incompatibility," and warnings have been given both by an obstetrician (Greenhill, 1952) and by anaesthetists (Hingson and Hellman, 1951), who class it as the fifth most common cause of maternal anaesthetic death. Experimental work on the relationship of the various anaesthetic agents to the action of pituirrin has been carried out on dogs (Parsloe *et al.*, 1950). This incriminated the pressor principle as the cause of cardiac irregularities, and further demonstrated that these occurred in conscious or lightly anaesthetized subjects: deep anaesthesia appeared to protect against coronary constriction and arrhythmias. These workers also found that pitocin had no marked deleterious effects, and could find no definite evidence of that potentiation of pituirrin by cyclopropane suspected on clinical grounds.

From reading the reports of isolated cases purporting to show cyclopropane-pituirrin incompatibility one may sometimes feel that the fatalities or near-fatalities could be explained on other grounds; but the large number of these

reports compels the belief that in the human subject, whatever may be the case in dogs, there is an unfavourable synergism which may lead to cardiac arrhythmia or arrest. Up to the present all these catastrophes appear to have resulted from the use of pituirrin or "pitressin," and writers have sometimes expressed the opinion that had pitocin been used all would have been well. But it must be remembered that the makers of pitocin do not claim absolute purity for their product, and that for every ten oxytocic units there is probably present at least half a unit of vasopressin, and gross cardiac irregularity has been reported in a patient under cyclopropane from as little as 3 units of pitressin given subcutaneously (Greene, 1942). Intravenous administration may be expected to produce a more intense effect.

Death in the case reported above can best be explained as resulting from the administration of vasopressin, albeit in a very dilute form, to a patient with an impaired coronary circulation who was in the stage of heightened vagal reflex activity associated with emergence from cyclopropane anaesthesia. The occurrence of ventricular fibrillation from the cyclopropane alone seems very unlikely. The administration had been brief (10 minutes), and in the first plane, with respiration gently assisted throughout, five minutes had elapsed from its discontinuance, and the patient had recovered sufficiently to make purposive movements of her head and arm: then cardiac arrest occurred about a minute after the start of the pitocin drip.

So far as a single case can indicate anything, this one should draw attention to the following facts: (1) that numerous fatalities have been attributed to the combination of pituirrin and anaesthesia, particularly with cyclopropane; and (2) that pitocin, though highly purified, is not entirely free from vasopressin. It is not too much to recommend that the pitocin drip should be used strictly in accordance with the accepted principles as regards rate of administration; should not be used during or immediately after anaesthesia with cyclopropane; and should be avoided in patients who may have coronary disease, which means in effect those over 40 years of age. Those using this method of treatment are ordinarily careful to avoid the danger of exciting excessive uterine contraction, but should also realize the possibility of other adverse effects on the mother.

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