pleocytosis. Of those in Group E, one was taken post mortem and resembled those in the previous group; one was heavily contaminated with blood, and showed a mixed pleocytosis, normal net protein, glucose, and chloride content; while the third was, from the analysis, consistent with anterior poliomyelitis. Of the eleven cases in Group F, all the fluids were normal except those which proved to have some other intracranial lesion such as tuberculous meningitis, head injury, or lateral sinus thrombosis. The four cases in Group G had normal fluids.

From these analyses the importance of a *full* examination of cerebrospinal fluid in cases suspected of poliomyelitis seems to be established. It will be noted that in the cases clinically "doubtful," but ultimately established as poliomyelitis, the cerebrospinal fluids showed either pleocytosis or significant changes in chemical composition, sometimes both, while on the other hand complete normality of the fluid in all respects enabled poliomyelitis to be excluded in the great majority of cases. The finding of a normal chloride and glucose value will exclude any meningitis which, clinically, might be hard to differentiate in the early stages. We were unable from these analyses to obtain any definite information as regards the changes in the fluid at different stages of the disease; the history of onset in a number of cases was not reliable.

In two patients diphtheria infection was present, but in the first of these there was strong clinical evidence also of anterior poliomyelitis affecting both right limbs, and the comparison of the two spinal fluid analyses is interesting. The first had a pleocytosis of 15 lymphocytes per c.mm., protein 50 mg. per 100 c.cm., a trace of globulin, with a Lange curve 001110000000, glucose 61 mg., and chlorides 760 mg. per 100 c.cm. The second case, which showed no evidence clinically of anterior poliomyelitis, had a pleocytosis of 34 lymphocytes per c.mm., protein 25 mg. per 100 c.cm., no globulin or Lange curve, glucose 76 mg., and chlorides 850 mg. per 100 c.cm. One patient with palatal paresis might well have been considered to be post-diphtheritic, but bacteriological and clinical evidence favoured a diagnosis of poliomyelitis, as did the analysis of the cerebrospinal fluid. Three of the cases which were diagnosed as anterior poliomyelitis had facial paralysis. These are of particular interest in that, in the absence of any epidemic and without the analysis of the cerebrospinal fluid, they would probably have been missed. In all three there were definite changes in the fluid of the order stated under Group A.

In our series there was one known contact, a brother and bedfellow of a fatal case. The clinical signs were indefinite, but the cerebrospinal fluid showed characteristic changes.

Conclusions

Detailed analysis of spinal fluid is a valuable adjunct in the detection and diagnosis of poliomyelitis and polioencephalitis.

The finding of a completely normal fluid practically excludes a diagnosis of this disease.

Slight pleocytosis is a constant feature and a few polymorphs are commonly present in the early stages.

Slight protein increase is usual and develops with progress of the disease.

Globulin, if only a trace, is always found. The Lange gold curve often affords useful corroborative evidence.

Our thanks are due to Drs. Thomas Evans, Tighe, Pugh, and Farr Davies, of the Swansea Borough Health Department, for their collaboration, and to Mr. Leonard Snow for the chemical analyses of the fluids.

ACUTE YELLOW ATROPHY OF THE LIVER

TWO CASES, WITH ONE RECOVERY

BY

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The recent recording of a case of liver atrophy by Millar and Park (1939) has stimulated the presentation of the following two cases having certain points of similarity, which I believe to be of considerable significance.

Case I

A previously healthy primigravida, aged 21, was seen as an emergency on account of lack of progress twenty-four hours after labour started. The os was two fingers dilated; there was no obstetrical abnormality save that contractions were feeble, irregular, and ineffective, though very distressing to the patient. A diagnosis of primary uterine inertia was made and a quarter grain of morphine administered; labour pains ceased and the patient slept for a few hours. The following day contractions recurred at intervals, but no progress was made: the patient took very little nourishment, and vomited after drinking milk.

On the third day, after catheterization and a hot enema, labour proceeded slowly, and by evening the head was on the perineum, but the patient was unable to deliver herself and was getting very tired. Delivery was therefore completed by forceps under light chloroform anaesthesia lasting some twenty minutes, a very small amount of chloroform being used. The total duration of labour was sixty-eight hours, during which the patient had taken very little nourishment and a minimum of fluids. Her general condition was fairly good considering the length of labour, though she was very tired.

The first day of the puerperium was uneventful and the patient appeared much better, but a restless night followed, and when seen on the second day she was drowsy, had marked tachycardia, a normal temperature, and had vomited curdled milk on one occasion. The blood pressure was normal and the urine contained no bile, albumin, or sugar. The drowsiness rapidly increased to the verge of coma; the vomiting persisted, the vomit becoming "coffee ground" and later black from altered blood; and a trace of jaundice appeared, but there was no alteration in liver dullness. The severity of the condition was increasing rapidly and the patient was transferred to hospital, where she was treated with intravenous saline and glucose; but coma deepened, and death ensued within a few hours of admission. In hospital lumbar puncture showed the cerebrospinal fluid to be normal, and the urine contained a little albumin and acetone. No other abnormal constituent was noted, though tyrosine and leucine were not tested for. A necropsy was performed, at which the liver was found to be normal in size, but section revealed widespread necrosis. The whole body was deeply jaundiced, the lungs showed general oedema, and a few subpericardial haemorrhages were found in the heart, but there were no other significant findings. The pelvic organs were healthy. The cause of death was said to be necrosis of the liver.

Case II

A normally healthy woman, aged 32, was submitted to induction of labour at the eighth month on account of increasing pre-eclamptic toxæmia, which treatment had failed to control. It was a second pregnancy; the first, eleven years previously, had been terminated a fortnight before full term for the same reason. The patient had enjoyed good health between the two pregnancies, and all investigations had failed to show evidence of loss of kidney function. Grossly septic tonsils had been removed in the interval as a possible source of danger. On the day of induction there was slight generalized oedema, the systolic blood pressure was 155, and the urine, which was only six ounces in amount during the

twenty-four hours, contained 2 grammes of albumin per litre. Under short ether anaesthesia bougies were introduced into the uterus about midday, and following the anaesthetic there was a moderate amount of vomiting, which persisted at intervals through the night. Labour began the following morning and was completed spontaneously after fourteen hours, the baby being alive and well. Chloroform was administered during the second stage of labour, approximately one ounce being used.

Following delivery the patient slept badly and complained of nausea and retching with a very little vomiting. She was given 50 c.cm. of 20 per cent. dextrose intravenously on the first day of the puerperium; this relieved the symptoms, and she was able to take fluids. The urine increased in amount to 32 ounces during the first twenty-four hours after delivery. Early on the morning of the second day the patient became very restless and began to vomit again, at first small amounts of mucus and blood, changing to "coffee ground" and later black vomit. She complained of great weakness and was inclined to be apathetic; there was slight jaundice, which increased rapidly throughout the day. Liver dullness was diminished, the lower border being two fingerbreadths above the costal margin. Temperature was 97.6°, pulse 120 and of poor volume, and the systolic blood pressure 150; the tongue was moist but furred, and reflexes were very brisk. A diagnosis of acute yellow atrophy was made, and later confirmed by consultants. The intravenous dextrose was repeated, followed by two intravenous injections of a pint of 10 per cent. glucose at intervals of six hours. Insulin, 10 units, was given with the first pint, but not thereafter. Calomel, one-quarter grain hourly, to 2 grains, was followed by half an ounce of magnesium sulphate. Fluids were not well tolerated by mouth at first, though the vomiting practically ceased.

Throughout the succeeding night the patient was gravely ill; she was pale, drowsy, and very weak, and the pulse feeble, irregular, and at times uncountable. The bowels moved well, the stool being pale but not clay-coloured. There was some improvement on the following day (third of puerperium), drowsiness decreasing and the pulse strengthening; but it was only temporary, for by the fourth day the drowsiness increased to stupor, the pulse was poor, and jaundice was very pronounced. Urine, however, was passed freely, and continued so throughout; the amount of albumin decreased steadily, though bile pigments were now present in varying amount. There was no further vomiting, fluids being freely taken when the patient was roused from her stupor. Anahaemin 2 c.cm. was injected and fluids were pushed orally, fruit juices, glucose, milk with marmite, and ice being given in quantity. On the fifth day the patient remained comatose throughout; it was impossible to rouse her, though in spite of this she swallowed automatically whenever her mouth was filled from a feeding-cup. Temperature was 99.6°, the pulse varied from 116 to 146, and the blood pressure was lower. Towards evening respiration tended to be stertorous, the pupils were widely dilated, and there was some twitching of the facial muscles. On the sixth day her condition was practically unchanged, but respiration was more normal, the pulse improved in quality, and towards evening it became difficult to get fluids in by mouth, the patient appearing to resent interference.

On the seventh day liver dullness was found to be restored, the pulse improved further, and the patient roused once and spoke for the first time for three days. Improvement continued all day, and she awoke spontaneously in the evening and asked what had happened. Jaundice was still pronounced; the urine contained bile pigments, but albumin was less than 0.1 gramme per litre. The blood pressure was approaching normal, and oedema had almost disappeared. Thereafter improvement was rapid, though there was some mental confusion for a few hours after the patient regained consciousness. Within a fortnight she was able to sit up in a chair for a few minutes and, though convalescence was protracted, recovery was eventually complete and the patient has since remained in good health. The urine and blood pressure are normal, and she is able to lead her ordinary active life. The only legacy of this grave illness appears to be a very infrequent digestive disturbance lasting a few hours, usually following the taking of rich food.

Comment

The two cases of acute liver atrophy here recorded present certain features in common. Both occurred in puerperal women; in both chloroform had been given, the total amount being small; and in each case the onset of symptoms had been preceded by vomiting with restricted food and fluid intake. In Case I the period of restricted intake was three days, but it was at a time when a great deal of energy was being expended. The extent of the diminished intake and its significance was not appreciated until reflection and inquiry afterwards. In the second case diet had been of necessity restricted for some three weeks because of pre-eclamptic toxæmia, and fluid intake had been minimal for twenty-four hours following induction of labour, because of post-anaesthetic vomiting. In each case a patient who was partially exhausted and who is believed to have been partially dehydrated, though not to a degree recognizable clinically, was given a substance highly toxic to liver cells. The dangerous potentialities of chloroform in this respect have been shown by the work of Whipple and Sperry (1909), Opie (1910), and others.

It is suggested that these facts have an important bearing on the aetiology of acute yellow atrophy: that exhaustion and dehydration are predisposing factors to liver damage of peculiar significance. The case of Millar and Park (1939), previously mentioned, lends support to this view. It is further suggested that a patient who is vomiting and dehydrated, from whatever cause, should be regarded as a potential candidate for liver atrophy, and the administration of any protoplasmic poison, or drug known to affect liver cells, be done with extreme caution, preferably preceded by glucose saline intravenously. These cases also emphasize the importance of maintaining the strength and fluid intake of women during prolonged labour.

With regard to treatment these two cases are also instructive. Case I received no treatment until the condition was well advanced and the patient almost moribund. This was due largely to delay in diagnosis and failure to appreciate the indications of treatment. On the other hand, Case II was treated early and vigorously with glucose and abundant fluids, both orally and intravenously. At one period 50 ounces was given by mouth in five hours. Also, quite fortuitously, intravenous dextrose had been given before the liver condition became apparent. Although it is admitted that in Case I, which ended fatally, the liver damage was probably more severe and progressed extremely rapidly, yet, on the other hand, Case II, which recovered, was suffering from a severe degree of pre-eclamptic toxæmia absent in Case I. It is impossible to know whether Case I would also have recovered if treatment had been adopted as it was in Case II. Rightly or wrongly, recovery in Case II is attributed to the use of glucose and abundant fluids, and it is believed that the early and energetic use of glucose and fluids is of prime importance in the treatment of acute yellow atrophy. A search of the literature has shown that the majority of the few reported cases of recovery have been treated with glucose and their recovery attributed to that. Thus Eden and Holland (1937), Grant and Miller (1936), and Duncan and MacLachlan (1933) have reported cases, and Millar and Park's case (1939) was treated with glucose and fluids intravenously.

Other methods used in the treatment are difficult to assess in value. Insulin was given once in this case, but was discontinued partly because of lack of facilities for

obtaining blood-sugar estimations and partly from doubt as to its value. It has been used more extensively in other cases, notably by Grant and Miller, and Millar and Park.¹ Anahaemin and marmite were adjuvants of theoretical value in the treatment, and at least seem unlikely to be of any harm.

Lastly, the recovery is of interest from the prognostic standpoint. It is the custom to regard acute liver atrophy as an invariably fatal condition, and in Case II death certainly seemed imminent and inevitable to those of us who watched; but the patient survived, illustrating that recovery can occur even in what appears the most hopeless of cases.

I am indebted to the Dean of the Faculty of Medicine, Edinburgh University, for permission to publish these two cases, which have already been embodied in a thesis for the degree of M.D. (1938).

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PUERPERAL AGRANULOCYTOSIS FOLLOWING SULPHANIL- AMIDE TREATMENT

RECORD OF A FATAL CASE

BY

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In view of the widespread use of drugs of the sulphanilamide group it is considered imperative to publish the following case.

Case History

A married woman, aged 24, previous ante-natal record normal, except for an attack of influenza in February of this year, was confined on May 31, 1939, in her own small flat. The birth was normal. The attendant was gloved and masked. A sterile drum of dressings was in use.

On June 2 at midnight, following the finding of a cockroach in the bed, the patient had an attack of hysterics and her temperature rose to 104°. In the morning the temperature was normal and continued so, with only small variations for the next six days. On June 10, however, it rose to 100°. A swab was taken from the vagina, and the morbidity was reported to the medical officer of health. The swab later was stated to be showing haemolytic streptococci Grade A.

On June 11 and 12 she received in all 3 grammes of pron-tosil album, and on the 13th, the temperature being normal, she was given one gramme only. Next day her temperature suddenly shot up to 103.6°, and she was seen by the senior of us in consultation. The patient looked ill, but not markedly anaemic; the tongue was brown and the uterus tender; the pulse rate was 140. She was urged to go to hospital, but for private reasons she refused. It was decided to move her into a room which was more airy and sunlit.

For the first twenty-four hours 6 grammes of sulphanilamide were ordered; for the second day 4 grammes; and for the third day 3 grammes, gradually lessening the dosage according to symptoms. The temperature subsided. She was indeed remarkably well, with no toxic symptoms whatever until June 25, when she had another rise of temperature which may or may not have been "drug fever." She was given on that and the following day 1 gramme of sulphanilamide, thrice daily, and on the 27th, as her general condition was much improved and the temperature normal (she was sitting up in bed manicuring her nails when seen that morning by her doctor), the drug was reduced to 1 gramme twice a day.

Next day, without any previous complaint or warning, she suddenly spoke of having a sore throat and feeling hot and husky. When seen by the senior of us, although the throat condition was not typical, being only red with oedematous tonsils, it seemed certain that hers was a case of threatening agranulocytic angina. The pulse was 140 and the temperature 104.6°. On this occasion she was too ill to object to immediate removal to Queen Charlotte's isolation block.

CONDITION ON ADMISSION

The patient was very pale and ill-looking. She was fully conscious, and was hyperacute mentally; temperature 103.4°; pulse 140; respirations 26. The tongue was dry and rather "beefy" in appearance; mucous membranes were pale; there was no jaundice. Nothing abnormal was found in the abdomen, heart, or lungs. On vaginal examination the uterus was observed to be normal in size and mobility; the cervical canal was just patent, and there was no induration in the parametrium. Lochia were practically absent. The throat showed an acute follicular tonsillitis, the tonsils being much enlarged and engorged, and the pharyngeal wall red and slightly oedematous.

In view of the history and clinical findings a provisional diagnosis of agranulocytosis was made, this being confirmed by examination of a blood film, which showed a marked leucopenia and total absence of polymorphonuclear cells. At this time the haemoglobin was 67 per cent., leucocytes 850 per c.mm (lymphocytes 90 per cent.; monocytes 10 per cent.; no polymorphs seen in 150 white cells).

PROGRESS OF CASE

As soon as the diagnosis was confirmed 20 c.cm. of pentnucleotide was given by intramuscular injection and a continuous-drip blood transfusion by Marriott's method was started: 1,100 c.cm. of citrated blood was given in the next thirteen hours. The condition underwent no great change during the next twenty-four hours, but during the following afternoon a difference was noticed in the character of the voice, and a mild inspiratory stridor became evident. At this time there was a false membrane on the right tonsil, and severe oedema of the right arytenoid cartilage and the false cord on the same side. The vallecular surface of the epiglottis was also slightly oedematous. In view of this new development instruments were prepared for urgent tracheotomy, and inhalations of tinct. benz. co. given hourly. At the end of the transfusion the total leucocyte count had fallen to 680 per c.mm., the differential percentages remaining the same. The general condition had deteriorated slightly, and the pulse was very rapid and weak. The throat was sprayed with cocaine and adrenaline at intervals in an effort to reduce the oedema.

Twenty-eight hours after admission the temperature was 105.6° taken in the axilla, and the pulse 156. The stridor was rather more pronounced, but did not at any time warrant the desperate step of tracheotomy on a patient so ill. She remained wonderfully cheerful, and was making jokes and carrying on an intelligent conversation only ten minutes before she died, thirty-eight hours after admission.

The total amount of pentnucleotide given during the period in hospital was 100 c.cm. Had the true diagnosis not been made, this case would undoubtedly have been certified as an acute streptococcal septicaemia, and it seems probable that