by Lord Dawson[7] as examples of "acholuric jaundice," since he does not consider a normal blood fragility incompatible with this diagnosis, and further states that, while the marrow response in acholuric jaundice is usually normoblastic, it may be megaloblastic, with a high colour index type of anaemia. Though the fragility of the erythrocytes was not investigated in the present case, any such diagnosis appears to be ruled out by the co-existence of a hyperplastic marrow with a low percentage of circulating reticulocytes. In haemolytic anaemia, death may occur in the presence of extensive marrow hyperplasia, if blood destruction runs ahead of even markedly increased blood formation; but, in these circumstances, the circulating reticulocyte percentage is high. Conversely, as emphasized by Lord Dawson,[7] death may result from diminished marrow output, even though blood destruction may not be excessive; but, in these cases, the small number of reticulocytes in the circulation can be shown at necropsy to have resulted from marrow aplasia. Low circulating reticulocyte percentage and hyperplastic marrow cannot coexist (as they did in this case) unless there is defective maturation and emigration of the marrow cells—the characteristic feature of pernicious anaemia. As already noted, the highly characteristic findings were present in this case, not only of active megaloblastic proliferation in the marrow (with little emigration of new red cells into the circulation), but also of considerable leucopoietic activity (with nevertheless a leucopenia in the circulating blood). The conclusion seems justified that, clinically and pathologically, this case satisfied all the criteria of pernicious anaemia.

The question of whether the lack of response to treatment resulted from the use of an inactive liver preparation, or from the case being truly a "liver-resistant" one, cannot be definitely answered. It can only be said that the particular preparation used has, in the hands of other workers, given apparently uniformly successful results.[1 2 4 10 12] It is stated that the reticulocytes usually commence to rise within twelve to twenty-four hours of the first injection,[12] and the maximum reticulocyte response should occur on the sixth or seventh day. It would thus appear that in the case under discussion sufficient time was given for the signs of improvement to have appeared had they been going to do so. It is regrettable, alike on humanitarian and on scientific grounds, that no opportunity occurred of noting whether or not any other preparation might have had a beneficial effect. Had such arisen, it would have been strong evidence in favour of the inactivity of the substance first employed. As it is, it can only be said that the conclusion may or may not be justified that the preparation used was inactive. It may be that variations in activity occur even in different samples of the same product, as was recently emphasized by Wilkinson[13] in the case of stomach preparations, but certainly no case of failure of any sample of this particular product appears to have been reported hitherto.

The possibility exists that this may have been a true "liver-resistant" case. That such cases occur, when oral liver therapy is employed, is admitted by most observers; Naegeli and Gloor[9] give the figure as 10 per cent. of all cases. The general opinion, however, appears now to be that the lack of response is due to inability on the part of such patients to absorb the active principles when the liver is administered by the mouth, and that no undoubted case of pernicious anaemia should fail to respond to parenteral administration of a suitable liver preparation (Davidson,[5] Gänsslen [8]). Prior to the introduction of preparations suitable for injection, Davidson and Gulland[6] had suggested marrow aplasia as a possible cause of failure of liver therapy. While the marrow in the present case was not investigated in many different parts of the body (as, according to Sheard,[11] is, strictly speaking, necessary), the investigation showed that at any rate a large part of the marrow was highly active. Yet the therapy employed should, according to the observers already quoted, have been quite sufficient to initiate a remission. In the absence, however, of definite proof of the activity of the liver preparation employed, it is impossible to decide whether this case was genuinely "liver-resistant" or not.

SUMMARY

1. A case is described which, clinically and pathologically, presented the features of pernicious anaemia.

2. It failed to respond to intravenous injections of a liver preparation which has been found by other workers to be highly effective.

3. It is suggested either (*a*) that not all samples of this preparation are equally potent, or (*b*) that the case is an example of "liver-resistant" pernicious anaemia.

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THE NOMENCLATURE OF ECLAMPSIA*

BY

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The text of our paper is the following case:

Mrs. McG., aged 26, a 3-para, had had two normal confinements. She attended the pre-natal department once, in September, 1931, but failed to return. At that time there was no albumin, but the feet were greatly swollen. She was admitted to the hospital on October 5th with a history of having had two fits. She was given morphine 1/2 grain at 11.30 a.m. On examination she was found to be about thirty-three weeks pregnant; general condition good; restless. Pulse 70, tension fair; blood pressure 122/70; semiconscious. Gastric lavage with good results. Colonic lavage, excellent result. Catheter was passed, but there was no urine in the bladder. At 10.45 p.m. the patient was still semiconscious. At 12.30 p.m. colonic lavage with excellent result. Morphine 1/4 grain given on account of restlessness. Submammary saline given; blood pressure 118/70. Still semiconscious. On October 6th, general condition fair, patient in labour; stillborn foetus, 4 lb. 12 oz., delivered spontaneously at ten hours. There were signs of consciousness returning, and patient seemed better; colonic lavage achieved a good result, but the patient relapsed into a more comatose condition; blood pressure 142/70; blood urea 30 mg. per cent. At 6.15 p.m. she had a fit lasting three minutes; morphine repeated. Patient had further twenty-nine fits before 11.40 p.m., totalling 31 in all. She died at 11.47 p.m.

* Read before the Obstetrical Section of the Royal Academy of Medicine in Ireland, March, 1932.

The post-mortem report was atypical for eclampsia, and exemplifies not only the danger of fits in the multipara, but also the difficulty of determining whether a patient has eclampsia or not.

The post-mortem findings were as follows.

Right Kidney.—Not enlarged ; slight cortical congestion and pallor of medulla ; pyramids slightly injected.

Left Kidney.—Multiple small cortical haemorrhages ; not enlarged. Capsule strips easily. Microscopical sections show marked cloudy swelling of the epithelium of the tubules, and in many places this has gone on to fatty degeneration. There are scattered interstitial haemorrhages ; the medullary region shows slight increase in the interstitial tissue, which suggests an old-standing interstitial nephritis.

Liver.—Not enlarged ; normal. No haemorrhages. Microscopical sections show cloudy swelling of the liver cells. There is a good deal of congestion all over.

Post-Mortem Lesions in the Typical Eclamptic

Kidneys.—" The kidneys are acutely inflamed, and closely resemble the kidney in the nephritis of scarlatina. They are large, soft, and congested. The capsule strips easily, and the glomeruli and tubules are thickly packed with blood and epithelial casts. The epithelium of the tubules is in a state of cloudy swelling " (Solomons, in Tweedy's *Practical Obstetrics*). " Symmetrical total necrosis of the cortex. Immense firm cloudy yellowish areas of necrosis are infarctions involving more or less completely the whole cortex, with thrombosis of intrarenal, arterial, venous, and capillary branches in which Hertzog found hyaline fibrin thrombi " (Kaufman, vol. ii, 1310). " A glomerulo-thrombosis—that is, degenerative changes in the vessels and epithelium of the glomeruli associated with similar changes of varying intensity in the epithelium of the convoluted tubules. There are no signs of inflammatory or atrophic change unless the process has been engrafted upon a pre-existing disease. In other words, the renal lesions are the result, not the cause, of the process " (Fahr).

Liver.—According to Adami: " In typical cases abundant necrosis in this organ: these recall the focal necrosis seen in many infectious and toxic conditions, but they may be so extensive as to give the appearance of that wide destruction of the hepatic parenchyma seen in acute yellow atrophy." Schmorl, quoted by Williams, says: " Irregular-shaped reddish or whitish areas scattered through the entire organ and originating near the smaller portal vessels. Microscopically, they are areas of necrosis involving the periphery of the individual lobules and portal spaces in which blood cells may or may not be present. The formation of necrotic areas is due to degenerative changes following thrombotic processes in the smaller portal vessels, and these are areas justifying the diagnosis of eclampsia."

Definition of Eclampsia

It will thus be seen that the post-mortem results in the case under review and in the typical eclamptic differ so greatly that this case cannot be classed as one of eclampsia, and it seems to us that Fahr makes a point when he stresses the fact that the renal lesions are the result, not the cause, of the toxaemic process. Whether the kidney lesion precedes the toxaemic symptoms should in most instances be demonstrated by pre-natal care, but the irregular attendance by the Rotunda patients makes it difficult to carry this out.

We could quote many other cases to exemplify our point, but for the present we shall look for a definition. We define eclampsia as the occurrence of fits in a pregnant or puerperal woman which would not have occurred if she had not been pregnant. Williams does not go so far, and defines eclampsia as an acute toxaemia occurring in the pregnant, parturient, or puerperal woman, which is usually accompanied by chronic and tonic convulsions. He states that " while the convulsions are by far the most striking clinical manifestations of eclampsia, and even give the disease its name, instances are occasionally met with in which they are absent."

We cannot find a definition of eclampsia in the monograph by Stroganoff. We consider the necessity for a definition of the highest importance from a statistical point of view, and we cannot stand alone if statistics are to be of the least value. We must include in our statistics of eclampsia (until it is proven otherwise) these pregnant or puerperal women who die having had fits, unless the post-mortem results reveal absolutely atypical lesions. If the patient does not die she too must, for the present, be included, and if she dies and a necropsy is impossible, then she also is grouped as " eclampsia." Every year since the beginning of the present Mastership there have been cases of doubtful nomenclature, and these have been included in the various tables. This year however, as will be seen in the report, there is a separate table for toxaemias of unknown nomenclature.

Previous Cases

The following are some problematical cases.

Case I

1926–27 Report. 1-para, admitted as eclampsia. At 10.30 a.m. baby was delivered with forceps ; at 12.30 p.m. after the uterus had been emptied of clots, rapid collapse set in, and the patient became pulseless and unconscious. A definite convulsion was reported to have occurred, and she soon died. It seems possible that this was a " death fit " and not an eclamptic one, but this case is included in the eclamptic statistics.

Case II

1927–28 Report. A primigravida, aged 42, was admitted at thirty-five weeks with a history of having had fits during the last four days before admission. She had been semi-conscious from the time of the last fit. Slightly cyanosed ; able to project her tongue, but made no effort to speak. No ocular or other paralysis ; broncho-pneumonia in both lungs. Blood pressure 118 ; heart sounds normal ; reflexes exaggerated ; skin hypersensitive. Consulting physician confirmed diagnosis of pneumonia, and suggested that subconscious state was epileptic ; she remained aphasic. Examination of the cerebro-spinal fluid showed marked increase of lymphocytes and of globulin ; no tubercle bacilli found. Seen by a neurologist, who stated that the patient was possibly suffering from encephalitis, but the diagnosis was arguable. She died five days after admission. All toxaemic tests were negative. Blood urea 25 mg. per cent. ; albumin never above a trace.

The post-mortem findings were: *Liver :* Pale, enlarged, fatty ; small white patches resembling tubercles ; no haemorrhage or necrosis. Microscopically, some congestion of intralobular veins. The small patches resembling tubercles are small areas of a focal fatty change. No evidence of necrosis or haemorrhage. *Kidneys :* Somewhat enlarged, pale ; slight irregular fibrosis. Microscopically, congestion and parenchymatous nephritis ; some area of an early fibrosis and cysts ; some fatty changes. Haemorrhage at the inferior surface of the temporal lobe. No tubercles.

Case III

1928–29 Report. A 9-para—an atypical eclamptic, who was classed as such. The kidneys showed evidence of chronic interstitial nephritis. The liver was enlarged, friable, and greasy. Sections showed marked congestion, especially round the central vein. Liver cells cloudy and swollen, with a good deal of fatty degeneration.

There were two cases of mania in this report. Both had fits, but the history and the post-mortem reports were against eclampsia.

In the report for 1929–30 there was one primipara who was admitted as an eclamptic. She was reported by a nurse to have had some sort of fit. As the post-mortem report showed the typical eclamptic signs she was included in the eclampsia statistics ; if she had not had a fit she would not have been so included.

In the present year, the report for which has not been published, there will be found two cases of death: (1) a 10-para, who was admitted comatose—the post-mortem

findings were absolutely atypical; (2) the 3-para described at the beginning of this paper.

Enough has been said to draw attention to the fact that the time has come to review our ideas on eclampsia. For statistical purposes "fits" were, in the past, considered a necessary accompaniment of eclampsia. It should now be decided whether fits are a necessary factor, and whether the treatment suitable for the typical eclamptic is suitable also for the atypical—that is, for the chronic nephritic. There is no doubt that the ordinary eclamptic who has not had a severe cerebral haemorrhage will recover with careful palliative treatment, but the woman with nephritis will often fail to do so.

TOOTH EXTRACTION AND CHRONIC INFECTIVE ENDOCARDITIS

BY

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It is recognized that many chronic diseases, especially of the rheumatic type, such as arthritis, fibrositis, neuritis, iritis, etc., are due to the repeated absorption of toxin from a chronic focus of infection with streptococci—generally the *Streptococcus viridans,* but sometimes haemolytic streptococci. One of the commonest situations for this focal infection is at the apex of a tooth, where the toxin is produced under tension and readily absorbed. It has become almost the general practice to recommend patients suffering from one of these rheumatic manifestations to have an *x*-ray examination, and, if marked apical rarefaction is revealed, to have the offending tooth or teeth extracted.

Danger of Lowered Resistance

Fortunately, even if a large number of teeth are removed at one sitting, the operation is not generally a very serious matter, and recovery is speedy and normal. But if for any reason the patient's resistance against streptococcal infection is low, there may be very serious danger. As Sir William Willcox[1] has pointed out:

> "The resistance of a person to a dental infection may be broken down by the constant dosage of the blood stream with toxic products from the focus of infection. A condition of sensitization then results. . . . I have, on several occasions, seen fatal septicaemia and malignant endocarditis follow extraction of infected teeth in a patient in poor health with a low immunity."

It is to this grave danger that I especially wish to draw attention. It may, and certainly does, happen that chronic infective endocarditis comes on without any obvious cause, although in these cases the same germ, generally the *Streptococcus viridans,* which is present in the blood, may be cultured from the apex of an infected tooth. This suggests that the tooth was the primary focus of infection in a patient whose blood shows an abnormal deficiency in bactericidal powers against this organism. But blood infection is more likely to occur in a patient with a very low degree of immunity if blood and lymph channels are opened up by the trauma of tooth extraction, especially if the extraction is a difficult one, requiring more force than usual.

In recent years local anaesthesia by infiltration of the gum and tooth socket with an anaesthetic such as novocain has been very widely practised. Where there is obvious septic infection of the gums a local anaesthetic is not often given, but in apical infection, only revealed by *x*-ray examination, it is quite usual for extraction to be performed under local anaesthesia. I think there can be no doubt that forcing a fluid under considerable tension into the comparatively rigid and resisting tissues of the gum and periodontal membranes must tend to carry any germs which may be present in these tissues into the lymphatics, and so to the blood stream, with a danger, if the blood should happen to have no bactericidal power against the infecting organism, of starting a serious and fatal blood infection, such as subacute infective endocarditis. Two cases of this disease following tooth extraction under local anaesthesia are recorded in the *British Medical Journal* (July, 1931) by Dr. L. Abrahamson. In each case there was pre-existing valvular disease, and in both local anaesthesia was used.

I had the opportunity of seeing, not long ago, another case in which chronic infective endocarditis followed immediately upon extraction of a tooth.

Illustrative Case

The patient, a lady of about 50, was in a poor state of health, and had been advised to have her teeth examined. The radiologist found evidence of alveolar absorption in most of the teeth, but especially in three of them. He advised that, owing to the state of her health, little should be done at the moment, but recommended that one of them, which showed the greatest evidence of damage, should be extracted. This was done on October 26th, 1929, but I have not been able to ascertain whether local anaesthesia was employed. On the following day her temperature rose slightly, and continued a subfebrile course, from 99° to 100° or 101° F., during the remainder of her illness.

Haemolytic streptococci were cultured from the tooth socket, but were not found in the blood. The leucocyte count was 8,000, polymorphs 73 per cent., and the polynuclear count showed a marked shift to the left. Streptococci were also cultured in the patient's blood, which had no bactericidal effect upon them. The pathologist concluded that it was probable that there was a low-grade blood infection, although no growth had been obtained from the blood.

Ten days later she was visited by a London consultant, who reported that heart and lungs were sound, and gave a good prognosis as to recovery. A month later another blood examination and culture was made; leucocytosis had now increased to 13,000, polymorphs 77 per cent., but still no culture was obtained from the blood. The consultant, who had been kept informed of the progress of the case, expressed his belief that she was suffering from a low-grade type of septicaemia from a focal infection in connexion with the teeth, and strongly urged the advisability of the extraction of more teeth, as he believed that she would not improve until the focus had been removed. Three teeth were accordingly extracted between December 18th and December 28th *under local anaesthesia.*

The temperature rose somewhat after the first extraction, and her general condition became rapidly worse. I saw her for the first time on January 4th. She was then in a very serious condition, obviously suffering from endocarditis and myocardial infection. She died on January 10th, 1930.

The mode of onset of the symptoms and the course of the disease clearly indicate a blood infection with subacute endocarditis originating from the first tooth extraction, and very much aggravated by the three subsequent extractions under local infiltration, which introduced a larger number of streptococci into the blood stream. The febrile condition was not due to repeated doses of toxin from an infected focus, but to the elaboration of toxin in the blood from the blood infection with streptococci. Removal of more teeth materially aggravated the infection, adding fuel to the fire.

Commentary

The danger of extracting teeth with apical streptococcal infection is a real one, as these cases show, and I feel convinced that the danger is increased if local anaesthesia by infiltration of the gum is made use of.

Unfortunately, it is not at present feasible to estimate the patient's blood resistance to the infecting organism unless a culture can be made and tested against the