ACUTE LYMPHOCYTIC MENINGITIS IN "EPIDEMIC CATARRHAL JAUNDICE"

BY

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The purpose of this article is to record the occurrence of acute lymphocytic meningitis in a case of epidemic catarrhal jaundice and to criticize the terms "epidemic catarrhal jaundice" and "infective hepatitis." It is suggested that the infectious disease described under these names is not of necessity a condition affecting the liver, but is in fact a general virus infection, such as influenza, in which the primary site of invasion is frequently the gastro-intestinal tract. The advent of hepatitis and meningitis should be regarded as an indication of increased invasive power in subjects whose resistance is low. The conception of influenza should be generic and not specific, so that it may include a number of virus diseases epidemic in nature which at present have not been identified.

The objection to the terms "epidemic catarrhal jaundice" and "infective hepatitis" is that they give a false impression of the disease they represent, because they do not include the diarrhoeal cases, of which there are many, and the simple gastric types, in neither of which jaundice occurs. In support of this view some personal observations are described.

A Gastro-intestinal Epidemic in Letchworth

During the past 15 months there has been prevalent in Letchworth an infectious disease characterized by acute gastro-intestinal disturbance and frequently jaundice, obstructive in type. Three distinct forms have been observed: (1) the diarrhoeal group; (2) the vomiting group; (3) the jaundiced group. These forms have occurred repeatedly in the same household. The diarrhoeal variety has been more commonly seen. The incubation period has been difficult to assess, but may be short or as long as four weeks. There were no symptoms referable to the upper respiratory tract.

The Diarrhoeal Group.—The onset was abrupt, with diarrhoea, colic, and tenesmus, some patients vomiting once or twice during the first few hours. Slight general abdominal soreness was present, but there was usually little constitutional disturbance, and fever was mild or absent. The frequent watery motions continued for 1 to 5 days, then ceased abruptly. In a few cases recovery was delayed and small evacuations of clear mucus were passed in decreasing frequency for 3 to 5 weeks. Only in the acute stage was a fleck of blood to be seen in the motions. In several typical cases cultures from a stool passed within the first 24 hours revealed no pathogenic bacterium.

The Vomiting Group.—In these cases the onset was sudden, with shivering, epigastric discomfort, nausea, and vomiting. Sometimes one or two loose motions were passed on the first day, but subsequently constipation was the rule. There were considerable malaise and prostration, and continuous fever, which rose to 102°, persisted for 4 to 6 days, then fell by crisis. Vomiting continued during the period of fever.

The Jaundiced Group.—The clinical picture was similar to that of the vomiting group, but epigastric discomfort was more severe, amounting to pain. Patients complained bitterly of this symptom. Repugnance to food was usual, being associated with marked nausea and vomiting, which continued until the fourth or fifth day, when jaundice appeared. Thirty-four jaundiced cases have been observed, and in nearly all of them the liver was palpable and tender; sometimes the enlargement was considerable. In only one case was the spleen definitely felt, and this accompanied a much swollen liver. Jaundice may be slight, visible only in the urine or eyes for a day, or deep and fluctuating, persisting for five weeks. The average case was yellow for 6 days. A considerable degree of debility was present after convalescence was established, which delayed return to normal health for 4 to 6 weeks.

A Case of Acute Lymphocytic Meningitis

A man aged 27 developed meningitis *pari passu* with jaundice. His case was made more perplexing by the fact that he is a proved case of pulmonary tuberculosis, in which clinical arrest was achieved one year ago.

On Dec. 20, 1942, he became shivery and complained of headache. Vomiting occurred once or twice each day, and his temperature fluctuated between 99° and 101°. On Dec. 25 the conjunctivae became definitely yellow, but were clear the next day. His headache varied in intensity, but on Dec. 30 its severity became agonizing, with paroxysmal shooting pains between the temples. The patient did not look ill though he was obviously suffering considerably with his head. There was no neck rigidity, a questionable Kernig's sign was present, arm and leg reflexes were sluggish, abdominal reflexes were absent, plantar responses were flexor, and there was no papilloedema. The urine gave a green reaction with Benedict's solution. On admission to hospital lumbar puncture revealed a slightly opalescent fluid under increased pressure. Much relief from headache was obtained after 30 c.cm. of fluid had drained away. Examination of the c.s.f. showed a small fibrin web-cloth. A cell count gave 544 mononuclears (mainly lymphocytes) and 24 polymorphonuclear leucocytes per c.mm. The chloride content amounted to 710 mg. and protein to 75 mg. per 100 c.cm. Sugar was absent, and globulin increased. A scanty centrifuged deposit gave the following results: Gram film—no organisms seen; Ziehl-Neelsen stained clot—no tubercle bacilli seen; cultures on blood legumin agar and in peptone broth were sterile after 24 hours' incubation.

Jan. 1, 1943.—Lumbar puncture performed and 25 c.cm. of clear colourless fluid under increased pressure allowed to escape. Cell count, 300 per c.mm. Reflexes still sluggish, but abdominal reflexes now present.

Jan. 3.—Vomiting ceased. Temperature normal.

Jan. 5.—Patient looked well, sitting up in bed. Arm and leg reflexes were easily obtained. Lumbar puncture performed and 20 c.cm. of clear fluid under slightly raised pressure drained away. Examination of c.s.f. showed a clear colourless fluid with no clot. A cell count gave 336 mononuclear cells (mainly lymphocytes) and 56 polymorphonuclear leucocytes per c.mm. The chloride content was 715 mg. and protein 80 mg. per 100 c.cm. Sugar: Fehling reduction present. Globulin slightly increased. Convalescence was uninterrupted except for intermittent headache of mild degree for three weeks.

An intensive course of sulphathiazole, which was well tolerated, was given by mouth for five days (12, 8, 6, 6, 6 g.) after his admission to hospital. Since the cerebrospinal fluid became clear in 48 hours it would seem that the drug was beneficial.

Conclusion

It seems reasonable to deduce from these observations that the current epidemic in Letchworth is a virus infection primarily affecting the gastro-intestinal tract; that the weight of infection more commonly falls on the small and large bowel, producing an acute catarrhal ileocolitis, the degree of gastritis being minimal and hepatitis absent. Less often the stomach bears the brunt of the infection and colitis is minimal. In the present epidemic the majority of gastric cases develop hepatitis in greater or lesser degrees of severity. Approximately one case of jaundice has been seen for every six cases of diarrhoea—i.e., an incidence of 14%. Uncommonly the virus invades the leptomeninges, causing an acute lymphocytic meningeal reaction.

A number of severe cases of influenza, as distinct from febrile catarrh of the respiratory tract, have occurred recently in which diarrhoea with colic and abdominal discomfort was the initial phase. After 36 to 48 hours invasion of the respiratory tract occurred, starting as a tracheo-bronchitis and later becoming a bronchiolitis with pulmonary congestion. Outbreaks of jaundice in other parts of England have been reported in which the upper respiratory tract seemed to be the primary site of invasion.

The influenzal epidemic has different features each year. It may be gastric or intestinal with vomiting or diarrhoea, gastro-hepatic with vomiting and jaundice, tracheal with cough and substernal soreness, pharyngeal with pain in the throat, or simple fever with malaise. Retro-orbital pain and headache are almost constant and often severe, but may be slight or absent in the gastro-intestinal forms. Whichever type invades the community, it seems to breed true to a remarkable degree for about a year. The cases which differ from the current

form frequently start with the usual symptoms, and thus a different variety becomes established imperceptibly.

What benefit is to be derived from describing epidemic catarrhal jaundice as a separate clinical entity? It is stated that outbreaks of the disease often accompany an increased incidence of diarrhoeal disorders and that the initial symptoms may be of the "influenzal" type. Only one form of the disease is described by this name, and therefore it is misleading. These facts surely support the adoption of a wider conception of influenza.

Summary

It is suggested that the application of the term "influenza" be generic; that the names "epidemic catarrhal jaundice" and "infective hepatitis" are unsatisfactory, and that "influenzal jaundice" or "hepatitis" would convey a clearer conception of the disease.

A case of acute lymphocytic meningitis occurring in influenzal jaundice is described.

I wish to thank Dr. P. F. Wilson for his permission to publish this case, and the pathologist, who desires to remain anonymous, for allowing me to include his reports on the cerebrospinal fluid.

PSEUDOSCLERODERMIA

BY

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The following case of pseudoscleroderma arising from multiple deficiency may be of interest owing to the rarity of the condition.

Case History

A man aged 63 was admitted to hospital on July 15, 1941, complaining of stiffness in his legs, which prevented him from walking. He stated that he had been perfectly well until approximately one month before admission, when his right knee-joint suddenly swelled and became painful, forcing him to rest in bed. This swelling was attributed to a slight injury received to the same knee two days earlier which caused only momentary discomfort. After a few days in bed he noted that the skin of both his legs below the knee was becoming darker in colour than usual, the right leg being more involved than the left. This discoloration extended, and within the next seven to ten days it had involved the skin all over his body, being most pronounced on the face and neck, the backs of the hands to the wrists, and the legs from mid-thigh down. During this time he had been rising to attend to his own wants, but about 14 days before admission he began to have difficulty in straightening his legs at the knees. This stiffness progressed, and for some days before admission he was confined to bed with his knees fixed in a position of semiflexion. He stated that he had been feeling tired for an indefinite period, and that for the past month his bowels had been loose. There was no history of sore tongue or of Raynaud's syndrome.

The patient was unemployed, and his total income was 16s. 6d. a week from public funds. His expenditure was 4s. 6d. a week for his bed in a lodging-house, 2s. for tobacco, and the rest for food, etc. He did not drink alcohol. He cooked for himself, and lived mainly on pies, sausages, white bread, and scones, never eating fruit or any vegetables except a very occasional potato, and using condensed milk and margarine in place of fresh milk and butter. There was no previous illness of any note.

Clinical Condition

Routine examination revealed a small, thin, wasted man with a light-sepia-coloured skin with uniformly darker areas on the face and neck, backs of hands, and legs from mid-thigh to mid-dorsum of the foot. There was no special pigmentation around the nipples, on the pubes, or on points where pressure from clothing normally occurs. He was edentulous, had pale mucous membranes, a dry glazed but not inflamed tongue, atrophic ribbed finger-nails, pure white luxuriant hair, and patches of brown pigmentation on his buccal mucosa. There was no circumcorneal injection or cheilosis. Both corneae appeared healthy, and there were no petechiae or evidences of deeper haemorrhages. He appeared comfortable, but was slightly inattentive and confused. The skin around both his legs from 6 in. to 9 in. above the knee-joints to about the middle of the dorsum of his feet, but not on the soles, was brown in colour, thick, hard, and glossy to touch, and could not be moved on the underlying tissues. The skin elsewhere, although discoloured, was of normal consistency and mobility. The thickened skin was raised slightly above the normal skin, and the junction between was sudden (within 1/4 in.) and uneven. The legs were

not swollen and were not tender on pressure. Sensation over the affected area was dulled but not entirely absent. Both legs were held flexed at 45 degrees at the knees, and movement at these joints, which were not swollen, was painless but limited to a range of 45 to 60 degrees flexion by the tightness of the surrounding skin. Movement at the ankle-joints was also slightly limited. Movement at all other joints was normal. Further examination revealed no physical defect, and the remaining points of particular interest which helped in making a diagnosis are:

Skin temperature steady at 97.4°; pulse 75 to 80 a minute, regular; blood pressure 145/80. Test-meal (including histamine): no free HCl. Faeces 4 to 6 soft pale motions daily; total fat 33.9 g.—split fat 27.2%, unsplit fat 72.8%. Urine: routine tests negative; ascorbic acid (estimated as reducing substance), nil; creatin, 14 mg. per 100 c.cm. Blood: W.R. negative; plasma proteins, normal; urea, etc., normal; B.S.R. (Westergren), 6 mm. per hour; plasma ascorbic acid, 0.10 mg. per 100 c.cm.; sugar tolerance, normal curve; R.B.C., 3,310,000 per c.mm.; Hb, 38%; C.I., 0.58; W.B.C., 8,200 per c.mm. Film showed poor filling of red cells, anisocytosis and poikilocytosis, and a normal differential white count. Radiographs of knees showed only slight atrophic arthritis. Cuff test (Hess), negative. Microscopical examination of biopsy from affected skin resulted in the following report:

"The tissue consists mostly of vascular scar tissue. Enveloped in it are small foci of adipose tissue and dense fibrous fascial bands; at one side is striped muscle, which, at margin of scar tissue, is partly atrophied, partly hyperplastic (sarcolemmal cells proliferating). There are recent haemorrhages in the scar and also scattered granules of old blood pigment (previous haemorrhages probably). The appearances suggest scar formation in and adjacent to muscle and perhaps accentuated by haemorrhage."

Diagnosis

On the history and findings recorded above a multiple deficiency state was diagnosed, obvious deficiencies being nicotinic acid, ascorbic acid, and iron. The general pigmentation was considered to be part of the pellagroid change, and the thickened skin on the legs to be the result of this plus very minute multiple haemorrhages, the result of the vitamin C lack. The probability that other deficiencies aided in producing the curious localized change in the legs was great, but it was impossible to estimate their part in doing so. The diagnosis was made, therefore, of pseudoscleroderma the result of vitamin deficiency, and support was lent to this by the earlier records of a precisely similar change occurring in the legs of old people with scurvy (Pfeiffer, 1918). Other causes of the changes that were considered and excluded on the facts which have been given were: (a) true symmetrical diffuse scleroderma (sclerodactylia); (b) chronic cellulitis of legs with, as superadded causes of the general pigmentation, Addison's disease, haemochromatosis, and chronic vermin infestation of the skin. The presence of creatine in the urine was considered normal at the patient's age.

Treatment

Treatment was designed to test this diagnosis, and was conducted in various stages. The first stage was the maintenance of the patient for a period on the ordinary hospital diet, in order that its action could be assessed; the successive stages consisted in the addition to this diet of the obviously absent vitamins, in order that their action in promoting cure could be assessed also. Ascorbic acid was replaced first, mainly because the condition had been described before in association with scurvy.

Table showing Results of Treatment

Clinical Feature	Stage I: 18/7/41 to 18/8/41 Ordinary Hospital Diet	Stage II: 18/8/41 to 8/10/41 Ord. Diet + 7,000 mg. Vit. C in 14 Days, then 200 mg. Daily by Mouth	Stage III: 8/10/41 to 24/1/42 Ord. Diet + 200 mg. Vit. C + 200 mg. Nicotinic Acid Daily by Mouth	Stage IV: 24/1/42 to 9/3/42 As Stage II + 1,000 I.U. Vit. B.I.M.I. Daily
Blood { R.B.C. Hb ..	3,970,000 50%	4,150,000 66%	5,000,000 75%	5,000,000 79%
Bowels	Stools still frequent and soft	Improved but not normal	Normal	Normal
Mental state	As on admis- sion	Slight improve- ment	Marked im- provement to normal	Normal
Pigmentation	" "	Slight improve- ment	Marked im- provement	Normal
Skin thickening	" "	Very slight improvement; smaller area involved Knee move- ment 35°-60° flexion	Great improve- ment: small slightly thick- ened area on skin only re- mains Knee move- ments full and free	Completely healthy skin