Salmonella typhi was isolated from the blood clot. Three days later a further blood culture grew *Salm. typhi*. Chloramphenicol was given from the twenty-third day for a period of 10 days, and after this the fever settled. A blood culture on the thirty-fourth day was negative. On the forty-fifth day the patient was discharged quite well except for a slight bilateral foot-drop. One year later he was quite well and had just completed harvesting his rice fields by hand.

DISCUSSION

The common complications of typhoid fever are perforation, haemorrhage, and changes consequent on the profound toxæmia. Neurological symptoms and signs, apart from a clouding of consciousness sometimes described as a "typhoid stupor," are not a pronounced feature of typhoid fever. Occasionally a patient may suffer from peripheral numbness and tingling, but as a rule this is fleeting and insignificant. The standard textbooks (Huckstep, 1962) make only a cursory mention of neurological complications. In this patient, however, the neurological changes were the dominant features of his illness, and the possibility of a persistent infectious disease was not considered until he was found to be still febrile at a time when recovery from his muscle paralysis had begun. His clinical course, apart from the neurological changes, was typical of enteric fever, and the results of the agglutination test, isolation of *Salm. typhi* on two separate occasions, and response to chloramphenicol, confirm the diagnosis of typhoid fever.

Watson (1967) discussed 12 cases in which *Salm. typhi* was isolated from the blood as a manifestation of the carrier state. His cases did not show any of the clinical features of typhoid fever, and the agglutination titres were low, indicating an absence of infection. In the present patient the agglutination titres and the clinical course were typical of typhoid as seen in Ceylon.

Haymaker and Kernohan (1949), in their pathological study of 50 fatal cases of Guillain-Barré syndrome, looked for the presence of bacterial infection in 13 cases, and concluded that their studies "yielded a diversity of organisms, so that no one organism could be incriminated." Melnick and Flewett (1964), investigating the part played by infection in the pathogenesis of the Guillain-Barré syndrome, could only relate this disease to preceding viral infections. The clearest evidence they could find for a bacterial infection was the development of the Guillain-Barré syndrome in a patient 10 days after prostatectomy. Melnick and Flewett (1964) showed that common

viruses such as varicella, mumps, herpes zoster, Coxsackie, E.C.H.O. 6, and herpes simplex have been associated with this syndrome. Infectious mononucleosis and infectious hepatitis, too, have also been so associated (Davie, Ceballos, and Little, 1963; Gautier-Smith, 1965). As Watters and Barlow (1967) point out, the recovery of viruses from the cerebrospinal fluid and brain, and rising titres to viral agents, are not necessarily proof of the aetiology. Powles and Malpas (1967) reported two cases of the Guillain-Barré syndrome in patients with chronic lymphatic leukaemia, and Jenkins and Toole (1964) recorded two cases of polyneuropathy with albuminocytologic dissociation in the spinal fluid after exposure to insecticides.

With the strict criteria of Guillain, Barré, and Strohl (1916) and Osler and Sidell (1960) this patient falls into the category of the Guillain-Barré syndrome. The association of this syndrome with a variety of disorders, particularly viral infections, would favour the concept that the pathological lesion seen within the nerve tissue itself is due to an immunological process. The favourable response to steroids in some patients (Heller and DeJong, 1963) and mercaptopurine (Palmer, 1965) in others would favour this concept.

We thank Dr. K. B. Sangakkara, Medical Superintendent, Kandy General Hospital, for his help and advice.

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Zieve's Syndrome and Porphyrinuria in an Alcoholic

Brit. med. J., 1969, **1**, 96-98

In 1958 Zieve described a syndrome consisting of transient hyperlipaemia, jaundice, and haemolytic anaemia which was associated with the ingestion of large amounts of alcohol and which improved rapidly once alcohol was withdrawn. All the patients had a fatty or a cirrhotic liver or both. Further cases have since been reported (Haber, 1961; Kessel, 1962; Losowsky Jones, Davidson, and Lieber, 1963; Ström, 1963; Fukuda, 1964; Smith, Lonergan, and Sterling, 1964). All of them were men aged 25 to 65 years. Symptoms included anorexia, nausea, diarrhoea, and vomiting, with a history of recent loss of weight (5 to 10 kg.), yet many of them had an excellent appetite soon after hospital admission.

An interesting presenting feature was pain in the upper part of the abdomen, varying in intensity and changing in location;

it was described as cramps or dull pressure, at times simulating an acute abdomen. Pain was present in nearly all the cases and persists for 2 to 14 days. Low-grade pyrexia was a constant finding, persisting for weeks after treatment despite clinical improvement. Objective and symptomatic improvement usually began rapidly after admission. The moderately enlarged tender liver rapidly reverted to normal, and the mild abnormal biochemistry became normal within 10 days. The hyperlipaemia was due to an increased concentration of all lipid factors, including cholesterol (levels of over 1,000 mg./100 ml. were attained), but it reverted to normal within a few days of admission. The haemolytic anaemia was never severe. The haemoglobin settled at about 10 g./100 ml., with a reticulocytosis of 5-15%. Studies showed an increased red cell fragility and a moderate decrease in the red cell survival time, without much increased splenic uptake. Stool occult blood tests were negative.

Treatment is simple: a protein-rich diet and supplementary vitamins. Transfusions are unnecessary. The anaemia is compensated by increased bone-marrow activity manifesting as erythroid hyperplasia with occasional large phagocytic histio-

cytes loaded with lipid granules. The prognosis is good. The syndrome does not seem to be rare, and the majority of reports stem from the United States. The following case is of interest because of the associated transient porphyrinuria, which suggests a possible pathogenesis of the abdominal pain.

CASE REPORT

The patient, a 48-year-old man, drank heavily during the three months before admission. He complained of anorexia, loss of weight, and tremor. Admission was precipitated by the onset of severe abdominal pain in the right upper quadrant. The pain was persistent, aching, at times colicky, and radiated to the umbilicus. His stools were dark, and his urine was described as being a deep crimson colour. There was recent paraesthesiae of the legs. He gave no relevant past history, nor was there a family history of porphyria.

On admission he was pyrexial and icteric with no cutaneous stigmata of chronic liver disease or porphyria. His abdomen manifested diffuse rebound tenderness, but borborygmi were heard. The liver was palpable 4 cm. below the costal margin. The stool occult blood was negative. In addition to the coarse tremor of the hands he had decreased pin-prick and touch sensation of the legs.

The laboratory findings were characteristic of Zieve's syndrome: haemoglobin 12.5 g./100 ml., haematocrit 33%, reticulocyte count 5%, white cell count 9,800/cu. mm., serum amylase 600 i.u./l., serum total bilirubin 10 mg./100 ml. (conjugated 9 mg./100 ml.), alkaline phosphatase 28 K.A. units/100 ml., serum aspartate transaminase 60 i.u./l. Serum proteins, urea, and electrolytes were normal, but the serum was frankly milky, with a gross rise of all lipid components (see Table I) the cholesterol on admission was 900 mg./100 ml. Urine analysis showed strongly positive bilirubin and urobilinogen, and in addition a strongly positive porphobilinogen and urinary porphyrins. Urinary porphyrin assays are recorded in Table II. Within two weeks most biochemical and haematological values reverted to normal (see Chart). The milky serum cleared

TABLE I.—Blood Lipid Levels in mg./100 ml.

	Normal Range	Admission	Days after Admission	
			3	25
Glycerol ..	0.5-1.7	25	2.7	1.0
Triglycerideglycerol	7.5-18.0	441	56	19
Neutral fat ..	70-170	4,250	550	190

TABLE II.—Urinary Porphyrin Levels

Urine	Normal Range (μ g./24 hours)	Days after Admission	
		1	7
Porphobilinogen ..	0-2	4.2	1.6
Coproporphyrins ..	120-200	600	192
Uroporphyrins ..	5-30	120	42

Changes in haemoglobin, reticulocyte count, serum amylase, cholesterol, and bilirubin levels during the three weeks after admission to hospital.

by the fifth day after admission. The Coombs test was negative, red cell fragility was slightly increased, and the red cell survival time was 12 days. Sternal bone-marrow aspiration showed normoblastic hyperplasia and no increase in iron. Lipoprotein electrophoresis showed a marked increase of beta-lipoprotein. Severe fatty change with slight portal fibrosis, but no cirrhosis, excess iron, or Mallory's bodies were seen on liver biopsy. Serum calcium and phosphorus levels were normal.

The patient's condition rapidly improved, the abdominal signs disappearing within five days and the paraesthesia, jaundice, and hepatomegaly within seven days. Therapy consisted of parenteral vitamin K and a normal ward diet only.

DISCUSSION

The pathogenesis of the main features of Zieve's syndrome are disputed (Blass and Dean, 1966). The hyperlipaemia has been suggested to be due to an episode of massive mobilization of fat to or from the fatty liver (Zieve, 1958). Another suggestion (Zieve, 1958) is that there is a diminution of the normal plasma lipid clearing factors—for example, heparin, albumin. The hyperlipaemia may in some cases be caused or potentiated by an associated pancreatitis (Albrink and Klatskin, 1957; Gross, 1958), yet most cases have normal serum amylase and urinary diastase levels. Gross (1958) postulated that the hyperlipaemia is due to damage of the pancreatic alpha cells with insufficient production of a hormone that regulates the blood lipid levels, but different from glucagon, which is also produced by the alpha cells. Losowsky *et al.* (1963) postulated that a low level of lipoprotein-lipase activity is responsible for the hyperlipaemia, and that this enzyme in normal quantities is responsible for clearing serum in man; why it is low in Zieve's syndrome is unknown.

The haemolytic anaemia is thought (Zieve, 1958) to be based on the conversion of lecithin to lysolecithin—a powerful haemolysin. The abnormal lipid lysolecithin is produced from lecithin (normally present in the serum) through the action of a pancreatic lipase—lecithinolipase; the conversion is achieved by the substitution of a hydroxyl radical for a fatty acid.

The jaundice is attributed to intrahepatic cholestasis with varying degrees of hepatocellular damage (Kessel, 1962). This is suggested by the biochemical findings of high serum bilirubin and alkaline phosphatase levels with normal or slightly raised transaminase levels.

Many theories have been postulated for the abdominal pain. Garunas (1957) and Corazza and Myerson (1957) considered "packing" of the liver with fat. Klatskin and Gordon (1952) suggested fat embolism from liquefied fat arising from sites of fat necrosis. These theories do not explain why there is pain when the lipids return to normal. Abnormal lipid metabolism (Kessel, 1962) in nerve cells or nerves similar to those in diabetic neuropathy or tabetic gastric crisis would explain the discrepancy between the early reversal of the blood lipids to normal yet the persistence of pain and its apparent independence of the serum lipid level. A toxic (alcoholic) neuropathy (Kessel, 1962) or a nutritional deficiency neuropathy has been suggested, yet lack of correlation with the other clinical and biochemical findings is against these two hypotheses.

I suggest that the pathogenesis of the pain in Zieve's syndrome may lie in an abnormality of porphyrin metabolism secondary to the chronic ingestion of alcohol. A review of the literature (Zieve, personal communication, 1968) shows no previous recording of abnormal porphyrin metabolism. It remains to be decided whether, in my patient, the pain in Zieve's syndrome is due to a variety of secondary acquired porphyria, whether the porphyria is a coincidental finding, or whether the porphyrinuria is a temporary phenomenon due to the alcohol effect on liver metabolism and unassociated with abdominal pain. Recent literature (Gajdos, 1968; Palma-Carlos and Palma-Carlos, 1968; Shanley, Zail, and Joubert, 1968) has drawn attention to the experimental production in animals of

temporary porphyrinuria after ethanol administration. I feel that my patient manifested Zieve's syndrome and a variety of secondary acquired porphyria with abdominal pain, paraesthesia, and porphyrinuria, and that this may be responsible for the abdominal pain in Zieve's syndrome. Clearly future patients with Zieve's syndrome need to be investigated for abnormalities of porphyrin metabolism.

I thank the Wellcome Trust for their financial support. I should also like to thank Professor Sheila Sherlock for permission to study the above patient, who was under her care, and Dr. I. A. D. Bouchier for advice in the preparation of this paper.

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Home-made Cider: Source of Lead-poisoning

Brit. med. J., 1969, **1**, 98

Lead-poisoning is an industrial disease reportable under the Factories Act, 1961. Because of the Public Health Act, 1936, there is little chance of commercially prepared food and drink or public water supply containing lead in appreciable quantities, and of course certain factories in Great Britain are subject to regulations governing the use of lead and lead-containing materials. There are no regulations, however, governing such domestic use of lead as is here described.

CASE REPORT

A 49-year-old man was admitted to hospital in April 1968 with severe epigastric pain of 24 hours' duration. The pain was constant, did not radiate, and was becoming progressively worse. He had vomited several times, but had had no diarrhoea. For five years before admission he had been having similar attacks of abdominal pain; he thought he had been slower mentally since Christmas 1967, and he had noticed that a tremor had developed in his hands.

He was a slight pale man, but was not clinically shocked; his pulse was regular, 100/min., blood pressure 140/85, temperature 36.6° C. He was writhing in bed and appeared to have considerable epigastric pain. Rectal examination showed nothing abnormal and there was no evidence of intestinal obstruction either clinically or on x-ray examination. His haemoglobin was 56%, the packed cell volume 25%, and there was basophilic stippling of the red cells. Closer examination showed a dark blue line round the gingival margins. It was thought that the patient might be suffering from plumbism.

There was no radiological evidence of lead-poisoning in the skeleton, red cell fragility and plasma electrolytes and proteins were normal. Routine urinary analysis showed no protein, sugar, or acetone, and the creatinine clearance was within the limit of normal; however, qualitative urinary analysis showed porphyrins to be grossly in excess of normal. Blood and urine samples sent to the department of pathology at the London Hospital for lead estimation gave these results: blood lead level 375 µg./100 ml. (normal 60–80 µg./100 ml.) and urinary lead 260 µg./100 ml. (normal 8–12 µg./100 ml.).

On questioning, the patient stated that he drank about a quart (1.1 litres) of his own home-brewed cider each day, and that he had done so for about 30 years. During the process of making the cider, apple juice was poured on to a lead-lined tray at the base of the press. Here presumably was the source of the poison.

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A diagnosis of lead-poisoning was made and treatment instituted. This consisted in giving 2 g. of sodium calciumedetate each day intravenously. Seven doses were given. By the end of treatment his blood lead level had fallen to 55 µg./100 ml., and his urinary lead to 12 µg./100 ml. At this stage his haemoglobin had risen to 69%, he felt very much better, the tremor in his hands had disappeared, and he seemed to be sharper mentally.

Six weeks later the following figures were obtained: blood 12 µg./100 ml., urine 13.5 µg./100 ml. He had, of course, been counselled to drink no more of his own brew.

DISCUSSION

Beer and cider drawn through lead pipes, wine from lead-glazed earthenware pots, and soft or acidic water allowed to stand for any length of time in contact with lead pipes or cisterns have all been reported as causing lead-poisoning. The press which had been used to make our patient's cider was 120 years old and made of oak. Over the years the collecting-tray at the bottom of the press had shrunk, and so a watertight lead covering had been put on some 30 years ago to prevent loss of the apple juice through the cracks. While the slightly acidic juice was in contact with the tray a certain amount of lead was dissolved, as evidenced by a concentration of 5.95 mg. of lead in each litre of cider. This is considerably less than the lead content in home-made wine (120 mg./l.) reported by Lane and Lawrence (1961) from this hospital, although their patient had been drinking the wine for only four months.

Both our patient and his father had drunk the cider, and it is interesting to note that the latter had been admitted to hospital in 1948 and 1958 with acute abdominal pain and had had laparotomies on both occasions. Nothing pathological had been found at either operation, but in 1958 his blood film had shown basophilic stippling. Unfortunately, no investigations could be carried out on him, since he died in 1966 of an unrelated illness. We must assume that he too was suffering from chronic lead-poisoning and that this had been the cause of his abdominal pain.

My thanks are due to Professor F. E. Camps and his colleagues of the London Hospital, and to Dr. A. Lawrence, pathologist to St. Luke's Hospital, for their invaluable help. I am grateful to Dr. G. A. MacGregor for permission to publish this case.

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