used was a synthetic product, and the maximum benefit of the protective substances may be obtained only when given in the form of natural foods.

Summary

When comparing two groups of women for a period extending from the later months of pregnancy until six months after delivery, one of the groups being supplied with supplements of ascorbic acid, it was found that there was a deficiency of vitamin C, as measured by saturation tests, in both groups; the deficiency was naturally greater in the group without the supplements.

The incidence of suppurative mastitis in both groups taken as a whole was very high. When approximately 250 expectant mothers were followed up over a period of six months following delivery it was found that 25% suffered from breast abscess. It is to be noted that, with few exceptions, these patients were delivered in hospital.

There was no reduction in the incidence of mastitis in the group receiving the supplements or in those who gave evidence of a satisfactory intake as judged by saturation tests.

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ACUTE IDIOPATHIC PORPHYRIA

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In the porphyrias uroporphyrins are excreted in the urine, in contrast with coproporphyrinuria, which occurs in many diseases. The porphyrias have been reviewed in detail by Mason *et al.* (1933), Waldenström (1937), Chandler *et al.* (1939), Roger *et al.* (1939), Dobriner and Rhoads (1940), and Nesbitt (1944).

Waldenström (1937) has described five types of acute porphyria: (a) Latent porphyria—an asymptomatic form in which uroporphyrin is excreted continuously or intermittently, for years, in the urine. (b) Abdominal type—onset sudden, with colic, vomiting, obstinate constipation, and tympanites. (c) Nervous type—onset sudden, with pareses of the extremities, convulsions, confusional states, coma, or bulbar paralysis. (d) "Classic type"—both abdominal and nervous symptoms. (e) Comatose type—abdominal colic, rapid onset of coma, and death.

In all types tachycardia and hypertension occur during the acute attack. In nearly all cases the urine contains uroporphyrin-III, with but traces of the series-I isomer; occasionally the latter predominates (Turner, 1938; Golden, 1943). Sometimes acute porphyria occurs during the prolonged administration of trional, tetronal, or sulphonal, and these have been regarded as "toxic" porphyrias (Mason *et al.*, 1933; Nesbitt and Watkins, 1942), but Waldenström considers that the division between toxic and idiopathic groups is very questionable.

The diagnosis is established by the demonstration of porphyrin in the urine. In some cases the freshly voided urine is normal in colour and contains porphobilinogen (Vahlquist, 1939), which changes to porphyrin on standing or heating. The presence of porphobilinogen is recognized by Watson and Schwartz's test (1941). The reddish-brown colour of the urine which contains porphyrin is due to the formation of coloured substances such as urofuscin, uroresin, and indirubin from colourless chromogens (cf. Turner, 1938; Watson, 1939).

The porphyrin may be present as a zinc complex (Turner, 1938; Chandler *et al.*, 1939; Nesbitt and Watkins, 1942) which has absorption bands indistinguishable in position, if a hand spectroscopy only is used, from those of oxyhaemoglobin—differing, however, in that the β band is more intense than the α band, whereas in oxyhaemoglobin the reverse is true.

A few cases have been reported (Backer-Gröndahl, 1935; Schie, 1939) in which the symptoms closely resembled those of the "abdominal type" of the disease but the dark-coloured urine contained no detectable traces of porphyrin. Waldenström (1939) described a similar case, but during a remission of the disease the patient excreted pathological amounts of porphyrin.

The case described below is put on record for three reasons: (a) it was under continuous observation for two years, during which four exacerbations of the disease occurred; (b) in one of these the porphyrin output was followed quantitatively from day to day; and (c) in several relapses the clinical picture varied.

Case History

The patient, a sheet-metal worker aged 19, was admitted to St. Bart's for investigation on April 4, 1942. He was quite well until June, 1941, when he had a fairly sudden onset of dull aching pain round and below the umbilicus. This soon became colicky in nature and severe, but the pain did not radiate. Attacks lasted for two or three hours and had no relation to food or exercise. Nausea, vomiting, and obstinate constipation were prominent features of the illness. Some two weeks later he had five "fits" in one morning and was admitted to a hospital with a *Bact. coli* infection of the urine and a B.P. 150/110 but no other abnormal signs. The urine was free from lead, and the C.S.F. and a radiograph after a barium enema were normal. The urinary infection cleared satisfactorily, the B.P. returned to normal, and he was discharged in three weeks.

Second Attack.—In Jan., 1942, he was readmitted to hospital with symptoms similar to those in the first attack. The urine was reported as normal, but the colicky pains persisted for a few days. B.P. 160/100. He was discharged within three weeks.

Third Attack.—On March 28, 1942, he complained of aching in the limbs followed by colicky abdominal pain, vomiting on one occasion, and obstinate constipation. On April 4 he was admitted to this hospital for investigation, when, in addition to the above history, he reported having lost a considerable amount of weight during the past six months. On examination the fauces were injected, there was slight tachycardia (pulse 90), and the B.P. was 160/120. There was slight tenderness in the abdomen below the umbilicus and the liver margin was just palpable. The urine was dark brown in colour, of sp. gr. 1032, without protein, ketone bodies, or blood. It reduced Benedict's reagent, and Schlesinger's test for urobilinogen was strongly positive. Examination of the fresh urine with the direct-vision spectroscopy showed no abnormal absorption bands, but on standing for some hours it darkened and the two-banded spectrum of porphyrin became visible in a half-inch layer. An amyl alcoholic extract of the fresh or of the stale urine showed the α , β , and γ bands of alkaline porphyrin, converted by hydrochloric acid to acid porphyrin. Toluene-soluble red pigments were also present.

Investigations.—Hb, 118%; R.B.C., 5.5 millions; W.B.C., 6,800, with a normal differential count. There was no punctate basophilia. E.S.R., 1 mm. in the first hour. Serum bilirubin was normal. Blood W.R. and Kahn tests were negative. The reducing substance in the urine was proved to be glucose. A glucose-tolerance curve gave the following result (blood sugar in mg. per 100 c.cm. followed by time in hours, in parenthesis, after the test dose of glucose): 88 (0); 148 (1/2); 140 (1); 125 (1½); 115 (2). Urine specimens before the test dose and two hours afterwards contained sugar, which indicates a low renal threshold for glucose. Radiographs of the lungs, abdomen, and kidneys were normal. The skull was normal except for a small pituitary fossa (transverse, 8 mm.; vertical, 3 mm.; and interclinoid measurement, 1 mm.).

Course of the Illness

Nausea and constipation were marked, but abdominal pain did not amount to more than discomfort below the umbilicus. The

patient lost weight very rapidly, as shown by Fig. 1; and on April 28 (fourth week after admission) he had an epileptiform attack associated with cyanosis and widespread clonic movements but no incontinence. B.P. remained about 150/110, and tachycardia persisted. By the sixth week increasing weakness of the large muscle groups of his arms and legs was apparent, and there was fibrillary twitching in the deltoid and pectoral muscles. Reflexes were absent

FIG. 1.—Weekly variations in the patient's weight: —. Average weekly pulse rate: ----. No observations made: Black rectangles: Duration of abdominal symptoms. Shaded rectangles: Time during which barbiturates were given. The arrow: Sulphathiazole given.

in both arms, and pain sensation was blunted on the trunk and face. Within two weeks he became so weak as to be unable to move his hands or arms, and his voice was very hoarse and feeble. There was gross wasting of all muscle groups in the arms, forearms, and hands; fibrillary twitching had ceased. He had difficulty in standing because of weakness of the legs. Knee- and ankle-jerks were present and equal, with the plantar responses Babinski-negative. He sustained a burn from a hot-water bottle on his leg, and it was found that sensitivity to pinprick was impaired in both legs (it had been normal a week earlier), but position sense was normal. For a period of six weeks he was unable to feed himself. By the tenth week his voice was stronger, his weight was increasing, and there was some return of power to the flexor muscles of the arms. Six weeks later there was still gross wasting of the pectorals and deltoids, biceps and triceps groups, forearm muscles, especially the ulnar group, and of the intrinsic muscles of the hands. The arms could not be abducted. Full flexion and extension of the elbows were possible, but without power. There was bilateral wrist-drop. Touch, vibration, and position sense were normal, but there was blunting of pinprick sensation, especially on the hands, and the tendon reflexes were absent. Abdominal reflexes were absent. The muscles of the legs were of good tone and there was no wasting. All leg movements were weak but incomparably stronger than those of the arms. Tendon reflexes were normal.

Fourth Attack.—From the 20th to 22nd weeks he complained of much abdominal pain and was constipated. His weight decreased considerably (Fig. 1), but there was no extension of paralysis. By the 30th week his legs were normal, but his arms were still grossly wasted and weak, without tendon reflexes yet with enough power slightly to abduct the arms and dorsiflex the wrists. Sensation in the arms was normal, but there were no abdominal reflexes. Within two weeks marked improvement was apparent. The arms could be moved relatively easily and all the tendon and abdominal reflexes had returned.

Fifth Attack.—During the 32nd week he again complained of slight abdominal pain and constipation and, though this was associated with loss of weight, there was no extension of paralysis. From this time there was gradual but continued recovery of muscular power and the wasted muscles regained their normal contours. By the 52nd week the patient was able to help in the ward and could support the weight of a laden tray and perform fine movements with his fingers.

Sixth Attack.—On April 16, 1943 (54th week), a small pustule appeared on the ring-finger of the right hand and lymphangitis developed next day. Sulphathiazole was started, but was discontinued after 9 g. had been given. On April 21 he vomited and experienced severe abdominal colic, and his limbs felt very heavy. He had been losing weight for four weeks. The only abnormal signs were tachycardia and a B.P. of 160/130. During the succeeding week he suffered from marked insomnia and was at times mentally confused. The power of his shoulder-girdle muscles diminished rapidly and in 10 days he was practically unable to

move his arms. Simultaneously, the muscles wasted rapidly and there was a further marked loss of weight. The distribution of the weakness and wasting was as in the third attack, but in addition he had tenderness of both quadriceps and knee-jerks were absent. At this time there was no hepatic involvement as judged by the bromsulphthalein dye excretion test. The legs soon recovered their normal power, but even after three months—long after the abdominal and mental symptoms had disappeared—there was gross weakness and wasting of both arms (the right more than the left), abduction being very poor. By the 73rd week movements of the large joints of the arms were good and reasonably strong. The dorsal interossei of the hands, especially the first, were still very weak and wasted, and the power of the lumbricals was poor. Eighty-seven weeks after admission the small muscles of the hands had recovered to a considerable extent—enough to enable him to weave. Improvement continued until his discharge on April 8, 1944, when his weight was steady. He was then working at occupational therapy for several hours a day and could write without difficulty. His urine still contained considerable amounts of porphyrin and of urobilin.

Five months after his discharge the patient was working as a clerk for six hours a day; weight 138 lb., pulse 72, B.P. 124/72. His urine contained a great deal of porphobilinogen and urobilinogen, and yielded much porphyrin and moderate amounts of the associated red pigments on standing. At this time a single specimen of the urine of each of his parents was examined, but neither contained porphyrin.

Comment

Fig. 1 records the patient's weight and pulse rate throughout his stay in hospital—that is, from soon after the start of his third illness until his discharge. The gross loss of weight which preceded each relapse is well shown, as was the recovery of weight when the symptoms subsided. The fourth and fifth attacks, which were minor episodes clinically, were also associated with a definite fall in weight. The greater loss of weight associated with the sixth attack was in keeping with the fact that it was comparable in severity with the third illness. Each point on the pulse-rate curve represents the average reading for the week. Tachycardia was a marked feature of the condition, with peaks in the curve of pulse rate corresponding to each relapse. The black rectangles indicate the duration of abdominal symptoms—namely, pain alone, or with vomiting and nausea. The shaded rectangles denote the duration of administration of phenobarbitone. The arrow represents the point at which sulphathiazole was given.

Excretion of Porphyrins.—Prof. C. Rimington kindly investigated quantitatively the output of porphyrins in the urine by

FIG. 2.—Lowest chart: Day-to-day excretion of uroporphyrin in mg. during the fourth attack (cf. Fig. 1). Middle chart: Corresponding excretions of coproporphyrin in the urine. Upper chart: Daily variations in pulse rate.

methods which he has published elsewhere (1943). He found that uroporphyrin-III predominated in the urine, the isolation of which as its octamethyl ester completed the clinical diag-

nosis. Coproporphyrin-III and a very small amount of coproporphyrin-I were also found. Fig. 2 represents the day-to-day excretion of uroporphyrin and of coproporphyrin from the 19th to the 23rd week after admission. The daily variations in pulse rate are also charted. An increase in porphyrin excretion was associated with a rise in pulse rate, though the correspondence was not exact.

Conclusion

The administration of sulphonamides or of barbiturates may precipitate an attack (Mason *et al.*, 1933; Waldenström, 1939; Nesbitt and Watkins, 1942). Phenobarbitone, 1 gr. twice daily, was given for periods of several weeks during the third and fourth attacks, but there was no evidence that the drug affected their course adversely. The onset of the sixth relapse cannot be attributed to the administration of sulphathiazole, as the patient had then been losing weight for about four weeks—a sign, in his case, of pending relapse. A noteworthy feature of the disease is the degree of restoration of function of the paralysed muscles, which in this patient appeared nearly complete.

Summary

A patient complaining of attacks of abdominal pain, constipation, and fits was found to be excreting uroporphyrin-III in his urine and to be suffering from acute porphyria. A marked decrease in body weight preceded the onset of symptoms.

In the course of three years he experienced six relapses, in each of which the symptomatology varied. Recovery now appears to be complete although porphyrinuria persists.

In one attack the daily variation in porphyrin excretion was determined.

The clinical features of the disease and methods by which the diagnosis may be confirmed in the laboratory are described.

We wish to thank Dr. Geoffrey Evans for permission to publish this case.

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SIMMONDS'S DISEASE DUE TO POST-PARTUM NECROSIS OF THE ANTERIOR PITUITARY: CARCINOMA OF STOMACH

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Although the papers by Sheehan (1938, 1939, 1940) and Sheehan and Murdoch (1938, 1939) have clarified knowledge as to the causation of Simmonds's disease and stimulated interest in this condition, descriptions of cases due to necrosis of the anterior pituitary lobe resulting from post-partum collapse are still rarely seen in the clinical journals. The following case may therefore be of interest. It is reported alone, although other presumptive cases have been seen in this department during the past few years, including that of a woman who had amenorrhoea dating from the birth of her last child when she was 30, and who died, aged 39, of carcinoma of the bladder, with an extensive neoplastic spread in the pelvis. Post-mortem examination revealed splanchnicemia and (both to the naked eye and in serial sections) the typical atrophy in the anterior pituitary. Owing to her general condition, however, few investigations had been done during life.

Case Report

Mrs. W., aged 59, was referred for investigation on Feb. 23, 1943, by Dr. F. M. Rose, of Preston. She gave a history of progressive

tiredness and loss of 1 st. in weight over the past year, and anorexia and numbness of the fingers since an attack of influenza in 1942. She had mentioned epigastric pain to her doctor, but told me that there had been no pain, vomiting, epistaxis, or dysphagia. She had had four pregnancies; her son was aged 37, the middle two children had died at 11 months and 2 years old, and her daughter was 27. The first three confinements were uncomplicated, but at the birth of the last child, when the patient was 32, there was severe haemorrhage and she was in bed seven weeks or more from weakness. She menstruated 5 months later, and again, for the last time, four months after that. After the delivery she did not lactate, and the breasts, from being large, became very small. Loss of hair was soon noticed (especially axillary and pubic), and she gained 1½ st. in weight. A year passed before she regained her strength. Sensitivity to cold developed, becoming more pronounced during the last year. No change in sex feelings could be recalled. The patient's daughter-in-law said that she had been pale for 15 years or more, but the pallor had become more grey over the past year, and the cheeks were sunken. No psychological changes had been noted, such as peevishness, unkindness, absentmindedness, faints, fugues, or attacks of coma.

Examination.—Height, 5 ft. 1 in.; weight, 6 st. 11 lb. The pallor and wasting gave the clinical picture of cachexia; face wrinkled, cheeks sunken, no glossitis; axillary and pubic hair absent; scalp hair thin; eyebrows very thin; breasts flat and atrophic; soft quick pulse, with occasional dropped beats (B.P. 100/60); oedema of lower legs; nothing abnormal felt in abdomen. Physical examination otherwise negative.

Blood Counts, 1943

	Hb Haldane	R.B.C. (mills.)	Anisocytosis	M.C.V. (c.μ)	Mean Diam.	Leucocytes	
						Total	Neut.
Feb. 23	100	4.4	Slight	86	7.7μ	6,400	2,900
Mar. 17	95	4.2	"	—	—	8,400	4,500
April 2	74	3.7	"	—	7.8μ	—	—

Blood Chemistry

	Feb. 23	Mar. 12	Normals
Bilirubin (mg./100 c.cm.)	0.7	—	9—11
Calcium	—	8.5	9—11
Chlorides	568	570	560—620
Cholesterol	125	132	120—230
Phosphate	—	4.2	3—4.5
Phosphatase	—	15	3—13
Potassium	25	24	18—21
Protein (g./100 c.cm.)	—	7.1	6—8
Sugar (true) fasting (mg./100 c.cm.)	65	—	65—100
Glucose-tolerance test (50 g.)	80—150—70	—	—
Urea (mg./100 c.cm.)	25	—	—
Sodium	297	—	300—325

Progress.—Feb. 23: Urine normal. Feb. 25: B.M.R., -9%. Fractional test meal: Histamine-fast achlorhydria without evidence of stagnation or organic lesion. March 9: Glucose-tolerance test—normal curve; electrocardiograph, "T₂ inverted" (Dr. Harold Isaacson). March 12: B.M.R., -37%. March 24: Insulin sensitivity test (Fraser and Smith, 1941). As there were clinical grounds for suspecting pituitary insufficiency, one-third of the standard dose of insulin was used—i.e., 0.1 unit per 3 kg. of body weight. After 1.4 units of insulin had been given intravenously the blood sugar fell from fasting level of 78 mg. per 100 c.cm. to 38 mg. per 100 c.cm. in 45 minutes and 30 mg. per 100 c.cm. in 60 minutes. In the healthy subject symptoms of hypoglycaemia should not persist after this one-hour point. As the patient then showed slight clouding of consciousness and a slight squint, the test was cut short by 50 g. of glucose orally, and an intramuscular injection of 0.42 c.cm. of 1:1000 adrenaline. The lowest figure for the systolic blood pressure was 82 mm. Hg 40 minutes after the insulin. She was admitted to hospital for a rest and was discharged two days later feeling no ill effects.

[The following explanation of the insulin sensitivity test is quoted from Fraser and Smith (1941): "The rate of the initial fall in the blood sugar differentiates normal or increased insulin sensitivity from insulin resistance; and the speed of the subsequent return to the fasting level will indicate any tendency to persistence of hypoglycaemia—that is, a delay in return will indicate 'hypoglycaemia unresponsiveness,' which may be found mainly in hyperinsulinism, hypo-adrenocorticism, or panhypopituitarism. Thus the characteristic result of this test in panhypopituitarism is a normal rate of fall associated with an abnormally slow return to the fasting level, or 'hypoglycaemia unresponsiveness.'"]

The accompanying Graph shows the slow and prolonged fall of the patient's blood sugar and the typical delayed rise. Fraser and Smith's "index of hypoglycaemia unresponsiveness" is 320 (normal 550±70). The result of this test, therefore, was further evidence for the presence of a lesion in the anterior hypophysis.