Clinical Notes and Cases.

A CASE OF PELLAGRA.

By E. Barton White, M.R.C.S.Eng., L.R.C.P.Lond.,
Medical Superintendent, Bristol Mental Hospital; and

A. L. Taylor, M.D.Leeds,
Pathologist, Bristol General Hospital and Bristol Mental Hospital.

Pellagra in this country is a comparatively rare disease, and so far as records show, only two cases have previously been encountered at the Bristol Mental Hospital. A third case which has recently come under observation may justify some description and comparison with the two previous ones, which were reported fully in 1927.

Since 1909, when the late Prof. Robertson of Edinburgh described the condition in a Shetland girl, practically all the pellagra cases in this country have occurred amongst patients suffering from one or other of the psychoses; the vast majority therefore have been met with in mental hospital practice, and we owe much of our knowledge of the condition to the late Dr. G. A. Watson, Pathologist to the Lancashire Mental Hospitals, who described no less than 54 cases which he observed personally.

Our attention was attracted to the present case in July, 1931, when she was undergoing verandah treatment, by the excessive pigmentation of the exposed skin compared with that of her neighbours, who were only slightly sunburned. Subsequent investigation confirmed the diagnosis of pellagra, which pursued an unusually acute course, death supervening within two months of the onset.

Family history.—Very poor. The mother was a certified patient in the hospital at the time of patient's admission, suffering from melancholia, with delusions of unworthiness and persecution, and gradually drifting into dementia. The father had died at 72 from cardio-vascular changes. The only sister was said to be frail and under-nourished. One of the three brothers was healthy; the other two suffered from pulmonary tuberculosis, one of these dying in August, 1931.

Personal history.—The patient was a single woman, æt. 26, the eldest of five children. Had worked in a cardboard and paper factory, but was frequently absent through ill-health. She had been in a sanatorium on two occasions as an

early case of pulmonary tuberculosis. She was always unstable, either depressed or excited, and was said to have had a nervous breakdown 14 months previous to admission. Had suffered from indigestion and gastric trouble for some years. Menstruation scanty and irregular. Admitted to this hospital in March, 1928, certified by her doctor as follows:

"Agitated, restless and confused; has delusions that her sister has made her deaf and that her father has robbed her of money; also hallucinated, hearing her mother screaming. Is probably suffering from pulmonary tuberculosis."

Condition on admission.—Patient was a brunette with sallow complexion, poorly nourished and showing signs of recent wasting. Height 4 ft. 9¾ in., weight 6 st. 4 lb. Signs of tuberculous disease at left apex. Pulse 120; faint presystolic murmur at apex. Temperature 97·8°, rising to 99·0°. Teeth in poor condition, but no obvious pyorrhœa. Urine, acid, specific gravity 1016, trace of albumen, no sugar. Blood-count: Red blood-cells, 5,050,000; hæmoglobin, 90%; leucocytes, 4,000. Thyroid gland not enlarged. All reflexes normal, but pupils dilated; no nystagmus, no ankle clonus. She was resistive and difficult to examine, but sensation in the limbs appeared below normal. Mentally she was dull, mute and solitary, negativistic and resistive to all attention. She lived in a state of phantasy, sometimes laughing and muttering to herself, and was at times hallucinated. She refused her food and was faulty in her habits. A diagnosis of katatonic dementia præcox was made.

Progress of case.—Physically there was some improvement during the eighteen months following admission, and the pulmonary condition remained stationary, with normal temperature, but negativism, including refusal of food, persisted throughout the illness, and in spite of periods of enforced feeding by tube, at the end of the second year her weight had dropped to 6 st.

Onset and Course of Pellagra.

The onset of pellagric symptoms commenced in July, 1931, when, as stated, the light-dermatitis was first noticed. This appeared as a dusky red erythematous rash over the face, ending abruptly at the scalp margin, with pigmentation most marked over prominent points. It extended over the ears, ending at the posterior margin of the helix. The submental region was clear, but the rash appeared over the front of the neck in a symmetrical butterfly-wing pattern, missing the hollow of the suprasternal depression and accentuated along the anterior margins of the sternomastoid muscles. The dorsa of the hands were similarly affected, the knuckles showing the deepest pigmentation; the rash extended upwards to an oblique line running across the outer aspect of the forearms, its extent coinciding precisely with the area exposed to sunlight.

Under suspicion of pellagra the patient was removed from the verandah to a shaded part of the dormitory, and subsequently all the cardinal features of the disease rapidly developed:

(1) *Dermatitis.*—The character and distribution of the rash was typical of the disease, and almost identical with that of the cases previously reported. After removal to subdued light the affected skin did not recover, but became dry and scaly, tough and thickened, with loss of elasticity. Cracks appeared in the skin-folds, and persisted as shallow ulcers surrounded by greyish-red pigmentation. The eruption on the hands extended round to the thenar and hypothenar areas with a definite pigmented line of demarcation, and ulceration developed between the fingers. Sores appeared at the corners of the mouth and fissures on the lips. There were

numerous cracks on the face, which became infected, and in three weeks thick scales or scabs were shed from between the suppurating areas.

(2) *Stomatitis.*—The tongue became swollen and dark red, showing teeth indentations and marginal ulcers. Ulceration also appeared on the gums and in the buccal cavity, in spite of every effort to keep the mouth clean.

(3) *Diarrhœa.*—This had not previously been noticed, and first made its appearance some ten days after the skin eruption. It continued intractably till death. The stools were frequent, watery in character and contained particles of undigested food; blood was not noticed, and cultures failed to yield dysenteric or other pathogenic organisms.

(4) *Nervous lesions.*—These were slight in character, and not readily discovered owing to the obvious difficulties in examining a resistive patient. Sensation, however, as shown by muscular response to pin-pricks was definitely impaired, particularly below the level of the elbows and knees.

The patient subsequently went rapidly downhill, in spite of a special dietary including milk, raw eggs, Benger's food, oranges and lime-juice, calculated to restore vitamin deficiency. As there was persistent refusal of food no solids could be given, and emaciation became extreme. During the last two weeks she showed signs of septic absorption and the temperature rose to 101°. Death finally occurred in September, 1931, two months after the appearance of the first symptoms.

Post-mortem Findings.

The body was that of a very emaciated, prematurely aged female, showing a faded dermatitis of the face and neck and over the dorsum of the hands. Weight 3 st. 7 lb.

Tongue and pharynx.—Irregular shallow ulcers were present at the sides and on the dorsum of the tongue in its posterior half. Pharyngeal wall pale and smooth. Buccal mucosa ulcerated.

Thorax.—Pleuræ: Old adhesions over both upper lobes.

Lungs: Generally congested, with patchy areas of bronchopneumonia in both lower lobes. There was much puckered scarring at both apices, and in the left apex an area of active tuberculous caseation 1½ in. across.

Heart: No gross abnormality. Valves healthy. Myocardium pale and flabby.

Abdomen.—There was complete absence of omental and mesenteric fat. The stomach and intestines throughout were remarkably thin and atrophic, and practically devoid of contents. Internally the stomach showed flattening of the rugæ, and a pale thin mucous membrane to which small shreds of mucus were adherent. There was some submucous hæmorrhagic stippling, commonly seen as a *post-mortem* change. The small intestine was thin and atrophic, and tore readily under slight tension. Its mucosa was pale, and the

valvulæ conniventes were small and widely separated; the Peyer's patches were very ill defined. The large intestine was similarly atrophied and showed small areas of shallow ulceration in its sigmoid portion, but with little evidence of inflammatory reaction surrounding them. Microscopically the atrophic changes described were most advanced in the small intestine, although readily demonstrated also in the stomach and large bowel. All parts of the wall were greatly thinned, and their wasted appearance contrasted strongly with the normal tissues sectioned as controls. It was difficult to assess the amount of damage in the mucous membrane owing to the auto-digestion which here rapidly supervenes after death, but it was clearly seen that the intestinal villi were smaller, shrunken and widely separated, and showing surface desquamation in remarkable degree as compared with the normal controls. The submucous and muscular coats were narrow, and in the former very few scattered cells were found, mostly lymphocytic in type. The Peyer's patches and solitary follicles shared in the general atrophy and were diminished in both number and size. In the large bowel a similar condition was found, and in many places the crypts were cystic and lined by a flattened epithelium very suggestive of reversionary atrophy. The shallow ulceration in the sigmoid colon was clearly a terminal dystrophic event, and here inflammatory reaction was entirely lacking.

Abdominal lymph-glands were not enlarged.

Liver and kidneys were slightly enlarged and showed considerable fatty changes.

Spleen much enlarged, and on section very soft and friable.

Microscopically these organs showed the typical appearances of acute toxæmia, without doubt due to terminal infection.

Endocrine glands.—The thyroid, thymus, pituitary, suprarenals and ovaries presented no abnormality to the naked eye, and were normal histologically.

Nervous system.—The brain and spinal cord showed no gross macroscopic lesion, and were examined microscopically for degenerative changes. In the dorsal cord these were slight but quite definite; by the Weigert-Pal method small areas of demyelinization were demonstrated in the posterior column of Goll and also in the antero-lateral columns on both sides. In sections stained by hæmatoxylin and eosin, under high-power magnification, the affected areas were found to contain degenerated fibres and numerous corpora amylacea, indicative of long-standing tissue breakdown. Nerve-cell changes in the cornua were relatively slight.

Commentary.

The clinical and pathological features of the case above described conform in all essential particulars with the classical description of pellagra, although in the present instance the course was unusually acute.

The case presents an interesting comparison with the two previously reported from this hospital; all were young adult females in the third decade; all were suffering from one or other form of dementia præcox; further, all showed refusal of food. In each case symptoms of pellagra came on after mental disease was fully established, and in each the syndrome was typical, *viz.*, an association of light-dermatitis, stomatitis, gastro-intestinal disturbance and sensory loss due to spinal cord degeneration. All three cases were fatal in periods varying from two to eight months.

The ætiology of pellagra is still a controversial and unsettled question. Many authorities favour the view that a preliminary avitaminosis is essential for the production of the disease, and hold that a dietary deficiency in vitamin B is an important factor, basing their views on the work of McCarrison and Cramer, who showed that gastro-intestinal atrophy may be produced in experimental animals by depriving them of this substance in the diet. Other theories which have received various support suggest a deficiency of protein, either quantitative or in biological value, an infective agent, and endocrine deficiency. A full discussion of these divergent views has been presented by Kimber (this journal, 1927, lxxiii, p. 443), and need not be repeated here. There is as yet no general agreement, and we incline to the view expressed by Kimber and Watson, that pellagra should be regarded as a syndrome which may result from a number of different factors, while holding that deficiency of the appropriate vitamin is the most important agent. It appears to us reasonable to suppose that the gastro-intestinal disturbances are the first to be established, followed by abnormal absorption of toxic substances, resulting in the peculiar light-dermatitis of the disease. The typical skin-lesion recalls the light-sensitiveness found in congenital porphyrinuria, but absent in the acquired hæmatoporphyrinuria of sulphonal poisoning. Porphyrin is a structural unit common to all hæmoglobins and chlorophylls; it is iron-free, and composed of four substituted pyrrhole groups. One variety, coproporphyrin, is normally present in the bowel, and it may be that the atrophied gastro-intestinal wall in pellagra becomes pervious to this photodynamic pigment and excessive quantities are absorbed. Similarly the toxic absorption from the small bowel may well account for the spinal cord changes, which resemble closely the subacute combined degeneration of pernicious anæmia. Indeed, in the initial stomatitis and smooth sore tongue, with bouts of diarrhœa and the not infrequently reported achlorhydria, pellagra has many points of contact with this disease.

In the present case the light-dermatitis first suggested the diagnosis, and diarrhœa was not noticed until later, but the markedly atrophic condition of the bowel wall demonstrated *post-mortem* suggested that the intestinal lesion had been present much longer than was suspected on clinical grounds, while histologically the cord changes were quite definitely of chronic type.

The diagnosis of pellagra is readily made once the typical syndrome is established, but it appears that by this time treatment is practically hopeless, and in the present case, as well as in the previous ones encountered, the disease proved rapidly fatal. It would seem therefore advisable to regard all mental hospital patients who refuse their food as potential pellagrins, and to anticipate the possible approach of the disease by carefully revising their dietary, so as to ensure an adequate protein and vitamin content. In this connection it is important to note that the so-called vitamin B is in reality a complex substance consisting of at least two allied but distinct factors; B1, deprivation of which leads to the disease beri-beri, and B2, which is thought to be associated with pellagra. In dogs deficiency of this fraction leads to the disease black tongue, and in rats to a dermatitis with loss of fur. Both factors are present in birds' eggs and yeast, but B2 is more abundant in milk, meat, green vegetables, potatoes and roots. The constitution of a suitable dietary for all suspected cases should, therefore, be a simple matter; but it need hardly be said that the persistent refusal of food so frequently encountered amongst mental patients is itself a great stumbling-block, and may indeed of itself be an important factor in precipitating the onset of the disease.