frequently played. Here we found submerged stones and weeds literally covered by the larvae and pupae of *Simuliidae*. We also came across small swarms of the winged forms, and captured numerous specimens which have not yet been determined.

The second case is reported by Dr. D. Owen Williams, of Glandovey, Cardiganshire. He says:

After receiving last Saturday's issue of the BRITISH MEDICAL JOURNAL on the subject of pellagra, it occurred to me that I had recently attended a woman aged 63 or 68 at Borth, a seaside resort in Cardiganshire, who has had an erythema-like dermatitis on the backs of both wrists and hands. They were swollen, brownish-red in appearance, with scales coming off, and I thought that it might be a form of psoriasis. It caused much pain of a burning character. Soothing ointment suited it, and some days it appeared much better, but it soon reappeared again. It comes on in the spring and the autumn. I saw her daughter on Saturday afternoon, and she told me that the patient was much better, and I find that she has had it for a considerable number of years (over twenty). But what was curious in her case was that she had a sunburnt (in appearance) erythematous rash on the bridge of her nose (brownish-red), over an inch in length and about half an inch in width and bilateral. She also had (on the upper lip especially) similar brownish-red sunburn-like patches on the edges of the lips which were also swollen and dry. These patches caused an itching pain. They have now disappeared. When I first saw the patient, on April 4th, she seemed to have had a cold, but with no temperature above normal. She told me that she suffered from intense pain in the head. She also felt a little depressed and occasionally had a little pain in the lumbar region, but there were no other nervous symptoms or signs. She seems to have kept her age very well, and is somewhat stout in appearance.

Behind the house there is the river Serry (two or three yards away), and beyond this again, extending for some miles, is the Borth bog, and running immediately past the back of the house there is a watercourse (very often filled with weeds). This is the first year she had anything on the nose and lips.

This is certainly a case at least for differential diagnosis. I have never heard of any similar case having occurred in the district. Some twenty or thirty years ago there were occasional cases of ague in the villages at the other end of the bog.

What struck me about this woman were the patches on the nose and on the lips, and when I read about pellagra it seemed somewhat curious.

So far I have not had time to see this case, but Dr. Williams's notes leave little doubt as to the possibility of its being a case of pellagra.

On July 15th, Dr. G. S. Blandy informed me of a possible case at the Napsbury Lunatic Asylum, and said that both Dr. L. W. Rolleston, the superintendent, and he would be very pleased to show me the case if I cared to go. This I did at once. I found a young woman suffering from that grave form of the disease known by the name of typhoid pellagra. The patient was lying in a state of coma vigil, with lower extremities in forced extension, the feet in plantar flexion. She presented intense neuromuscular excitement, tremors, subsultus tendinum, vivid hallucinations. She had been admitted on May 15th with slight fever, rapid pulse, and tendency to collapse, her mental condition being that of acute confusional insanity. About June 16th her physical condition became much worse, and she developed an intense stomatitis. On July 1st a pellagrous dermatitis appeared on face and backs of hands. On the face the eruption affects principally the middle of the forehead, the alae of the nose, the lips, and the chin. On the hands it occupies the backs, extending above the wrists, and forming a deeply pigmented band or cuff around each wrist. There are excoriations between the roots of the fingers and small pustules about the mouth. The mucosa of the lips, tongue, and inside the cheeks is markedly red and denuded. She has a tendency to loose stools. The urine contains albumen.

Dr. Blandy also told me of two other probable cases of pellagra which had died in the asylum—the one in July and the other in November, 1912.

The first was an old woman, aged 74, whose mental condition was one of confusion with motor restlessness and excitement. She was admitted on April 1st, 1912,

and had several syncopal attacks while in the asylum. In June she developed a pellagrous eruption and in fact under the date of June 10th we find the following entry: "She recently sustained a burn on either hand as the result of the action of the sun," but the eruption healed very slowly. Towards the end of June she became more demented, and after a severe heart attack she developed bronchial catarrh and died on July 3rd. The autopsy revealed extreme arterial degeneration and chronic nephritis.

The second case was that of a woman, 37 years of age when admitted in 1906. It was a case of manic-depressive insanity, the excited phase predominating. She suffered from stomatitis and diarrhoea, ascribed to her debilitated condition. She also developed a pellagrous dermatitis, but the only mention of it appears in October, 1912, when we find the following entry: "A troublesome dermatitis is only now beginning to clear up." Dr. Blandy remembers that the eruption appeared on the forehead, around the mouth, on the alae nasi and on the backs of the hands. It was supposed that it had commenced as a severe sunburn as the patient had been running about in the open air without a hat, but it continued for so long that this explanation was felt to be very insufficient.

The indigenous cases so far recorded are now sufficient, I think, to show that pellagra is certainly endemic and widely distributed throughout the British Isles. It is to be hoped, therefore, that physicians, especially those practising in rural districts, will soon learn to recognize it, and then we shall know something about its prevalence. My experience of the history, epidemiology and distribution of pellagra in several countries leads me to believe that there must be hundreds of unrecognized cases in Great Britain. As the cases already described amply prove, the disease is one of extreme gravity, and it is to be hoped that, following the example set by the United States, the Government will institute an inquiry.

With regard to the etiology of pellagra, the British cases absolutely disprove the maize theory of its causation.

NODULAR LEUKAEMIA.

BY

GORDON R. WARD, M.B.LOND.,
LONDON.

A PAPER by Reid, of Belfast, and others in a recent issue of the JOURNAL¹ raises anew the interesting question of the "associated syndromes" of leukaemia. These are four in number, and with the exception of one, chloroma, they are not necessarily a part of leukaemia, but may be met with in other conditions. These other conditions are rather indefinite when one looks at classical descriptions, and in consequence great confusion has arisen. The syndromes have been raised to the status of distinct diseases, and all classes of case showing them have tended to be included as examples of these diseases without reference to their proper classification.

An example will make this more apparent. There may be in leukaemia a great multitude of skin lesions—more or less definite tumour formations—and these may even be preceded by a "pre-fungoid" stage. Such cases have been included in the literature of dermatology as examples of "mycosis fungoides" and "lymphodermia perniciosa of Kaposi." But these titles also cover many cases which, whatever may be their true nature, are not examples of leukaemia. Hence it is correct to state that many cases reported as mycosis fungoides are in reality cases of leukaemia, and the frequent absence of blood examinations makes a final decision impossible. But it is not possible to assert that all such cases are examples of leukaemia.

The four "associated syndromes" are as follows: The first is the syndrome in which one finds symmetrical skull tumours, often of a green colour, but not always, and resulting in blindness, deafness, etc. There may also be lesions of other bones, or, rather, of the periosteum in other situations. This syndrome has usually been called "chloroma," on account of the green colour of the lesions. All cases with a green colour and some others are examples

of leukaemia, but a similar syndrome may arise in supra-renal sarcoma. The green colour may be found in the marrow, etc., of cases of leukaemia which have no skull lesions, and may be absent in the skull lesions of other undoubted cases of leukaemia. Hence the syndrome is unduly limited in one direction and unduly enlarged in another if we make the green colour an integral part of it. Hence the suggestion of the name "nodular leukaemia" for this and some other manifestations, in order that the existence of tumours might be apparent, while the connexion with leukaemia was at the same time not overlooked.

The second syndrome is that above mentioned as the "mycosis fungoides" syndrome. It lacks any other name, and hence is properly included as nodular leukaemia if a multiplication of names that subsequent research may render quite valueless is to be avoided. In these cases there are a number of nodules either just under the epidermis or in the deeper subcutaneous tissue, and these are very commonly more or less symmetrical in distribution. They may come and go with great rapidity, but this is by no means always the case. A similar syndrome may occur in cases of sarcoma, but the leukaemic nodule very rarely, if ever, ulcerates through the skin, whereas the sarcomatous nodule may easily do so.

The third syndrome is often described under the name of Mikulicz's disease. It is characterized by swelling of the lacrymal, parotid, and submaxillary glands. The swelling is usually chronic and painless, and does not tend to suppurate. As a matter of fact this "symmetrical glandular syndrome" is not infrequently of greater extent than would appear, for, besides the glands mentioned, the mammae or ovaries or testes may be affected. The swellings are always symmetrical, and microscopically show an infiltration of the gland substance with cells similar to those seen in the blood. I would include examples of mammary swellings in the syndrome whether the salivary glands were infected or not, since there seems to be no reason to suppose that the problem of their involvement is in any way different from that of the other glands. This syndrome is met with in mumps, and in some other conditions, but rarely.

The fourth syndrome is that of persistent priapism. This of course may be met with in other conditions, but the most common single cause of persistent priapism has been shown by Warthin to be leukaemia. This, like the others, is of the nature of an infiltration, although some of the infiltrating cells may multiply *in situ* and give rise to more or less distinct nodules standing out from the surrounding infiltration. If the infiltration itself is too slight to be appreciated clinically the nodules will appear to be the sole lesions. But even in the case of skull nodules this is not, as a matter of fact, the case; there is always infiltration as well as nodule.

What, then, is leukaemia, if it can be associated with all these different syndromes, not as a result but as a primary and determining factor? In the first place, we are entitled to say that it is one of a definite group of diseases—that is, the generalized affections of blood-forming tissues. In this group are also Hodgkin's disease and the Gaucher type of splenomegaly. It is possible, but not yet proved, that multiple myeloma should be included. In all of these there is something acting which calls into activity the cells of all blood-forming tissues, marrow, glands, spleen, and often thymus and liver. In each of these places autopsy may reveal foci of active growth identical in all places but not of the nature of metastasis nor replacing the original tissue of the part except by passive pressure. All these foci are, in fact, proliferations of cells pre-existing in those positions. In Hodgkin's disease and in Gaucher splenomegaly there is a considerable body of opinion that the endothelial cells are the ones to be stirred up in this way to new and abnormal growth. These endothelial cells are almost certainly those of the lymphatic spaces and channels. In leukaemia we are not so sure what cell is affected first, although we know that a great variety of cells results—just as in Hodgkin's disease the abnormal cells are not all of the same type. But whatever cell it be it is very closely associated with the lymphatic channels, so closely that one cannot avoid the conclusion that it is the carrying off of these cells by these channels which produces the sudden changes in size of spleens, etc. This change is

even more marked in the case of skin tumours or nodules. Whence do these come? Probably from lymphatic cells in association with lymphatic channels, for the only parts of the body in which these nodules may not be met with are precisely those in which lymphatic channels are not found—namely, the nerve tissues and cartilage. They may be found in the choroid plexus or on the periosteum, but no nearer. There is no particular difficulty in understanding that whatever calls forth such undue activity in normal blood-forming tissue may also call into existence blood-forming tissue in any part of the body where lymphatic cells and channels are found—in fact, it is clinically certain that this is the case.

It will be noted that this class of case is sharply separate from malignant growths—"cancers." These eat into surrounding tissues, they consume even bone. Leukaemic nodules infiltrate, but do not destroy, and they never touch bone. Other growths cause a reaction in the surrounding tissue—there is no reaction to leukaemic nodules. Sarcoma cells may eat their way through a vessel, and thus a very few fragments of tissue may escape into the blood stream, or they may grow as a solid cord through the length of a vessel, but the cells of leukaemia have natural access to vessels without destroying the walls—hence they are found in the blood stream in enormous numbers, but never as fragments of tissue, always as single cells. There is not on record any case of undoubted sarcoma in which the cells were found in the blood stream during an ordinary blood examination, there are no cases of any sort in which it was alleged that cells of any but a small round-celled sarcoma reached the blood stream, and these latter on investigation are found to be of no value when subjected to criticism. These statements are, of course, not made from a perusal of the literature of the whole world, but yet after considerable attention to the matter.

Leukaemia, as one of the generalized affections of blood-forming tissues, is distinguished by the type of cell involved. It differs plainly from that met with in Hodgkin's disease or in Gaucher splenomegaly. Nevertheless, although constantly different from these, it is not constantly the same. This is because the most specialized cells proliferate first. The stimulus may act on a primitive cell, but at first it is able to send out its children in the clothing to which the world is accustomed. But later the hurry begins to tell, and the daughter cells are less specialized; later still, the primitive cell itself comes forth, and then, as a rule, the patient dies.

The difference between the two types of leukaemia is more difficult to lay down, and, even if an individual view could be stated, it would not be accepted. Fortunately the treatment is the same, so that such a statement would be of theoretical rather than practical interest at the moment.

REFERENCE.

¹ BRITISH MEDICAL JOURNAL, June 21st, 1913.

A CASE OF ECTOPIA CORDIS.

By WILLIAM ROLLAND, M.D.,

HONORARY ASSISTANT SURGEON, BOLTON INFIRMARY.

As these cases are of such rarity that they may be looked upon as teratological curiosities, it seems desirable that a recent example of the condition, which occurred in the practice of the writer, should be put on record.

The child was one of twins born on January 25th, 1912. As nearly as could be determined the pregnancy had only lasted six and a half months. The mother was a primipara, aged 38, under-sized, anaemic, and with a generally contracted pelvis. She was attended in her confinement by a midwife, and I was called in later to deal with a very adherent placenta, which had to be removed under chloroform. No history of congenital abnormality could be obtained on either side of the family. One of the twins (female) survived about six hours, its death being due to prematurity. It presented no abnormal condition. The other (male) was born dead, but death had evidently occurred only a short time before, probably owing to the pressure to which the heart must have been subjected during delivery.