above-mentioned solvents. The first account of the drug in English medical literature is in THE LANCET of Jan. 13th, 1900, and so far as I am aware it was first employed by Messrs. Parke, Davis, and Co. in 1899 as a preservative for their solutions of adrenalin.

On account of its local anæsthetic effect I was prompted to employ this drug in painful and irritable conditions of the stomach, such as gastritis, cancer, gastrodynia, ulcer, and especially in those cases of pain, vomiting, and hæmatemesis so frequently associated with chlorosis and scarcely yet completely removed from the category of gastric ulcer, with which they are by no means identical. In doses of five grains or more in petroleum emulsion it has a remarkably soothing effect both on pain and vomiting and exercises a deterring influence on fermentation, resembling in this carbolic acid. It was while using chloretone for this purpose that its hypnotic effect became apparent, and I have since employed it satisfactorily in ten-grain doses simply to procure sleep, though the state of quietude induced by the smaller doses is itself a very great alleviation of painful and protracted illness, such as the gastric conditions to which I have referred.

The local anæsthetic effects have been found of value in vaginal pruritus as exercised by a 0.4 per cent. solution in warm water, or by five-grain suppositories in hæmorrhoids. The sedative effect on the brain, similar to that of the bromides but more rapidly induced, associated as it is with a similar effect on the stomach, led to its early employment for sea-sickness, and it is in connexion with this distressing malady that its reputation has chiefly been established. Five grains in powder taken a quarter of an hour before embarking will generally insure complete immunity from sickness during the Channel passage even in rough weather, and the drug does not appear to lose its efficacy by repetition, as is the case with some others. A young French lady, who was invariably ill during the crossing to Dieppe, since being fortified with chloretone has only once suffered and that in a way which suggests a useful hint in prescribing. Having performed the outward journey "*tute, cito et jucunde*" under the influence of one of the five-grain powders of which she was provided with four, the other three were carefully deposited in a purse against her return after the summer holiday. Then accompanied by a friend, to whom she promised immunity from the discomforts of the sea on the strength of this new remedy, she confidently embarked and proceeded to share the remaining doses. One paper after another was opened but all were empty. In the hot weather the chloretone had evaporated and vanished, leaving nothing behind but disappointment and the prospect of a miserable voyage, which was amply verified in both cases. As negative evidence this was distinctive testimony to the value of the drug and has been subsequently remedied by inclosing it in impervious wrappers such as paraffin paper.

When taken at intervals in similar doses longer voyages have been undertaken without discomfort—such, for instance, as that across the Atlantic. The drug was taken about 20 minutes before meals two or three times a day during rough weather and the journey was completed without a qualm. A more general knowledge of this remedy will certainly save a large amount of discomfort and in those who suffer continuously will enable journeys to be undertaken which were formerly dangerous or actually impossible.

I have dwelt upon these effects of chloretone as they have led up to its employment in another class of cases for which we have hitherto possessed no efficient remedy. I refer to chorea. During the past 12 months the opportunity has occurred of exhibiting the drug in some 14 cases and the result has been so striking and uniform that though the number is small it is worth making known that those who have wider opportunities may further test its reliability. In these cases, both boys and girls between the ages of seven and 12 years, five grains of chloretone in half an ounce of petroleum emulsion were given three times a day for two and sometimes three days; there was in all of them such a marked diminution of the choreic movements that the dose was then halved and sometimes given only twice and even once a day according to the severity and progress of the case. The number of days in which the drug was continued varied from five to ten, by which time it was omitted and either steel wine with arsenic or cod-liver oil was substituted to meet the anæmia and feebleness which usually accompanied the disease. Under this treatment the duration of choreic movements was limited to nine days and the stay in hospital to three weeks on an average. This is a great advance in the treatment of chorea, which even with the advantage of hospital

régime usually extended to double and treble that time. These advantages consist in rest in bed with isolation and liberal dietary. When convalescing the patients were encouraged to knit or crochet or to use the hands in some such manner so as to practise purposive movements and also as a test of steadiness.

Many patients on admission were unable to feed themselves, experienced considerable difficulty in speech, and in some cases needed padding in their cots to prevent bruising in their uncontrolled movements. It was found that those cases which came under treatment early benefited most. Of the 14 which took chloretone, two were removed from the hospital before they were quite recovered on account of contracting rôteln, and two others resisted the treatment for a longer time—one, a girl, aged ten years, who had suffered from chorea for three years with short remissions, and another girl, aged seven years, who, after four months' chorea before admission, appeared rather to be cured by the relief of constipation, which had been a marked feature, this being effected in 21 days.

With any comparatively new drug exerting marked beneficial effects the question always arises as to drawbacks, and in the present instance there are some, though not of serious account. Two of the cases exhibited exfoliation of the skin on the hands and heels which gave rise to a suspicion of scarlet fever—one after ten days in hospital without fever or rash and the other shortly after removal on account of rôteln, of which there had been an outbreak in the hospital. The other 12 cases did not show this and the retention of one such case in the hospital and subsequent removal to the convalescent home did not lead to communication of scarlet fever to anyone else, so this exfoliation of the skin may be regarded as an occasional effect of the drug.

In two of the earlier cases treated, possibly owing to the physiological effect of chloretone being carried rather too far, there was marked somnolence, the child lying in any attitude in which he was placed and rousing only to take food. This passed off in a few hours on discontinuing the drug. The only other objection taken account of was the cost (4s. an ounce is somewhat expensive in hospital work), but considering the small quantity used and the comparative infrequency of the cases it is not serious and with increased demand it will no doubt be reduced.

As regards the permanency of the cure further experience is required; one of the cases cited was readmitted in about three months with a relapse, and on the other hand another was successfully treated which had relapsed after treatment by arsenic. Like the treatment of rheumatism by salicylates the effects of the specific drug requires to be followed by a tonic *régime* in most cases since the little patients are usually anæmic and feeble in addition to suffering from the spasmodic movements. Where endocarditis coexists salicylates can be combined with the chloretone or may be applied to the skin instead, but for the chorea itself chloretone appears to be as much a specific as the salicylates have come to be regarded in rheumatism.

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"PULMONARY HYPERTROPHIC OSTEO-ARTHROPATHY" OCCURRING IN A CASE OF CONGENITAL HEART DISEASE (!).¹

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THE patient, a young unmarried woman, aged 21 years, was recently admitted to University College Hospital under the care of Sir Thomas Barlow, to whom we are indebted for permission to publish the notes of the case. The patient had suffered from palpitation, breathlessness, and blueness since birth. During the last ten years she had suffered from pains in the limbs, both in the ankles and wrists and in the shafts of the long bones of the legs, more particularly after standing and walking. She had scarlet fever at the age of ten

¹ Report of a case shown at a meeting of the Clinical Society of London held on March 22nd, 1907.

years, but no other illness. There was no history of acute rheumatism or of syphilis in the family, the other members of which were quite healthy. The patient was very cyanosed and clubbing of the fingers, the toes, and the nose was well marked. A systolic murmur was heard over the præcordium, probably due to defect of the interventricular septum; it was best heard to the left of the sternum and in the third and fourth intercostal spaces, but was also audible at the apex beat of the heart and in the second intercostal space; it was not conducted towards the left clavicle. There were no signs of any of those diseases of the lungs which have hitherto been found associated with clubbing of the fingers and osteo-arthropathy; the tuberculo-opsonic indices observed on five separate occasions by Mr. D. Embleton were 0.96, 0.78, 0.96, 0.96, and 0.82. The blood examination showed 8,320,000 red corpuscles and 9300 white corpuscles per cubic millimetre; the percentage of hæmoglobin was 150 and the colour index was 0.94; the polymorphonuclear cells numbered 60.2 per cent., the small lymphocytes 19.9 per cent., the large lymphocytes 12 per cent., the hyaline cells 6.9 per cent., and the eosinophile cells 1 per cent. Besides the clubbing above referred to there was obvious swelling of both legs due to thickening of the lower ends of the tibiæ and fibulæ, and there was slight swelling of the bones of the forearms, of the wrists, and of the shafts of the metacarpal and phalangeal bones.

Radioscopic examination.—Compared with the corresponding bones of the patient's sister, who was quite healthy and of almost the same height and build, there was very considerable enlargement of the tibiæ and fibulæ of both legs, especially of the lower two thirds, more marked in the right limb; irregular bony deposits were present at the attachment of the interosseous ligaments to the adjacent tibiæ and fibulæ. The upper halves of the shafts of the femora showed increase of the mass of bone, but in a more marked degree, especially in the right leg; the head, the neck, and the lower halves of the femora appeared to be normal. The first and second phalanges of the fingers and thumbs, the metacarpal bones, the first and second phalanges of the toes, the metatarsal bones, and the bones of both forearms showed very slight thickening; there was no bony increase of the terminal phalanges of the fingers or toes.

This case is of special interest in several directions. In the first place it confirms the belief that Pierre Marie's sign-complex is not a feature of particular forms of lung disease only, such as bronchiectasis, tuberculosis, empyema, neoplasm, &c., for the patient was quite free from any signs or symptoms of pulmonary disease. The changes in the bones and the joint pains constitute "osteo-arthropathy" which, combined with clubbing, is known under the title given by Pierre Marie² as pulmonary hypertrophic osteo-arthropathy; the latter observer and Bamberger³ considered that the genesis of this sign-complex depended on the effects of toxins formed in the lungs; we consider that everything points to the absence of any toxic focus in the lungs of this case; tuberculosis of the lungs, the most common infection in congenital heart disease, may yield no physical signs and yet be present; that this is not so in this case is shown by the existence of normal opsonic indices above quoted—a condition of affairs which could not occur if a tuberculo-toxin were circulating in the system so widely as to produce the above diffuse osteo-arthropathy. A mechanico-toxic cause of clubbing and of osteo-arthropathy has been advanced recently by Bécclère⁴ and by Groedel⁵ and confirmed by an observation by Berent⁶; clubbing of the fingers has long been known to occur in one hand⁷ in cases in which an aneurysm has caused interference with the circulation of the limb and Groedel and Berent have shown that bone changes may also occur in such cases; the toxic substance or substances must in these cases be generated locally and be derivations of tissue metabolism. Their retention, owing to the obstructed circulation, is considered to be responsible for the clubbing and for the bone and joint changes. We consider that this case gives support to the view of Bécclère and of Groedel because the greatest bone change is noticed in the

lower extremities, gravity tending to increase the stagnation of the blood in these parts; that mechanical obstruction is in the first place responsible for the change is also shown by the fact that the patient has suffered for as long a period as ten years frequently and immediately from pain in the lower limbs on standing or walking.

This case is finally a unique one, for, so far as we are able to ascertain, there are no other reports in the literature of cases of congenital heart disease being associated with Marie's sign-complex in the absence of lung disease; Bamberger's eighth case was one of congenital heart disease but was complicated by the presence of tuberculosis, and Thorburn's⁸ case (footnote to his paper), though occurring in a boy, is not stated to be due to congenital as opposed to acquired heart disease; the latter association has been established by Bamberger. The distribution of the changes, mainly in the lower extremities of our case, is also very unusual and, as already stated, in the absence of any focus of disease in the lung supports the view that clubbing and osteo-arthropathy are due to the effects of tissue toxins normally generated at the periphery but prevented from being rapidly removed owing to the impairment of the circulation, in our case dependent upon congenital heart disease, in others upon the existence of lung disease, of acquired heart disease, and even, it is stated, of impaired action of the diaphragm in cases of hypertrophic cirrhosis of the liver.

Clinical Notes:

MEDICAL, SURGICAL, OBSTETRICAL, AND THERAPEUTICAL.

TWIN OVUM IN A TUBAL PREGNANCY.

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THE rarity of the above condition lends interest to the accompanying illustration from a case recently under my care.

The patient, aged 39 years, married in January, 1890, had a miscarriage at about three months in May of the same year, had a uterine polypus removed 12 months later, and in February, 1892, was delivered of an eight months' child.

Twin ovum in tubal pregnancy.

In 1896 she had a "false conception" (the description seems to point to hydatid mole), followed by an attack of peritonitis

² Pierre Marie, *Revue de Médecine*, 1890, tome x., p. 1.

³ Bamberger, *Zeitschrift für Klinische Medizin*, 1891, Band xviii., S. 193.

⁴ Bécclère: *Semaine Médicale*, 1901, p. 94. *Bulletins et Mémoires de la Société Médicale des Hôpitaux*, 1901, vol. xviii., p. 283. *Gazette des Hôpitaux*, 1904, p. 754.

⁵ Groedel: *Münchener Medizinische Wochenschrift*, 1906, S. 264.

⁶ Berent: *Berliner Klinische Wochenschrift*, 1903, S. 75.

⁷ Sir Thomas Smith: *Transactions of the Pathological Society of London*, 1871, vol. xxiii., p. 74. Canton: *Ibid.*, 1865, vol. xvii., p. 428. Ogle: *Ibid.*, 1858, vol. x., p. 103.

⁸ Thorburn: *Brit. Med. Jour.*, 1893, vol. i., p. 1155.