in the form of an aqueous solution of its sodium salt (thermiol) also has a marked action in the development of leucocytosis, and can likewise be applied to the treatment of tuberculosis. Both these acids contain an unsaturated carbon chain attached to a benzene nucleus, the former acid having a double linking and the latter a treble bond, as indicated by the following formulae:

Since these substances are far more active physiologically than benzoic acid, $\text{C}_6\text{H}_5\text{CO}_2\text{H}$, which does not contain the unsaturated group, one may assume as a working hypothesis that this action is in some way connected with the presence in the molecule of the double or treble linking, this junction being known to be a point of great chemical reactivity.

In the course of a series of clinical investigations carried out by Dr. Lovell Drage with the glycerinum sodii cinnamatis a demand arose for a drug having a more pronounced action, and the author was thereby led to consider in what way the physiological activity of cinnamic acid might be enhanced.

The employment of benzene derivatives as therapeutic agents has amply demonstrated the fact that the presence of an amino- (NH_2) or a hydroxy- (OH) group in the aromatic nucleus greatly increases the physiological action of the parent hydrocarbon, and it therefore seemed likely that the use of a substituted cinnamic acid containing one of these groups might bring about the desired effect. Since the employment of amino-compounds of the antifebrin type is often attended by unpleasant secondary effects, the author was in the first place led to employ a hydroxy-derivative, and to recommend the use of sodium ortho-coumarate, a substance having the structure of cinnamic acid, with a hydroxyl (OH) substituent:

A glance at the foregoing formulae will show that ortho-coumaric acid is likewise somewhat similar in constitution to salicylic acid, these two acids standing in the same relationship to each other that cinnamic acid does to benzoic acid. This likeness to salicylic acid was also a determining factor in the choice of ortho-coumaric acid for medicinal purposes, bearing in mind the beneficial action of the salicylates in certain pathological conditions.

For hypodermic injections the author prepares a 22 per cent. aqueous solution of the sodium ortho-coumarate containing a slight excess of the free ortho-coumaric acid. The dichroic solution is quite limpid and stable, and as the salt is extremely soluble in cold water, even a higher concentration may be employed if necessary.

In all the cases hitherto studied the solution has induced a rapid physiological action, the leucocytosis being well marked and resembling that effected by the cinnamate.

Experiments have also been instituted on the sodium salts of the two isomeric coumaric acids with the view of ascertaining whether the change in the relative positions of the active groups brings about any appreciable differences in their physiological effect.

Sodium para-coumarate, prepared by the Perkin-Fittig synthesis from para-hydroxybenzaldehyde, is a much less soluble salt than the ortho-compound and accordingly an 8 per cent. aqueous solution was employed. The results obtained with equivalent quantities seemed to show that the action was of a similar nature, but rather less intense than that produced by the ortho-salt.

Sodium meta-coumarate which was employed in 20 per cent. aqueous solution had a very marked physiological action, being apparently even more active than the ortho-compound. The meta-coumaric acid required for this preparation was produced synthetically from meta-nitrobenzaldehyde.

From a chemical point of view the action of the meta-

acid is of special interest. It is well known that benzenoid ortho-compounds and para-compounds in general often resemble one another in their chemical and physical properties, whereas they frequently both differ markedly from their isomerides of the meta-series. In the case of the ortho-coumaric and para-coumaric acids the groups (OH) and ($\text{CH:CH.CO}_2\text{H}$) are in sympathetic positions, and might accordingly be supposed to act conjointly, but in the meta-compound these groups are in apathetic positions with respect to each other, so that the meta-acid might be expected to exhibit the dual properties of a phenol and a cinnamic acid, each substituent producing its physiological effect to some extent independently.

The three isomeric coumaric acids are certainly physiologically active, but it must be left for further experiments to decide which of these is likely to prove to be the most serviceable therapeutic agent. The investigation is being extended to other compounds of a similar type, and it is hoped that it may become possible to correlate the physiological action of these substances with their chemical constitution (compare Drage, BRITISH MEDICAL JOURNAL, April 29th, 1905).

TWO CASES OF UNILATERAL CONVULSIONS AND PARALYSIS IN YOUNG SUBJECTS ASSOCIATED WITH EXUDATIVE ERYTHEMA.

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THE following cases deserve to be recorded, both because the combination of the non-embolic hemiplegia of early life with exudative erythema seems to have escaped notice by previous writers, and because all new facts ought to be published which may help to throw a sidelight on the pathology of that variety of paralysis. The remarks on the cases will come in most appropriately after the latter have been described.

CASE I.

Severe Gastro-enteritis in a Boy of 12 years; Right-sided Convulsions and Hemiplegia with Aphasia; Bedsores; Striae Atrophicæ; Erythema Nodosum; Conjunctivitis; Alveolar Inflammation.

J. T., sent by Dr. McCallum of Tarbolton, was brought to me on October 2nd. As it was afterwards found that he was making very slow progress at home, it was arranged that he should come into my wards in the Royal Infirmary, and he was admitted on November 3rd. Dr. McCallum informed me that the boy had, on several occasions, had rheumatism in subacute form, and that he was an inveterate cigarette smoker. He never, however, had scarlet fever, measles, whooping-cough, or, indeed—apart from rheumatism—any illness until June 12th, 1903. On that day, possibly as a result of prolonged bathing, he began to suffer from pain and stiffness in his joints. These symptoms subsided after a few days, and were followed, in the course of a few days more, by severe pain, vomiting, and diarrhoea, which continued for a fortnight and caused such wasting and exhaustion that the patient became almost comatose. At this time convulsions began. They involved the right angle of the mouth, the right arm, and the right leg simultaneously, and were strictly confined to the one side. The attacks recurred frequently throughout the first two days, and then became fewer and less severe, until they finally ceased, a fortnight after they began. The patient was insensible for about five days, and spoke no word for three weeks from the time when the convulsions began. During this period the evacuations were passed into the bed, a bed sore developed in the sacral region, and linear atrophy of the skin took place in numerous areas about the knees and thighs. So far as was observed, the temperature was subnormal throughout. A trace of albumen was recognizable in the urine for a time after the convulsions set in, but not before. There was no headache or vomiting. The right hemiplegia and aphasia dated from the convulsive seizures. Sensation was not affected. Before his illness patient was in the fifth standard at school, and was regarded as a smart boy.

Three weeks after the convulsions began, he first uttered the words "aye, aye," and since then he has regained a considerable amount of language. Even at the time of his original visit, on October 2nd, his mother stated that he understood everything that he heard, and this is certainly the case at present. He cannot, however, name all the letters of the alphabet, though he recognizes some words. His writing of letters is very bad, particularly when he uses the right hand.

There is still some paresis of the right side of the face. The power of the right upper limb is still defective, the dynamometer registering scarcely 5 kilos with the right hand, as against 13 with the left. There is slight contracture in the flexors of the elbow. There is some wasting of the muscles of the right forearm, and this atrophy is associated with slight tenderness, but no wasting is recognizable in the hand. The leg is scarcely affected, so that the gait is normal. The two calves are alike in girth.

The heart, lungs and urine are normal. Ophthalmoscopic examination reveals no morbid change in the fundi. Apart from the tenderness

of the weakened muscles in the right arm, there is no sensory abnormality, and there is no satisfactory evidence of neuritis. The knee-jerks are present. The striae atrophicae are still present. Over the patella and above it there are, on the right side four and on the left side five well-marked striae. Several similar striae, mostly of smaller size, are present at the outer side of the right ankle, and on the front and outside of the left leg at or above the ankle. Sensation in the region of these striae is undisturbed.

The temperature began to rise on December 26th, and reached a maximum of 102.4° on January 1st. On January 4th, an eruption of erythema nodosum was observed to be developing on the legs; and in the course of the ensuing week the lesions increased in number on the legs, a few appeared on the lower parts of the thighs, and one appeared on the right forearm. By the end of another week, the eruption had faded away, and was represented merely by haemorrhagic stains. As the eruption subsided, the temperature declined, but it scarcely attained its normal till January 24th. After the erythema subsided, patient suffered for a time from conjunctivitis.

The attack of erythema was not associated with arthritis or with subjective symptoms, but after the eruption had been out for a few days the nodules were very tender on pressure. A culture inoculated with fluid withdrawn from a nodule remained sterile after forty-eight hours. The blood which afterwards flowed from the puncture, as well as blood taken from the ear, showed merely a contamination with the staphylococcus epidermidis albus.

There was again an elevation of temperature from February 6th to 13th in connexion with a large swelling which developed on the outer aspect of the right upper jaw. Though it was punctured or incised on three occasions, no pus could be found in this inflammatory swelling, but after the third operation it rapidly subsided.

It will be seen that, so far as the unilateral convulsions and paralysis are concerned, this case is very similar to one of the so-called infantile hemiplegia. Moreover, the onset in connexion with an acute illness rather adds to the resemblance. It is well known that two opposing theories are held as to the pathology of such cases of hemiplegia, and the diversity of opinion is readily explained by the fact that the patient rarely dies while the lesion is recent. When the brain is examined at a later date it is usually found to be the seat either of sclerotic atrophy or of porencephalus, and these changes are particularly apt to involve the motor area of the cortex—namely, the cortical distribution of the middle cerebral artery. These later changes are consistent with either theory. Thus, on the one hand it is supposed that the cerebral lesion results from vascular obstruction, and Gowers favours the idea of thrombosis in the artery or in a vein on the surface. On the other hand, Strümpell has suggested that the disease is acute polioencephalitis—an inflammation of the grey cortex comparable to the poliomyelitis which gives rise to infantile paralysis.

The present case, it might perhaps be said, illustrates, rather than solves, the difficulty of determining which variety of lesion was present. On the one hand, the intense prostration, and the changes in the blood, brought about by the persistent vomiting and diarrhoea, were admirably calculated to favour thrombosis in the vessels, and particularly in the veins on the surface of the brain. Moreover, the absence of fever and of optic neuritis is, to a slight extent, in favour of a non-inflammatory affection. On the other hand, it may be urged that the remarkable series of lesions from which the boy suffered, involving, as they did, the digestive tract, the brain, the skin, the conjunctivae and the alveolus, pointed clearly to the presence in the system of an infectious agent which caused inflammation in the brain, as surely as it did in the other parts which have been named. The negative result of an examination of a small quantity of blood from the general circulation and from a cutaneous lesion cannot be regarded as sufficient evidence against this theory.

The development of linear atrophy of the skin is one of the interesting features of this case. These lines or striae are similar to those which are seen on the abdomen and breasts of pregnant women, and on the abdomen in cases of ascites in either sex. They may also develop spontaneously on the shoulders, buttocks, and thighs. As a rule, they are not associated with any disturbance of sensation, but in 1861 Wilks¹ recorded the case of a hysterical girl in whom tender striae atrophicae developed on the legs and trunk. The same writer observed striae on the limbs, and especially on the knees, of a lad who had disease of one knee-joint. A similar localized change in the skin has occasionally been reported as following an injury to a nerve (Wilson,² Ohmann-Dumesnil³), or as following herpes zoster (Barie⁴). Bradshaw⁵ described a condition almost identical with that existing on the knees and thighs of the present patient as having appeared in a girl of 13 during a relapse of enteric fever; and Duckworth⁶ met with hyperaesthetic striae in a lad of 15, three months after

enteric. Shepherd⁷ has observed atrophic striae without disturbance of sensation, after enteric fever, in a male aged 15; in this case the fever was followed in addition by double parotitis, paralysis of one facial nerve, paresis of the legs, and fits. Atrophic striae have been noted by Osler⁸ after scarlet fever.

It is very likely that striae atrophicae developing in the course of acute diseases are often due, as under other circumstances, to prolonged stretching of the skin; for example, by pressure of the bedclothes upon the feet or upon the patellae. In such a case as the one just described, it is safe to assume that the vitality of the skin generally was much reduced.

CASE 2.

Right-sided Convulsions and Hemiplegia in a Girl aged 18; Strabismus; Optic Neuritis; Erythema Multiforme; Local Asphyxia.

Jeanie S., aged 18, housemaid, was admitted to the Royal Infirmary on June 11th. She had been found on the road unconscious about 5 p.m. on the 9th, and was then "kicking." There was reason to believe that she had been unconscious for five or ten minutes. With the aid of two friends she was able to walk home, a distance of two or three minutes' walk. It was afterwards ascertained that she had suffered from severe headache from the 7th until the onset of the attack just described, when her leg suddenly gave way and she fell down and remembered nothing more. A second convulsive attack set in at 9 p.m. and continued for about twenty minutes; the movements were confined to the right side, and, having begun in the arm, spread to the leg, and then to the face. The head was turned to the right. The bowels and bladder were not evacuated during the attack. Two other seizures of a similar nature took place during the night, and each was followed, after a few minutes, by vomiting. Patient was conscious and able to speak in the intervals. On the morning of the 10th she had twenty-four attacks of the same kind between 4.30 and 5.30, with continuous unconsciousness and occasional vomiting. Occasional movements took place subsequently at the right shoulder, but without loss of consciousness. On the day of admission it was noted that she was deaf. The bowels were constipated.

Condition on Admission.—Patient was conscious. The mouth was drawn slightly to the left side, and the right arm and leg were powerless. The sense of pain, however, was preserved. There was no important change in the pupils, but an occasional divergent squint was observed. There was pain in the frontal region of the head. The urine contained a faint trace of albumen, but no sugar, blood, or tube casts. The defect of hearing, which was more noticeable on the left side, was associated with retraction of the membranes, but there was no perforation and no history of a discharge from the ears. Moreover, she had been dull of hearing all her life. (A later examination by Dr. Kerr Love showed that there was no diminution of bone conduction, and suggested that any deafness present was due to a catarrhal affection of the middle ear.) The pulse, respiration, and temperature were practically normal. The heart, lungs, and abdomen were normal.

June 12th. Right hemiplegia, but sensation preserved. No hemianopia. Right plantar reflex extensor, left flexor in type. Cutaneous reflexes absent on right side of abdomen. Marked hyperaemia of the trunk, especially on the back. Ophthalmoscopic appearances normal on both sides.

Previous History.—Patient had whooping-cough in childhood. She had rheumatic fever about four years before the present illness, and at that time round, red blotches appeared all over the body. Moreover, there had been some suspicion as to the state of the heart, and instructions were given that a blister should be applied over it. It was stated by a friend that the last menstrual period had been missed altogether, while at the preceding one the flow had been scanty. Previously, however, menstruation had been regular. The family history was very good.

On June 13th and 14th there were occasional attacks characterized by twitching of the right side of the face, and preceded by a cry or by complaint of pain in the right side of the face and right limbs. From time to time the right pupil, or it might be both pupils, would be dilated and insensitive to light.

On the morning of June 15th, there was observed a cutaneous rash, which could not be referred to any such agents as drugs or enemas. It seemed to take origin in an extension of the hyperaemia of the trunk, which has been already alluded to. In front of the trunk it was measly. In the upper limbs it was mostly measly, but at the flexures of the elbows it was more a uniform redness. About the wrists and backs of the hands and fingers it was papular. On the back of the trunk and buttocks it was measly. The fauces were red, the temperature was normal, and a blood count showed: haemoglobin 90 per cent.; red corpuscles 7,233,000; white corpuscles 21,800.

On June 17th the rash was in part fading, but on the backs of the hands and forearms it presented a very characteristic serpiginous appearance, with complete and broken circles and wavy lines constituted by bright red elevated skin. On different days cutaneous haemorrhages were observed, especially in front of the shoulders.

About June 18th signs of returning power began to be noticed in the right side. The headache, however, did not pass away, and on the 24th a convergent squint developed, apparently as a result of paresis of both external recti, but especially the right.

On June 26th it was noted that menstruation had occurred since admission. The urine still contained a trace of albumen. Patient had recently begun to complain of pain between the occiput and back of the chest, extending out to the shoulder on each side, but not accompanied by tenderness or rigidity. There had been no vomiting for several

days, and there was no significant change in the pulse-rate or temperature. Nevertheless, the ophthalmoscope revealed distinct though not severe optic neuritis on both sides. There was no epistaxis, distension of superficial veins, or oedema about the head.

The strabismus came and went, and on July 7th it was associated with diplopia. About this time patient vomited any medicine she got.

On July 17th the optic neuritis showed signs of subsiding, though a good deal of whitish exudation was still recognizable. Only a few small hæmorrhages were seen; the macular regions were unaffected, and vision was practically normal with each eye. The other cranial nerves were investigated in detail on July 20th, and the only changes that fell to be recorded were complete paralysis of the right external rectus, paresis of the left external rectus, and nystagmus while the eyes were being rotated from left to right.

Before the patient left hospital, on September 19th, the inflammation of the optic discs had subsided to some extent, and part of the left disc showed the pallor of consecutive atrophy. The power of both external recti had improved. Patient was able to walk, and the dynamometer registered 18 kilos for the right, as compared with 23 for the left. She continued to improve after her dismissal, but in the course of the next three months she had, on three occasions, a transient attack of right-sided pain. On December 17th the strabismus was scarcely appreciable; there was a slightly spastic condition of the right leg; vision was nearly normal with the right eye, though reduced to $\frac{1}{2}$ with the left; and the dynamometer registered 26 kilos with the right hand and 30 with the left. She was keeping free from headache and vomiting.

It may be mentioned that before she left hospital she was found to be liable to local asphyxia of the four extremities, but this liability was apparently of older standing than her recent illness.

In this case the early symptoms pointed clearly to a lesion involving the motor area of the cortex. On the one view, this would be thrombosis of a vessel on the surface of the brain, such as is met with in chlorosis. The age and sex of the patient, and the preceding amenorrhoea, would favour this hypothesis, while the subsequent optic neuritis would not be opposed to it. On the other view, the lesion would be acute localized encephalitis or meningo-encephalitis; and in favour of this hypothesis it might be urged that the paralysis of the sixth nerves showed that the meningitis had spread to the base. The optic neuritis would quite accord with this view, and the subsequent attack of erythema multiforme would suggest for the various inflammations a common origin in some blood infection.

It is to be noted that the theory of thrombosis, while opposed to Strümpell's, is not inconsistent with another theory of infection. Thus we may suppose that thrombosis is the primary local condition, and that in some cases this is, while in other cases it is not, of an infective nature. If it is infective it will tend to cause acute inflammation of the vessel wall, and this process may spread to neighbouring tissues, whether these be cortex, or meninges, or something else. Much will depend on the abundance of the infective agent in the blood, and in an individual who, through the general state of his constitution, the condition of his heart, and the state of his blood, is predisposed to thrombosis, the latter may occur in different places almost simultaneously, and in one place there may be marked signs of acute inflammation, while in other places there are not. Thus, in a man aged 55, who was sent to my wards by Dr. Edward Wright, and who showed a strong tendency to thrombosis, the process appeared to be simple in the case of the veins of the upper limbs and chest, whereas in the case of the right internal saphenous vein, the overlying skin was inflamed. This patient was the subject of right hemiplegia and almost total aphasia which set in gradually, no doubt in consequence of thrombosis in the left middle cerebral artery; and he also suffered from gangrene of portions of toes on both feet. There may also have been thrombosis of a renal vein, as he had hæmaturia for a few days. There was a history of prolonged alcoholic excess. The sounds of the heart were normal. Similarly, it is difficult to determine whether, and in what proportion of cases, an infective character is possessed by the thrombosis which so commonly develops in the femoral vein after enteric fever and childbirth, and in tuberculosis and other cachectic conditions.

It is likely enough that in cases of hemiplegia of the kind now under consideration the lesion is not a constant one; but it is reasonable to suppose that in many of them the primary condition is thrombosis, which may or may not, from the outset or at a later period, be infective in its nature, and thus liable to give rise to inflammation in its neighbourhood.

The association of exudative erythema with this disease does not find mention in the textbooks. In Osler's collection of twenty-nine cases of the erythema group with visceral manifestations,⁹ there is one (Case xv) in which a lad suffered from recurring transient attacks of hemiplegia, but such an illness is obviously quite different from that which sets in

with a series of convulsions, and leaves permanent weakness behind it. In another (Case xxi) there was meningitis from otitis media, but this again has no relationship to the disease now under consideration.

REFERENCES.

- ¹ *Guy's Hosp. Reports*, 1861, 3rd series, vii, 297-301. ² *Jour. Cut. Med.*, 1868, i, 140-147. ³ *Brit. Jour. Dermat.*, 1890, ii, 246-250. ⁴ *La Semaine Méd.*, 1888, p. 250, quoted by Shepherd, *Jour. Cut. and Genito-Urin. Dis.*, 1891, ix, 59-62. ⁵ *Liverp. Med.-Chir. Jour.*, 1888, xiv, 483, 484. ⁶ *Brit. Jour. Dermat.*, 1893, v, 357-359. ⁷ *Jour. Cut. and Gen. Urin. Dis.*, 1891, ix, 59-62. ⁸ Quoted by Radcliffe Crocker, *Dis. of the Skin*, 1903 (3rd edition), i, 648. ⁹ *Amer. Jour. Med. Sc.* 1895, cx, 629-646; *Brit. Jour. Dermat.*, 1900, xii, 227-245; *Amer. Jour. Med. Sc.*, 1904, cxxvii, 1-23.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

FOREIGN BODY IN THE AIR PASSAGE.

In December last I was asked to see a baby girl, aged 9 months, who, hitherto in perfect health, was stated to be beginning bronchitis. It had been suddenly seized with a violent paroxysm of coughing; several subsequent attacks had occurred, and were followed by ejection of fluid, due to reflex vomiting, in part at any rate. On auscultation and percussion no signs whatever could be discovered, and from the general appearance of the child, and an absence of all untoward symptoms, I felt able to give the friends complete reassurance. I visited the child on the following three or four days, and she still appeared well, though not quite so jolly and vigorous as usual. There was now, however, in addition to the paroxysms of coughing, a good deal of rattling in the trachea, and a distinct occasional rhoncus over a very limited area, midway down the scapula and a little internal to its inner border. At a period subsequent to this initial attack I was asked to visit the child again, and found physical signs and constitutional symptoms still lacking, though the recurrent paroxysms of coughing continued. Later on, it appears, the attacks, occurring every ten or twelve days, got more severe; copious mucus was ejected, sometimes, I learn, being stained with blood, after which the usual period of comfort and naturalness followed. The severest attack of all occurred a fortnight ago when out driving, and was so violent as to cause the nurse the greatest alarm. As the spasm of the glottis was sufficiently prolonged to effect discoloration of the face, the nurse held the child out of the carriage window, face downwards, and smacked it vigorously on the back, a procedure which produced relief. A few days later, as another attack was beginning the nurse adopted the same course, turning the child nearly upside down, and at the same time smacking the back, when, along with the usual flow of mucus, out jumped a small gold brooch! It is one fashioned like a safety-pin, $1\frac{1}{2}$ in. in length, with a circle of tiny pearls, measuring 1 cm. in diameter. It was unclashed, and the gold had turned almost black except at the pin point, which was perfectly bright. It had been missed on the morning of December 1st, within a few minutes of my first visiting the child, and a long search had been made—needless to say, in vain. It had been constantly used to secure the child's bib, but on account of its tendency to fly open the mother had long intended to discontinue using it. It had anchored itself for $4\frac{1}{2}$ months in some portion of the air passage, and there for $4\frac{1}{2}$ months had it been exposing the child to unsuspected but none the less imminent and vital risk.

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PERCY WITHERS, M.B., M.R.C.S.

PROTECTIVE POWER OF VACCINATION.

THE case reported by Dr. Neilson in the BRITISH MEDICAL JOURNAL of April 8th reminded me of a similar case in my practice several years ago. The patient was a woman, aged about 30 years, living at Tottenham. I found her in bed, suffering from small-pox. Her baby, an infant of 6 months, was at the breast, and had not been vaccinated, so I at once fetched some lymph and vaccinated the child. At the same time I advised a sister of the patient, who was in the room and showed no evidence of having been vaccinated, that it was possible she might not be infected with the disease if vaccinated at once. However, she positively refused the operation. Exactly fourteen days afterwards she developed confluent small-pox, was removed to hospital, and under skilful treatment made a good recovery, but with such an