ON THE USE OF ANTIPYRIN IN LARGE DOSES.

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AMONGST the coal tar derivatives recently introduced into practice none can compare in value with antipyrin, whether regard be had to the certainty of its action when appropriately administered, or to the manifold conditions with which it is capable of grappling.

Personally I have had hardly any experience of its deleterious effects—at least of a serious nature—when employed with due precautions. Once or twice it made the patients “feel very ill,” and, when pushed, vomiting was occasionally induced. In certain cases, too, a rash appeared upon the skin, generally of a measly or erythematous character, but this rapidly disappeared when the use of the drug was suspended, and was never a source of any uneasiness. In this opinion I am confirmed by the report of the Therapeutic Committee of the British Medical Association, appointed to make “an inquiry regarding the importance of the ill-effects following the use of antipyrin, antifebrin, and phenacetin.” “Out of 189 observers who report on antipyrin, no fewer than 138, or 73 per cent., have never observed any ill-effects at all worth mentioning. Considering how large is the experience of the action of this drug represented in these reports, this large proportion of observers who have no ill-effects to record is very remarkable. Almost more than any other fact could do, it seems to testify to the comparative harmlessness of this drug when properly administered. It is clear, then, if one may be allowed to judge from these reports, that ill-effects following the use of antipyrin are not only relatively but absolutely infrequent in their occurrence. One observer expresses his opinion that they are ‘rarer than the idiosyncrasies of the iodides or quinine;’ and certainly, so far as the above reports go, this would appear to be the case.”

But it must be admitted that this is contrary to the opinion of many, and I can only suppose that the drug has been impure, or the initial dose too large, or they have been unfortunate in giving it to patients with whom it disagreed in virtue of a peculiar idiosyncrasy, which it shares with many other valuable medicines. But if we are to fight shy of everything which disagrees with isolated individuals, we would not only have to deny ourselves the use of many valuable remedies, but also of almost every species of food and drink.

The following cases are good illustrations of the benefits which may be derived from the use of antipyrin in large doses, and the comparative safety with which it may be given, although such cases must be carefully watched, and the initial dose should not exceed 10 or at most 15 grains.

CASE I.—J. M., aged 9 years, was admitted to Ward 2 of the Western Infirmary on December 12th, 1889, suffering from fits of two and a-half years' duration. His father stated that he had previously been perfectly healthy. In both father and grandfather there was a history of so-called “hysterical fits;” in the father between the ages of 2 and 4, and in the grandfather between those of 45 and 57. An aunt had a “stroke” twenty years ago, from which she recovered, and is still alive. Six weeks before the first fit the boy had a fall, bruising his head just above the right ear, but there was apparently no injury to the bone. He recovered from this in about three days, and remained well until the first fit occurred, for which the parents can think of no other cause but the fall. At the beginning of the illness he had only about 4 to 6 fits daily, but they gradually increased in number until he had as many as 30 or 40. At the same time he complained of gradually increasing weakness in the right arm, but this after a time disappeared, when the left became similarly affected. Three months afterwards the fits entirely ceased after the application of blisters to the head. An interval of fifteen months ensued during which there were none, and throughout this time the general health remained perfectly good. About seven months before admission, with no apparent cause, they began again, at first only one occurring in twenty-four hours, but gradually they increased until they amounted to 40 or 50, the largest number in one day having been 57. There was no improvement until a few days before admission, during which time he had only 12 daily. The fits occur in sleep as well as while he is awake. They are sometimes preceded by pain in the left elbow, sometimes by headache, now frontal, and now situated on the side of the head, over the right ear. The headache sometimes only occurs immediately before the fits, and is sometimes of longer duration. Occasionally three or more fits occur together with very little interval, but there appears to be no status epilepticus. Drowsiness, lasting for a few minutes only, often succeeds the convulsion. The right side was at first the more severely affected, but

now is considerably less so than the left. The patient is perfectly intelligent. Numerous fits were seen, both by the house physician and by the nurses, and all presented similar characters, their duration being from one and a-half to two minutes. In all, with the commencement of the tonic spasm, the arms were thrown over to the right side, and either both rigidly extended, or the right flexed at the elbow and the left extended. The thumbs were bent into the palms; at the same time the head was violently twisted to the right, so as to look over the shoulder, and the eyes were rolled upward and to the right. Clonic convulsions followed, especially violent upon the left side, except in the face, where they occurred upon the right, and involved chiefly the zygomatic and the lower half of the orbicularis palpebrarum. The mouth was kept half open, and there was no foaming; the tongue was not bitten. Nearly all the fits were preceded by the epileptic cry. As consciousness was recovered, the patient sometimes burst into tears. There was occasionally incontinence of urine during the fits.

On examination all the organs were found normal. The gait was awkward and unsteady. Shortly after a fit there was slight exaggeration of the left patellar tendon reflex, and an approach to ankle clonus on the right side. There was a continuous dilatation of both pupils, which responded normally to light. Examined again on December 22nd, an hour and a-half after a fit, there seemed to be slight paresis of both upper and lower limbs, the left side being apparently a little weaker than the right. The dynamometer in the left hand registered 32, in the right 30 K.

The treatment, which was commenced on December 20th, consisted of rest in bed, regulation of the bowels, and the exhibition of antipyrin, commencing with 5 grains thrice daily, and increasing by 1 grain in every dose each day. On January 9th, 1890, 25 grains thrice daily were reached, and this dose was continued till January 16th, when it was diminished to 20 grains thrice daily. From the date of entrance till December 26th the average number of fits daily was 16.5; from then till December 30th, 13.2. On December 31st and January 1st there were 11 fits; on January 2nd and 3rd, 10 fits; and on January 4th, 3. They then ceased till January 28th, when the dose of antipyrin had been lowered for twelve days. There was then one slight fit, and the dose was again increased to 25 grains thrice daily. From that time there were no more, and the patient was dismissed on March 1st quite well. He continued the antipyrin at home, and a letter from his father, dated March 12th, stated that there had, up till then, been no recurrence.

CASE II.—L. E., aged 13, schoolboy, was admitted to the Western Infirmary on October 10th, 1892, complaining of twitching of the right hand and foot of four months' duration. The family history has no special interest, except that his mother is subject to rheumatism. He has never had scarlet fever or rheumatism, and there is no history of fright. In March, 1891, he had his first attack of twitching. It was confined to the right side, and affected both hand and foot, which could not be kept still, nor could anything be held in the hand. Swallowing was not interfered with, but speech was slightly affected. He attended the infirmary dispensary, and by the month of July had quite recovered. He remained well until June of the present year, when the twitching gradually returned, being confined, as before, to the right side. The attack is more severe than its predecessor. He has attended the dispensary for some time, but without material improvement. On examination typical choreic movements are seen in the right arm and leg, which cannot be held in any one position even for a moment. Anything placed upon the palm is at once jerked off. He spills at least part of any water he attempts to swallow, and so on. There is an occasional tendency to stammering. The right eyelid is affected, and the right pupil is much larger than the left. The pulse varies between 110 and 120. There is a faint apical systolic murmur. The temperature and the urine are normal. The case was treated by antipyrin. On October 11th he received 15 grains in three doses, and as the drug agreed perfectly it was rapidly pushed. On the 13th he had 30 grains, on the 15th 45 grains, on the 17th 60 grains, and so on, until on November 14th he was taking 60 grains thrice daily. He was about a fortnight under treatment before the symptoms began to abate, when he was getting 30 grains thrice daily, but from that time improvement was continuous, and he left the infirmary perfectly well on November 25th, the dose of antipyrin having been maintained until his dismissal at 50 grains thrice daily. On leaving he was instructed very gradually to diminish the dose, and up till the date of writing (December 6th) he has remained in perfect health.

CASE III.—M. W., female, aged 12, was readmitted to Ward 7 on December 17th, 1892, suffering from a violent attack of chorea of a month's duration. The family history is unimportant. About twenty-one months ago she had an attack of rheumatic fever, which confined her to bed for five or six weeks. She had not long recovered, when her mother noticed that she could not maintain any one position for any length of time. She was always fidgetting, and “strange movements were observed.” There was no history of fright. She was treated by a medical man, and improved, but the treatment was changed, and the movements returned. After about four months she began to lose strength, and could not do anything requiring exertion. She attended the dispensary for some time, and was finally sent into the infirmary by Dr. Dickson on December 21st, 1891. At that time the attack was a slight one. The movements consisted in a constant jerking of the head from side to side, and “fidgetting” with the hands. The left hand was most affected, but even there the movements were slight. The tongue was unaffected. All motion ceased during sleep. The treatment consisted in rest in bed, regulation of the bowels, and the administration of extract of malt with cod-liver oil. She was dismissed well on January 26th, 1892. She was readmitted on December 17th, 1892, with a violent attack of a month's duration. On this occasion the movements were so violent that she could not walk without falling, nor sit without being dashed about so as to injure herself. On admission she had several bruises upon her head and body, and it was necessary to tie her down in bed. A special nurse was required to watch her at night. All four limbs were attacked. She was treated on this occasion by rapidly increasing doses of antipyrin. On December 19th she took in all 12 grains; on December 18th she took 10 grains thrice daily; December 19th, 15 grains; December 21st, 20 grains; December 25th, 25 grains; January 6th, 1893, 30 grains; January 12th, 35 grains; January 14th, 40 grains; January 16th, 45 grains. The doses were not in-

¹ BRITISH MEDICAL JOURNAL, January 13th, 1894, p. 85.

² The cases were reported by Wm. R. Jack, M.D.

ceased beyond this point, as the drug then produced sickness. Since 35 grains were given it had caused slight headache. Improvement was very rapid. The special nurse was not required after forty-eight hours. By January 7th the patient was so far recovered as to be able to sit by the fire. Movements still persisted, but they became very slight, and were confined to the right hand and leg. After January 16th the drug was twice stopped for a day owing to sickness, and on January 23rd the dose was reduced to 40 grains thrice daily, and Easton's syrup was given. The dose of antipyrin was then gradually further reduced. Slight movement of the right hand persisted for some time, but this also finally disappeared. She was dismissed quite well on March 7th, 1893.

Did space permit many other similar cases, in which equally good results were obtained, might be quoted, but the above may be taken as fair samples of the whole; and I may sum up my experience in the following aphorisms:

1. Antipyrin is not the dangerous drug which some observers have led us to suppose.
2. It may be given with safety in large doses, even in the case of children, in most cases, although the initial dose must be small, and it must be slowly and cautiously increased, the patient always being carefully supervised.
3. In large doses it often yields surprisingly good results, and in chorea it is the only medicine from which cures may confidently be anticipated.

FORMATION OF A NEW SOCKET FOR AN ARTIFICIAL EYE.

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THE following unusual case, where after enucleation of the bulbus oculi, no socket remained to contain an artificial eye, and a new one was made by operation with satisfactory results, may prove of interest to those engaged in the practice of operative surgery.

The lady, B. W., who was the subject of treatment, describes the commencement of the deformity as follows: "When about 2 years of age, I had a violent attack of whooping-cough, after which my left eye was found to be so much injured, that immediate removal was deemed necessary. The operation was performed by — in April, 1870. For fifteen years my socket was left quite empty. In 1885 I went to Dr. Mackenzie Davidson, who, on examining my socket, said that unless it could be enlarged it would be impossible for me to wear an artificial eye."

Dr. Davidson enlarged the socket on several occasions by making incisions into the orbit, and keeping up dilatation of the space thus gained by tampons of various kinds, so that the patient was enabled to wear an artificial eye, and was for a time "exceedingly comfortable," while the eye "looked fairly well."

In the year 1890, however, the contraction of the socket had returned to such a degree that some further operations had to be done by Dr. Davidson, but these were unfortunately not successful in maintaining the required space, and the "socket closed up so that it was only with the utmost difficulty" she "could insert the tip of" her "little finger."

At this stage, in April, 1892, Dr. Davidson requested me to see the patient. There was no detectable diminution of the size of the bony orbital cavity, and I suggested the plan of operation which was subsequently carried into effect. Dr. Davidson was kind enough to transfer her to the wards of the Aberdeen Royal Infirmary, under my charge, and, on April 13th, 1891, the operation agreed on was performed as follows: A skin flap, A B C, Fig. 1, including the subcutaneous tissue and nutrient skin vessels, was dissected up from the temporal region, remaining attached by its base A C. The flap, which was about 3 inches long and 2 broad, was next divided into two tongues for about three-fourths of its length by an incision B D. Through the base of the flap an incision, shown at the line A C, was next carried, but so as to divide only the skin, the vitality of the flap being maintained by the vessels of its subcutaneous tissue, which remained undivided at its base. From the base A C a scalpel was carried beneath the skin and subcutaneous tissue into the shrunk socket, that barely held a pea, and the lids were freed and the socket enlarged by cutting upwards and downwards, parallel to the

surface, to an extent corresponding to the shaded area in Fig. 1.

After the bleeding, which was quite moderate, had been arrested by a few fine catgut ligatures and pressure, the flap was turned inwards behind the freed lids until it lay with its raw surface looking forwards and its cutaneous surface back-

FIG. 1.

wards towards the orbit, one tongue of the flap lining each lid within, and in this situation, having been adjusted in as natural a fashion as possible to the lids, it was secured by a number of fine catgut sutures in the position shown by the vertical shading in Fig. 2. There was so little of the natural

FIG. 2.

conjunctiva remaining that none of it was seen in doing so save over the caruncula lacrymalis, where it formed a small portion of the covering of the new socket. The temporal wound, now left raw by the turning in of the flap, as seen in Fig. 2 on the area shaded with horizontal lines, was next drawn together as far as practicable by sutures that approximated its edges.

In the new socket was placed a disinfected marble, Fig. 2A, of about the size of a normal bulbus, and the temporal wound was dressed with iodoform vaseline. All the steps of the operation were carried out under antiseptic measures, sublimate lotion of the strength of 1 to 1,000 being chiefly used.

The healing proceeded to a wish, and soon the temporal wound had cicatrised, leaving a scarcely visible mark. The

The quotations in this paper are taken from notes of her case written out by the patient herself.