after which the patient returned to her usual occupations. In a few weeks there was recurrence of ulceration, which again yielded to similar treatment, but which recurred again and again. At last I proposed to close the lids for six months, and for this purpose pared and united their edges, but before the period had expired the patient said that she no longer had perception of light. During the whole time of her illness the eye on which the Mules's operation had been performed never gave her a moment's uneasiness, and was never either congested or tender on pressure. She has continued to wear her artificial eye ever since, and seems hardly conscious of its presence.

In this case it will be seen that the possibility of sympathetic mischief had been present to the minds both of Mr. Teale and myself, and that, to me at least, the hypothesis appeared untenable. I should describe the case as one of corneal disease of peculiar malignity, probably neuro-paralytic in its essential character, occurring in a very unfavourable subject, and attacking the two eyes in succession under the influence of some common cause. I cannot find any facts in the history which give the smallest colour to the notion of sympathy, at least in the sense to which I think the word ought to be restricted.

CASE 3.—A girl, about fourteen years of age, went to St. George's Hospital in January, 1887, her left eye being disorganised by chronic inflammation. A Mules's operation was successfully performed, although the patient was so unlucky as to develop scarlet fever a day or two after the operation. This did not interfere with the healing, and she was discharged with a well-fitting artificial eye. In October, 1895, she came to me with interstitial keratitis of the right eye, of the ordinary type and of considerable severity, which ran a very chronic course, and from which she is now making a better recovery than at one time I anticipated. There has never been any tenderness of the Mules's stump, and there has been nothing in the case of the right eye to distinguish it from hundreds of others in which no cause of sympathy could be indicated.

CASE 4.—A single woman, about fifty years of age, had double cataract, for which I operated successfully on both her eyes early in the "eighties." One of them afterwards became the subject of painful and complete glaucoma, and after some ineffectual treatment I performed a Mules's operation upon it in 1887. The remaining eye was attacked by glaucoma in 1894 and was eventually lost. There was nothing to suggest "sympathy" except that the events were consecutive in order of time.

It will be seen from the foregoing narrative that I have met with four cases in which, after the performance of Mules's operation, the remaining eye has been attacked by serious disease. It is remarkable that the four cases were totally unlike in their origin and nature, and that the diseases attacking the second eye were also totally unlike. It is remarkable that neither the ordinary phenomena of sympathetic irritation nor the ordinary phenomena of sympathetic ophthalmitis were exhibited in any one of them, and that in none of them was there any tenderness of the Mules's stump. In most of the cases of supposed sympathy occurring after the lapse of years it has been recorded that the eye by which the sympathy was excited had become tender or painful shortly before the sympathetic outbreak. I am strongly of opinion that if in my cases the eyes on which Mules's operations were performed had been removed instead the subsequent occurrences would have been precisely the same, except that no idea of sympathy would have been suggested. Moreover, it must be remembered that sympathetic ophthalmitis of the ordinary type is by no means unknown after removal of the eye. Many cases of the kind have been recorded, and one of the most recent of them may be found in the *Annales d'Oculistique* for the present year. The question raised by Mr. Cross is one which deserves all the observation and all the acumen which can be brought to bear upon it. On the one hand, the superiority of Mules's operation over removal is as great as the superiority of excision of a joint over the amputation of a limb; and, on the other hand, even this enormous advantage must not be conceded to patients if it be attended by any measurable risk of destructive changes in the eye which remains sound. My personal experience induces me to believe, with some confidence, that the risk is purely imaginary, or, at least, that it has no better foundation than the occurrence of a certain number of coincidences.

Harley-street, W.

ON THE VALUE OF ARSENIC AND BELLADONNA IN THE TREATMENT OF CHOREA.¹

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DURING the summer of 1894 I had an opportunity at the Evelina Out-patient Department of testing the value of arsenic and belladonna in the treatment of chorea. I made notes of twenty-five cases the results of which I have briefly summarised.

CASE 1.—A boy, aged twelve years, had been suffering from chorea for three months. There was no history of rheumatic fever, but the father had been attacked by this disease. There were slight choreic movements of the face and eyes. The apex beat was perceptible in the fifth interspace, half an inch outside the nipple line, and there was a slight bruit audible in that area. Liquor arsenicalis in doses of twelve minims was ordered twice a day. After three days the twitchings were much improved, and after ten days they had disappeared.

CASE 2.—A boy was suffering from a fourth attack. The chorea was slight and limited to the left side, the apex was situated in the fifth space, and there was a long and loud presystolic bruit. Twelve minims of the liquor arsenicalis were prescribed three times a day. After seven days the movements had entirely gone, and oleum morrhue with vinum ferri was substituted.

CASE 3.—A girl, aged eight years, suffered from an attack two years previously. There was no history of rheumatic fever, and no cardiac murmur was discovered. There were twitchings of the face, tongue, and eyes. Liquor arsenicalis (10 minims) with bismuth mixture—a combination of subnitrate, tragacanth, and peppermint water—was given twice a day after food. Three days later the dose was increased to 15 minims. This dose, however, was followed by sickness, and a crop of herpes appeared on the lips; it was therefore diminished to 10 minims. After taking arsenic for fourteen days no visible improvement was apparent; consequently the drug was stopped, and tincture of belladonna was tried instead in doses of 15 minims three times a day, along with a carminative. After taking this drug for seven days the movements had disappeared, and tonics were administered in its place. The patient took phosphate of iron for fourteen days and was then discharged, as she had not exhibited any movements during that interval.

CASE 4.—A boy, aged seven years, had exhibited choreic twitchings for a period of three weeks. There was no cardiac bruit and no history of rheumatism, but of fright. After taking arsenic (10 minims) for ten days there was no amelioration. At the end of that time, also, he was sick after each dose, and an acute herpetic eruption with œdema of the right ear appeared. Tincture of belladonna in 20-minim doses with bismuth mixture was ordered every four hours during the day. On the fourth day the movements were decidedly better; after seven days they were no longer present and no toxic effects were observed.

CASE 5.—A girl, aged twelve years, was suffering from the eighth attack. There were now moderate choreic movements of the extremities and tongue which had existed for five weeks. Arsenic in 15-minim doses was prescribed three times a day. There was no cardiac bruit, but the heart's action was markedly irregular. After three days the movements were, if anything, worse; there was some soreness of the eyes and nose, with diarrhoea. Tincture of belladonna (20 minims) along with potassium bromide was ordered every six hours. After four days the movements were much improved, the hands could be held out perfectly still, and only twitchings in the left arm and face were left. The speech was good and the pupils, as is generally the case in chorea, were slightly dilated, but they reacted to light and accommodation. After a week the movements had quite gone. The pupils were then very wide and reacted but slightly to light.

CASE 6.—A girl, aged eleven years, had exhibited frequent and irregular movements of the left arm and leg for a week. There was no history of acute rheumatism, but her father

¹ A paper read before the North Tottenham Medical Society, Nov. 5th, 1896.

and brother had suffered from it. She was very anæmic; the apex beat was situated in the nipple line, and there was slight hypertrophy of the left ventricle. Whenever the limbs were thrown into spasmodic movements the heart's action at the same time became markedly irregular. She was ordered 15-minim doses of liquor arsenicalis twice a day. The movements gradually improved, but at the end of three weeks she still complained of much sickness of an evening and of abdominal pain after food. Belladonna, in the form of the tincture in 15 minim doses, with mistura carminativa, was substituted. A week later the movements became *nil* and did not reappear.

CASE 7.—A girl, aged eight years, had a fright three weeks previous to admission to hospital. There were movements of the hands and tongue. The heart sounds were normal, but the cardiac movements became irregular when the jerks occurred. A week's treatment with arsenic only appeared to aggravate the condition; she complained also of sickness, headache, and of an eruption around the mouth. Tincture of belladonna in 15-minim doses with peppermint water was prescribed instead. After a week the note read: "No vomiting, no headache, movements the same, pupils normal, herpes drying up." After three days' further treatment the movements were vastly improved, and after fourteen days had completely disappeared.

CASE 8.—A girl, aged eleven years, was suffering from a second attack, which was apparently the result of an examination at school. The left face and tongue were particularly affected. After three days' treatment with arsenic diluted with cinnamon water the eyes and nose became very sore, and tincture of belladonna in 10-minim doses was ordered three times a day in place of it. After three days the movements had subsided considerably, and after ten days' treatment the movements were extremely slight. She complained of blisters in the mouth and of a sore throat. Oleum morrhue with vinum ferri was now ordered instead. It is advisable, especially in the case of out patients, to discontinue the arsenic and belladonna as soon as the movements become insignificant, and then to give tonics in order to complete the cure. The remaining cases were much of the same character, and illustrated in the same manner the efficacy of these drugs.

During the last year eight cases of severe chorea, including one of chorea insaniens, have been admitted into the Tottenham Hospital. Condensed notes of three of these read as follows:—

CASE 9.—A boy, aged ten years, was admitted on Feb. 8th, 1897, with extensive choreic movements affecting all the muscles of the face, arms, and shoulders. Contractions of the sterno-mastoids caused him to turn his head from side to side. He had spasmodic and very violent movements of the trunk. Breathing and swallowing were unaffected. The heart's action was rapid, the pulse 90, but there was no murmur. A mixture of 30 minims of tincture of belladonna, and 6 minims of liquor arsenicalis, with mistura bismuthi, was prescribed every four hours. On the 11th he became a little quieter, slept during the day for a few hours, and well at night. He took food well. On the 12th he was much quieter, but if observed the movements became exaggerated. On the 13th he was much better; most movement was now to be seen in the lips and tongue. The first sound was reduplicated at the apex. There was some swelling of the parotids, and the urine measured 12 ounces. Potassium acetate in 5-grain doses was added to the mixture. On the 14th he was decidedly quieter, and the urine measured 18 ounces. On the 16th he was very much quieter, and no oscillations occurred unless he attempted to move. The urine amounted to 16 ounces. Syrup of phosphate of iron was now ordered and the arsenic and belladonna were discontinued.

CASE 10.—A girl, aged seventeen years, was an out-patient with chorea twelve years previously. She was frightened in February by a carriage accident, but no movements were perceptible until April 8th. On admission on April 14th she was exceedingly violent and restless, and the movements affected the limbs chiefly. The temperature was 99.2°F. On the 15th a mixture of 30 minims of tincture of belladonna, 6 minims of liquor arsenicalis, with bismuth mixture, was administered every four hours after food. On the 20th the movements had entirely disappeared. Massage to the arms was commenced and cod-liver oil with phosphate of iron was prescribed instead.

CASE 11.—The case of chorea insaniens occurred in a girl, aged fifteen years, with a history of rheumatism at the age of five years. The movements commenced about

five days before admission. The knee-joints were swollen. At the height of her violence chloroform was administered; she was taking belladonna for three days before, and subsequently for a week. At the end of this time she could walk, and all movements had ceased.

When estimating the value of a drug much care is required, and especially is this the case in chorea, since the natural tendency is towards recovery after about seven weeks, even if no treatment at all is adopted. If a drug is prescribed, and after a few weeks' perseverance it is found to be of no benefit, it is natural to seek a change, and the latter drug may receive the credit of the cure, which might have followed even if no drug had been administered. The observation of the cases here mentioned gives one the impression, however, and this is also generally acknowledged, that large doses of arsenic have a beneficial influence in subduing the movements, and this is best seen after the movements have existed for some time—weeks or months—that is, when a cure seems almost hopeless. The drug should be given after food, and the little patient should lie down for half an hour afterwards in order to avoid retching and sickness. Whilst looking up the literature I found a paper by Dr. Fuller, in the *Medical Times* of July 1st, 1859, on the Treatment of Choreic Patients by Belladonna. He gave large doses of the drug in twelve cases. One girl aged ten years, received 70 grains of the extract daily, the average dose for an adult being half a grain. She took 1000 grains in twenty-six days. Another took 37 grains of atropine in eighteen days, the average dose for an adult being one-fiftieth of a grain. During the administration neither fever, rash, nor erythema was noted. The pulse became quick and the urine scanty. Only in two instances was indistinctness of vision observed; four suffered from sickness and diarrhoea. There was no dryness of the throat, no headache, and no delirium. In two patients the belladonna was useless; in the remainder its efficacy was noteworthy. The drug was readily absorbed from the stomach, and passed out in the urine, from which it could be extracted. The phenomena of chorea appear to be due to a nutritive and functional disturbance or ataxia of the higher nerve centres. Post mortem a general tendency to dilatation of the smaller arteries within the substance of the brain accompanied with exudation is observed. This appears more especially in the corpus striatum and the regions supplied by the middle cerebral arteries; in other words, there is pronounced hyperæmia of these nerve centres. It is probable that the chief stress falls upon the Rolandic areas. Such vaso-motor ataxia might be induced by reflex disturbances arising within the digestive tract, by uterine irregularities, or by emotional disturbances. In the rheumatic diathesis the toxin may attack the motor centres directly.

It is, perhaps, permissible to make the following remarks in conclusion:—1. Belladonna appears to be most beneficial in recent cases, and its influence is sometimes very marked in severer forms. 2. In obviously rheumatic cases arsenic in large doses may be given a trial or may be combined with belladonna from the first. Belladonna may act by diminishing the excitability of the nerve centres or by imparting an improved tone to their vascular supply. 3. In the wards of a hospital it is perfectly justifiable to give to a child as much as 30 minims or more of tincture of belladonna every four hours for ten days or even longer. Certain precautions are necessary. The patient should be kept in bed and the urine should be daily measured. Small doses of potassium acetate may be added if it become much diminished or if the eyelids show any puffiness. In one child nocturnal incontinence occurred, and the dose was lessened. The occurrence of the papular erythema, which leaves raised circular lumps for a time, does not necessitate any diminution of the dose. Dryness of the throat and swelling of the parotids, should they occur, are merely temporary. The influence of the belladonna makes itself felt after about four days. Should no visible improvement occur before the tenth day it would be useless to continue with it. But in all the eight severe cases already referred to belladonna was of benefit, and is certainly worthy of further trial. As soon as the movements become trivial or occur only during exertion it is better to omit the belladonna, to commence massage of the affected muscles, and administer cod-liver oil and syrup of phosphate of iron or other tonics. The arsenic may be continued for a week or longer. For permission to publish the cases seen at the Evelina Hospital I am indebted to the courtesy of Dr. Soltan Fenwick, assistant physician to the hospital.

Edmonton.

VITALITY.¹

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VII.—THE INTERSTITIAL CIRCULATION IN ALL LIVING THINGS.—ITS DEPENDENCE ON VITALITY.

INTIMATELY associated with the matter of every living particle is water. Indeed, water is a constant and necessary constituent of all life. Its amount is considerable in proportion to the solids wherever vital phenomena are active. Living matter without water has probably never existed, and anything approaching desiccation results in death. Water, then, must be regarded as an absolutely necessary condition of life at all times, but the smallest amount that may be present without life ceasing has not been determined. As far as I have been able to ascertain, no evidence yet obtained supports the conclusion that life in the complete absence of moisture is possible, and it seems almost certain that water must have preceded the existence of any form of life.

Life involves the very free movement not only of material particles but of the constituent atoms of the living matter, many of which are being continually rearranged—placed in new positions with respect to one another. There is no such thing as a living particle having the same composition in every part, or remaining of the same composition from moment to moment. An isolated living atom of any substance in nature is not conceivable.

Whether the atoms are caused to move in the water in which they are suspended or are in some sort of chemical or other kind of combination with the elements of the water cannot be decided at present. The atomic movements and rearrangements here referred to are *vital movements*, but are, of course, invisible and not to be demonstrated; but the general movements so characteristic of living matter are well known, and can be studied without difficulty in the amoeba, in the colourless blood corpuscles, in pus and mucus corpuscles, and in many other particles of living matter or bioplasm; and these movements of living matter differ in essentials from every kind of movement known to take place in matter in any other state or condition, and are vital—that is, peculiar to, and characteristic of, life—the temporary living state of matter.

Not only is water necessary to living matter, but the fluid which bathes the living matter and the substance immediately around it must be continually changed. It is probable that neither the particles of living matter nor the fluid around it are ever in a state of rest—stagnation of fluid like the cessation of movement in living matter being immediately followed by death.

In all living forms there is evidence of the free and constant movement of interstitial fluid, and in organisms of complex structure consisting of tissues as well as of living matter the fluid is not only present in the living matter itself, but pervades every part of all the moist tissues, circulating freely among the structural elements, and keeping these in a state of health and activity. In some cases there are actual canals which are bounded by a thin layer of the tissue and thus separated from one another; in others the fluid pervades every part of the tissue, occupying minute interstices, which vary much in dimension and arrangement in different tissues, and in the same tissue at different ages. The free movement of fluid is, in fact, always taking place in living forms, whether there are true vessels arranged as a network of tubes in every part of the organism, or propelled by a special organ into large vessels directly connected with it, and so into smaller ones resulting from the division and sub-division of the trunk and its branches, and thus distributed to all parts. The free circulation in the living matter and in the interstices of the tissues is universal, and is one of the phenomena belonging to life itself. It is an "interstitial circulation," always independent of any propelling organ or power, or capillary attraction, adhesion or any motor action known in connexion with the non-living.

This unceasing movement and interchange of fluid which

takes place in the minute channels and interspaces between the microscopic elements of the tissues as well as in every kind of living matter is a necessity of life, and has been universally present in all things that have lived, including the most minute speck of independent living matter and the most gigantic and highly complex organisms. The interstitial circulation goes on even in the so-called non-vascular tissues which may be situated some distance from any vascular supply—from any blood- or lymph-carrying vessels. Even in the hardest textures, such as bone, and teeth, and shell, the circulation of interstitial fluid continues as long as any living particles, however minute, which have taken part in the formation of the tissue, remain. When tissue becomes hard, and dry, and inactive, there is, of course, no longer circulation of fluid in its interstices, and all changes indicative of life have ceased; and though still connected with and, in fact, forming part of a living organism, the tissue is no more living than if it had long been completely severed and preserved for many years in a museum. Through the agency of the interstitial circulation all nutrient matters after passing through the formed material are brought into close proximity with the particles of bioplasm that are to appropriate them, which living particles are concerned in the development, formation, and action of the respective tissues or organs. By the interstitial circulation the deterioration of tissue may be prevented, and damage which it may have sustained repaired. Abnormal formations and deposits may be removed through the circulation of the interstitial fluid, and may be taken up by it, changed, and dissolved. Although entirely independent of the organs of circulation and of any propelling power, mechanism, or apparatus, some of the interstitial fluid with its dissolved constituents is continually passing through the capillary walls where capillaries exist and mixing with the blood, some of its components taking part in nutrition while others are altogether removed from the organism by the action of various excreting organs.

The interstitial circulation of man and the higher animals is active long before the organs of circulation or the fluid to be propelled through the vessels exist, and before any vestige of the complex arrangement of nerve centres and fibres which regulate and control the blood circulation can be discerned. In fact, the ordinary circulating organs may be said to be subordinate and to minister to the interstitial circulation, and would have no meaning in the absence of the latter, which begins at the earliest period of embryonic life and before any structures or organs have appeared. The interstitial circulation never ceases as long as life lasts, and continues for a time after the heart has ceased to beat and the blood to circulate. In various pathological changes detrimental to some of the tissues and organs of the body of *vital importance* the interstitial circulation may still be carried on, but in its absence, development, nutrition, formation, repair, action, and the removal of the products of disintegration and decay would be impossible.

That "death" occurs when the heart stops beating and the blood ceases to circulate is certainly true with regard to the high and complex phenomena which characterise man and the higher animals, but some vital actions continue to be manifested in certain organs and textures after death in the ordinary sense has taken place. The formation of hair, nail, bone, and some other structures may continue for some time after death. In short, although the bioplasm of certain parts has ceased to live, that of certain tissues and organs of the body may retain its vitality for some time, which varies according to circumstances. The bioplasm concerned in the higher operations of the brain and some other parts of the nervous system may indeed be dead, while other forms of bioplasm continue to live, and for different periods of time after "death." In man and the higher animals the forms of living matter dying first are more dependent upon the steady supply of nutrient matters and the immediate removal of the products formed during their vital changes than the bioplasm taking part in the formation and action of simpler tissues and organs, and probably "die" the instant the interstitial circulation in them ceases to be carried on at the normal rate. "We" die some time before the death of many of the living particles taking part in the formation and action of some of our tissues occurs. In certain cases, as is well known, the multiplication of particles of bioplasm (leucocytes) continues for some time after death, and is associated with a rise in the temperature of the whole body amounting occasionally to three or four degrees during several hours after the blood circulation has

¹ Nos. I., II., III., IV., V., and VI. were published in THE LANCET of Feb. 22nd, April 11th, June 13th, Aug. 29th, Oct. 17th, 1896, and Jan. 23rd, 1897, respectively.