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TWO CASES ILLUSTRATING THE THERAPEUTIC USES OF THE NITRITES.

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THE following cases are briefly reported in illustration of the therapeutic uses of the nitrites :

CASE I.—*Large doses of nitrites in a case of angina pectoris: psychic effect of inert medication.*—Robert Gallagher, aged 63, laborer, single, native of Ireland, was admitted December 11, 1889. The following notes of his history were made by Dr. Harris, resident physician :

“He has always been a hard-working man, exposed to all vicissitudes of temperature and weather ; has used alcohol in moderation, but has never lost any time from work through drink. There is no venereal history. When a child he had chicken-pox, measles, small-pox and whooping-cough ; at 19 years of age, typhus fever ; and at 20, typhoid fever. At 33 years, an attack of acute inflammatory rheumatism confined him to bed for a number of weeks. Between the ages of 16 and 20 he had occasional attacks of syncope, which lasted for a few minutes. There were no epileptiform convulsions and no aura. In 1862 he came to this country and remained apparently in good health until 1884, with the exception of an attack of pleurisy and the following accidents : fracture of leg in 1872 ; fracture of skull in 1878, and three attacks of mild sunstroke. In 1884, while walking home from his work, he was suddenly attacked with sharp, stabbing pain in the left side, over the region of the heart, accompanied with what he called ‘sprinkles of pain’ running up the neck. The pain quickly passed ; he did not fall or lose consciousness. Shortly afterward the attack was repeated, being, however, much more severe. He felt as if his heart were being compressed between two hands, and as if he were being smothered by a weight upon his chest. There was a sense of impending dissolution. This attack also passed over quickly, but left him too weak to return to work for two days. A repetition of the attack occurred in two weeks. This time the pain ran into the left arm, giving the sensation of ‘sprinkling’ and numbness. Since that time, the paroxysms have been more frequent and more severe ; he has been growing weaker ; his appetite is failing. During nocturnal attacks he frequently loses consciousness for several minutes. There is no sensation of clutching at the throat, but the difficulty in breathing seems to be entirely in the thorax. The pain at times runs along the left shoulder and the back of the neck, terminating at the left mastoid process.”

After admission to the hospital, the attacks recurred almost daily, sometimes twice or oftener in the twenty-four hours. They were of two varieties, the more severe ones being followed by syncope and lasting longer than the others, which he termed "choking spells," and which consisted of paroxysms of cardiac distress and dyspnoea.

The patient noted that there was much less tendency to attack when the stomach was comparatively empty, and after meals he had always more or less pain and discomfort, though not amounting to a paroxysm.

His mother died of some spasmodic pulmonary affection at the age of 76; his father died of apoplexy at 75; one sister died from a heart trouble like his own, so he says, and one from old age. He has one sister living in Ireland and one in Philadelphia, who have attacks similar to his own.

When I took charge of the case, January 16, 1890, physical examination showed no pulmonary lesion, no prominence of the præcordium, no thrill, no visible apex beat. Upon percussion the heart dulness appeared to be slightly less than is usually found. The first sound of the heart was rather feeble and deficient in valvular tone. The second sound was good, therefore relatively accentuated. There was no murmur. The radial arteries were rigid; the temporal arteries tortuous, plainly visible and rigid. There was a marked arcus senilis. The face was anxious and haggard.

Urinalysis repeatedly made, failed to show either albumin or sugar. Urates and phosphates were constantly in excess.

The diagnosis of angina pectoris, the result of arterio-sclerosis, seems to be beyond reasonable doubt. While there was no evidence that either the sunstrokes or fracture of the skull had given rise to permanent cerebral lesion of a nature to account for the symptoms, there was undoubtedly a strong general neurotic element in the case, so that the frequency and, in part, the severity of the attacks had been increased by fear.

The treatment which had been instituted consisted of rest in bed, regulation of diet, due attention to the secretions and excretions, inhalation of amyl nitrite at the time of attack, and the administration of one drop of the centesimal solution of nitro-glycerin three times a day. I ordered the nitro-glycerin to be increased one drop at a dose, until physiological effects were obtained. After the dose had been raised to five minims three times a day, the patient remained for four days free from an attack. The paroxysms then recurred, and seeming to be uninfluenced by further increase of the drug *per os*, it was administered hypodermatically in doses of ten minims of the centesimal solution once, then twice, and finally three times daily. The attacks were partially controlled by this measure, so that a period of two weeks of comparative freedom was obtained before their recurrence; which, however, ensued upon the diminution of the number of hypodermatic injections to two in twenty-four hours.

Sodium nitrite was then administered internally, beginning with one-fourth of a grain and increasing the amount one-fourth of a grain at each dose, until finally a dose of five grains, three times a day, was reached. Under the administration of fifteen grains of sodium nitrite by the mouth, and forty minims of the centesimal solution of nitro-glycerin hypodermatically, in the twenty-four hours, the periods of quietude increased; though for a few days the tendency to continuous repetitions of the paroxysms during the night became so marked, following some mental disturbance, that even this active treatment had to be supplemented by the hypodermatic use of morphine with atropine at 8 o'clock, for several nights.

There having been no recurrence of paroxysms since April 16, during the last week of April the hypodermatic injections were reduced to one per diem, and the amount of sodium nitrite cautiously decreased. Improvement in the patient's condition continuing despite the mitigation of the treatment, and the hysterical element becoming more marked, it was decided to substitute for the nitrites hypodermatic injections of distilled water and pills of althea, without allowing the patient to be aware of the change. Improvement continued, so that the patient was successively able to get out of bed, to go around the ward and then the corridors in a rolling chair, and then to walk out for exercise. The hypodermatic injections were soon discontinued, but the pills were not withdrawn until some time in August, on account of the mental distress occasioned by tentative withdrawal. Sodium iodide and arsenic were then used, the indication being the condition of the arteries. In September, no recurrence having taken place, the patient was transferred to the out-wards.

The chief points of interest in this case are :

1. The large doses of the nitrites required to bring the affection under control.
2. The mental effect, when this control had been secured, of inert medication.
3. While the patient was taking his largest doses of active medicaments, the only perceptible physiological effect was a very occasional and quite transient flushing of the face.

CASE II.—*Influenza in a patient having chronic valvular disease. (Mitral incompetence and aortic stenosis). Treatment by atropine and strychnine, with amyl nitrite.*—William Hayward, aged 54, white, birth place Wales, residence Philadelphia, was admitted January 13, 1890. Ten days previously he had had slight chills, followed by slight fever. A few nights before admission he was picked up in the street unconscious. On admission he complained of pain in the left side of the chest, varying in intensity and situation. There was slight cough with scanty expectoration, which at times was tinged with blood. Temperature was 100°; pulse 100; respirations 32.

Diagnosis of catarrhal pneumonia, probably influenza, was made by the resident, Dr. Harris, who also recognized the chronic cardiac lesions to be described later. He was treated with digitalis and ammonium carbonate, a cotton jacket and turpentine stupes applied to the chest, alcohol freely administered.

This treatment was continued until the 16th, when I took charge of the wards. At that time the temperature, which had pursued an irregular course, falling as low as 96.4°, and rising as high as 102°, was 97° in the morning; the respirations were 44 and the pulse 76. The pulse and respirations had been as irregular as the temperature, the respirations varying between 28 and 56, the pulse always small and feeble, ranging between 48 and 80, though—probably under the influence of the digitalis—its usual range was below 60. There were at this time irregular areas of dull percussion over both lungs, more especially on the right; and at the right base quite a large patch corresponding probably to one-fourth of the lower lobe. The respiratory murmur was feeble throughout, and in situations corresponding with the dull percussion the auscultation signs varied from bronchial

breathing, on the one hand, to absence of breath-sounds, on the other. Both crepitant and sub-crepitant râles were present in varying distribution; the crepitant râles being principally confined to the area of apparently lobar condensation at the right base, immediately above which, pleural friction was plainly perceptible. There was no evidence at any time of effusion.

Palpation in the præcordial region showed the apex of the heart in the sixth interspace and the nipple line. Just above this a systolic thrill was easily perceptible, limited to an area of about the size of a dime. The impulse was feeble and heaving and visible in two interspaces. Percussion showed increase of cardiac dulness toward the right, reaching nearly to the right border of the sternum. At the apex, a blowing murmur, rather low-pitched, replaced the first sound of the heart; the second sound was not audible. This murmur was transmitted into the axilla, and could be plainly heard below the posterior inferior angle of the scapula. Occasionally an indistinct murmur was heard before the systole, just above the apex. Over mid-sternum and over the aortic cartilage, a systolic murmur, harsher in quality and higher in pitch, was heard, and was transmitted into the arteries of the neck. The second sound could not be heard, but was replaced by an indistinct murmur. The differences in pitch and quality between the aortic and mitral murmurs were quite easily recognized, so that there was no difficulty in determining the coincidence of mitral incompetence and aortic obstruction with accompanying regurgitation, both evidently chronic conditions. No history of rheumatism was obtainable in explanation of this, though the patient had been a soldier and subject to much exposure. There were histories of syphilis and of gonorrhœa. The patient had been short of breath, more or less, for ten years, especially upon exertion, so that he had not been able to do much work during that period. There had never been any dropsy; there was no albumin in the urine; the lips were quite blue; the face pale, pinched and anxious; the nails blue; the skin cold.

Diagnosis of the acute condition was influenza, combined lobar and lobular pneumonia. The digitalis was stopped and the patient placed upon atropine sulphate, $\frac{1}{30}$ of a grain, with strychnine sulphate, $\frac{1}{30}$ of a grain, every five hours; nitrite of amyl, five drops in alcohol, by the mouth, every three hours. Ammonium carbonate was continued, ten grains being given every hour at first, afterwards at longer intervals; and whiskey was ordered to be given according to circumstances. Hot-water cans, properly wrapped, were applied along the legs, and the cotton jacket to the chest continued.

On the 19th a deep red flush appeared upon the left cheek and spread gradually, until it involved forehead and eyelids and the margin of the nose. As there were several cases of erysipelas in the wards, there was no doubt as to the meaning of this. Strange to say, however, the temperature was not markedly influenced, varying between 97° and 99° , and continuing for the most part at about 97.6° , until the 24th, when the local manifestations of the erysipelatous process reached their height coincidentally with the development of a new area of consolidation in the left lung, which gave the characteristic percussion and auscultation signs of a basal lobar pneumonia. The local conditions in the right lung had been gradually ameliorating; these shortly became worse. On the 25th the patient had a temperature of 100° ; respirations 52; pulse 76. Ten drops of tincture of chloride of iron was then given every three hours, and an ointment of ichthyol applied to the face. Atropine was increased to $\frac{1}{30}$ of a grain, and strychnine to $\frac{1}{30}$ of a grain. In place of the ammonium carbonate, half a fluid drachm of the aromatic

spirits of ammonia was given every half hour, in one-half ounce of whiskey; and twenty drops of the fluid extract of coca was given every hour at a later period. The chest was actively dry cupped and counter-irritation kept up by sinapisms and poultices. On the 29th the temperature was, at 11.30 A. M., 96.2°; respirations 48; pulse 66; at 6 P. M., temperature 97.4°; respirations 52; pulse 84.

On February 5, the morning temperature was 97°; respirations 20; pulse 80. On February 8, temperature was normal. Atropine, strychnine, amyl nitrite, with alcohol according to circumstances, was now the treatment. The temperature continued to vary between 97° and the normal line, keeping usually below 98°, occasionally falling as low as 96.4°; finally, on the 29th of March, becoming and thereafter remaining normal. At this time the respirations were 18 and the pulse 72. The pulse was now regular, comparatively strong, and much fuller than it had ever been; alcohol had been discontinued. The patient continued steadily to improve in all respects, and when transferred to the Soldiers' Home was capable of a greater degree of exertion without dyspnoea, than he had been for many years.

The interest in this case, if we set aside the prolonged low temperature which was so common in cases of influenza, is almost exclusively therapeutic. The well known tendency of influenza to bring about death in cases of such marked cardiac impairment as this patient presented, led to the formulation of a gloomy prognosis; and the patient's condition during the height of his pneumonia, and again when the smouldering embers of the pneumonia were relighted by the erysipelas, was such as to justify the gravest apprehensions. Antipyretic medication was evidently counter-indicated, but had any of the coal-tar compounds been administered for the relief of pain, as was so common, and, I believe, so unfortunate a practice throughout Europe and America during the prevalence of the pandemic, doubtless the result would have been in accordance with our fears.

Again, upon first sight, the cardiac conditions would have seemed to emphasize the indication for digitalis presented by the pneumonia. When the case came under my care, however, it was quite evident that digitalis had been of no avail, while the interpretation of the physical conditions—including among these the great disproportion between pulse rate and respiration—which seemed to me most obvious, was a direct counter-indication to its employment. Both right ventricle and left ventricle were enlarged, but during the acute attack it was impossible to determine whether hypertrophy had kept pace with dilatation. The valvular conditions had largely to determine the choice of therapeutic agents. With the current of blood obstructed at its entrance into the aorta, and with an incompetent mitral valve

permitting regurgitation into the auricle at the moment of systole, it seemed evident that the most pressing necessity was to hurry the cardiac rhythm, so as to diminish the time and pressure of mitral leakage.

Prolongation of the diastole must have been futile so long as the aortic obstruction prevented the increased quantity of blood, which might accumulate in the ventricle during the prolonged diastole, from finding its way out, except backward through the incompetent mitral, through the auricle and pulmonary veins, into the pulmonic circulation; there to increase pulmonary congestion and, therefore, the difficulty of breathing. It is true that a strengthening of the muscular contraction, within limits, was also of prime importance; but the considerations just mentioned indicated that digitalis was not the proper agent by which to secure this strength, while its effect in heightening systemic blood pressure was an additional reason against its use. Atropine and strychnine were therefore chosen, while nitrite of amyl was given in order to diminish the load placed upon the heart, by lowering the blood pressure; in this way partially compensating for aortic obstruction. Amyl nitrite was chosen in preference to other nitrites by reason of the greater rapidity and greater fugacity of its effect; thus permitting a better control. Its internal use is new in this country, though long practiced in England by B. W. Richardson.

The result of treatment in this case seems to have proved the correctness of the theories upon which it was based.

Extraordinary tolerance of nitrites is occasionally encountered, but I have never met with a case so rebellious to their influence as the case of angina here reported; nor, on the other hand, have I ever seen a more striking manifestation of their power for relief of this condition when once the proper dosage had been reached. Attention should also be called to the hypodermatic method of administration, which, if carefully conducted, involves little risk of local trouble.

These two cases illustrate very well the applicability of the nitrites to two methods of restoring equilibrium of circulation. As the proper balance of function constitutes health, the aim of the therapist must be to re-establish that balance in the most feasible manner, and with the least alteration of functions other

than those implicated in the existing disturbance. Broadly speaking, he must choose between two methods: first, the direct method, that of elevating a depressed function, or depressing an unduly exalted function, to the normal level; second, the indirect method, that of depressing or elevating a normal function, to the abnormal level of a disturbed function with which it may be correlated. As the first case illustrates the direct method, *depression of abnormally exalted function*; so the second case illustrates the indirect method, *compensatory depression of normal function*.

It is to the insistence of Bartholow upon the utility of lowering peripheral arterial tension by the use of the nitrites in cases of impaired cardiac vigor, that the medical profession in America owes the knowledge which gives power to accomplish results that to the lay observer seem hardly short of miraculous.

