Treatment.

In advanced cases medical and general treatment is indicated, as surgery offers little prospect of cure, but when the disease is limited to the epididymis and seminal vesicle radical operation is indicated. It should consist of removal *en bloc* of the epididymis (or epididymis and testis), the vas deferens, the seminal vesicle, and when necessary a portion or the whole of the prostate. The operation can be accomplished through an inguinal incision by Loughnane's method, but if the prostate is involved Young's combined inguino-perineal method is necessary. Should the disease be secondary to unilateral renal tuberculosis the affected kidney must be removed first and the operation on the genital tract postponed to a later date.

In all cases tuberculin is of great value, but only after operation. In my experience it has not the least effect on well established urogenital tuberculosis, and should never take the place of surgery if removal of the disease is possible.

An Address

ON

**THE CONSTITUTIONAL FACTOR
IN DISEASE.**

DELIVERED BEFORE THE ULSTER MEDICAL SOCIETY,

BY

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(Concluded from p. 827.)

BLOOD PRESSURE AND CONSTITUTION.

DISCUSSIONS on abnormal blood pressure have in the past suffered from our ignorance as to what constitutes the normal. Stocks²¹ has recently investigated the blood pressure of 1,323 English boys, and the extensive investigations of Alvarez²² and his colleagues on 6,000 male and 8,934 female first-year students at the University of California have provided reliable figures for young adults. The statistics published by Symonds²³ of 141,840 applicants for insurance in an American company give additional data for all ages above 15, the smallest group (over 60) being no fewer than 1,889. In children there is a steady rise in systolic pressure from an average of 85 mm. at 5 to 101 mm. at 10 and 123 mm. at 15. Contrary to what might be expected, there is no rise with advancing years from 17 to 40, the average systolic pressure being 125 mm. in men and 115 mm. in women. After 40 there is a slow rise, the maximum average being 135 mm. for 60 and over, but there is no longer any difference between the sexes.

In healthy individuals of the same age, sex, and race considerable variations occur. Thus Alvarez and his associates found that among the students they examined 2.77 per cent. men and 11.74 per cent. women had a systolic blood pressure less than 105 mm., and 20.81 per cent. men and 3.75 per cent. women had a blood pressure over 140 mm. It is, of course, impossible to draw exact lines above and below which the blood pressure should be regarded as abnormal. For convenience I would suggest that hyperpiesia is present when the blood pressure is more than 25 mm. above the average normal for an individual's age and sex. This would give a limit of 150 mm. in men and 140 mm. in women up to the age of 40, and 160 mm. for both sexes at 60. According to this standard, 8.15 per cent. men and 3.75 per cent. women among the 15,000 healthy students examined by Alvarez had hyperpiesia.

No such sliding scale is required for hypopiesia. American writers generally take 110 mm. as the minimal normal figure, but Alvarez's investigations clearly show that this is too high. A preferable limit would be 105 mm. for men and 100 mm. for women. According to this definition it was present in 2.77 per cent. of the 6,000 men and 3.50 per cent. of the 8,934 women among Alvarez's first-year students.

There is no doubt that the tendency to hyperpiesia is hereditary. Long before the invention of the sphygmomanometer the familial occurrence of high blood pressure,

apart from disease of the kidneys, was recognized, and it was well known that many members of successive generations of a family might die from such results of high pressure as cerebral haemorrhage and cardiac failure, associated with arterio-sclerosis and hypertrophy of the heart. The tendency to hypopiesia is probably inherited with equal frequency. The actual cause of the high or low blood pressure is quite unknown, though it is probably, at any rate in part, due to variations in the activity of such internally secreting organs as the suprarenal, the pituitary, and the thyroid glands.

I believe that hyperpiesia and hypopiesia should be regarded as constitutional conditions or diatheses, being simply extreme degrees of variation from the average normal. They are not diseases and need never give rise to symptoms, but an individual with either condition is apt to react in a special way to toxæmias and to mental and physical fatigue.

The diffuse hyperplastic sclerosis of the arteries, described by Evans as a constant pathological finding in hyperpiesia, is, I am convinced, a result, like the cardiac hypertrophy, of the constitutional high blood pressure, and not its cause. Clinically hyperpiesia may be associated with apparently perfectly healthy blood vessels, especially in young subjects before the pressure has become excessive.

(a) Hyperpiesia.

So much has been written on the subject of hyperpiesia since the classical analysis of the condition by Sir Clifford Allbutt that I have little to add. I think, however, that too much time has been expended in looking for some toxic cause, when in reality true hyperpiesia, as distinct from the high blood pressure secondary to chronic renal disease, is not a malady but a diathesis—a constitutional inherited condition. So far as I know, Dawson and Ryle⁴ are the only recent writers who have laid much stress on this aspect of the subject. Ryle has pointed out that the stout, healthy looking, John Bull type of individual is generally the subject of hyperpiesia, which is not acquired but is inborn. Among his patients with hyperpiesia 62 per cent. were of this type, 18 per cent. of average build, 4 per cent. "lean and nervous," and 16 per cent. of poor physique. The question might arise whether the exceptions were really suffering from primary hyperpiesia; in the lean and nervous individual I believe that a high blood pressure is generally secondary to the mental state. I found during the war, in cases of functional hyperthyroidism associated with a high blood pressure, that simple hypnosis often resulted in an immediate fall, amounting even to 45 mm., when the state of anxiety in which the patient lived was temporarily removed. A boy of 16, recently under my care, had an acute attack of nephritis from which he recovered completely, except that the blood pressure remained constantly in the neighbourhood of 156 mm.; as his urine was normal, the blood urea not raised, and the urea concentration test gave a normal result when he came under my observation six weeks after the onset, I allowed him to get up, and told him that his prolonged stay in bed had at last cured him. The next day his blood pressure had fallen to 120 mm., and it remained at this normal level, the previous rise having apparently been due to continuous anxiety, although he always appeared cheerful enough, but bored at having to stay in bed.

The typical hyperpietic has certainly a hypersthenic habitus; he is well built, with broad shoulders and a short, deep thorax with wide costal angle; he has a ruddy complexion, and may be actually plethoric; he is often athletic, unless overindulgence in food and drink has led to a crippling degree of obesity.

Hyperpiesia is often an accidental discovery in an apparently healthy man of exceptional mental and physical vigour. But sooner or later symptoms appear, generally as a result of mental or physical overwork, prolonged worry, excess of food and drink and perhaps of tobacco, or an acute or chronic infection. In women symptoms may develop at the menopause.

The symptoms are generally not due to the high blood pressure itself, but to its effects on the blood vessels or heart. Thus arterio-sclerosis impairs the blood supply to various organs, such as the brain and kidneys, which become

functionally inefficient, though in the case of the latter the blood urea never rises to the extent it does in primary renal disease; the loss of elasticity of the arteries may render them incapable of withstanding the strain of the high blood pressure, so that retinal and cerebral haemorrhages and epistaxis may occur. In spite of its hypertrophy the heart may eventually be defeated in its attempt to maintain an adequate circulation against the great peripheral resistance; cardiac symptoms, such as dyspnoea and precordial pain, then develop. The only symptoms which may perhaps be directly due to the high blood pressure are headache and vertigo, though even these are often absent in people with a blood pressure exceeding 200 mm.

When symptoms once appear in people with hyperpiesia the prognosis is never good, as there is an ever-present danger of death from cerebral haemorrhage or cardiac defeat, though this may of course not occur for several years.

(b) Hypopiesia.

Although hypopiesia—an abnormally low blood pressure occurring independently of any organic disease—is as common as hyperpiesia, much less attention has been paid to it. It may be defined as a constitutional and often inherited condition, in which the systolic blood pressure is permanently below 105 mm. in men and below 100 mm. in women, without recognizable cause, such as tuberculosis, circulatory failure, severe anaemia, hypothyroidism, or Addison's disease. It is often discovered accidentally in perfectly healthy individuals. Further investigation generally shows that they are of hyposthenic habitus—thin, slouching, with long and narrow chests and acute epigastric angle. They are rarely athletic, and they generally choose a sedentary occupation.

Though not actually ill, the hypopietic is rarely very well. His most common symptoms are undue liability to mental and physical fatigue and a general lack of endurance, which is often in striking contrast with the heroic efforts he makes to carry on in spite of his disability. He is often subject to headaches, especially in the occipital region, and to attacks of vertigo, and more rarely of palpitation and syncope. He is generally pale, though not anaemic, and suffers from cold extremities. These symptoms are most likely to arise as a result of mental and physical strain or some acute or chronic infection or toxæmia, which would either have had no effect or only a slight and temporary one in individuals with an average blood pressure.

Fisher²⁴ found that the mortality of 3,589 persons, aged between 16 and 60, accepted for insurance, who had a systolic blood pressure of 100 mm. or less, was 35 per cent. of the expected mortality according to the standard American tables, whereas the general mortality among those insured by the company was 80 per cent. of the expected rate. According to Muhlberg,²⁴ the medical director of another insurance company, a low blood pressure after the age of 50 without any obvious cause is the best criterion we possess that an individual will live beyond his normal expectancy.

Treatment of Hyperpiesia and Hypopiesia.

People with hyperpiesia and hypopiesia should be made to understand that they are not suffering from a disease, but that a constitutional tendency has been discovered in them, which indicates the desirability of care in certain directions in order that the maximum of physical and mental efficiency may be attained and preserved. It would probably be wise, when possible, to avoid all reference to blood pressure, and it is certainly most undesirable that the patient should keep a record of its variations. The last few years have introduced a new type of hypochondriac, and blood pressure has become one of the favourite topics of discussion at tea-tables and in club smoking-rooms. I once spent an unhappy week at a large hotel in one of the British spas where hyperpiesia is treated; my fellow guests appeared to have no other interest than in comparing the variations in their respective blood pressures. I have often been consulted by patients, who looked and felt perfectly well, for "blood pressure," which they apparently thought was the synonym of a serious disease.

It is even more essential for the subjects of hyperpiesia and hypopiesia than for the average man to take adequate holidays. But whereas the hyperpietic should be taught to restrict his exercise within more moderate bounds than those to which he has probably been accustomed, the hypopietic should be urged to take as much exercise in the open air as he can without exhaustion, even if, as is often the case, he has in the past taken little or none. He will often find that a holiday in the Swiss mountains will make him more physically efficient than he had thought was possible, and he may become an expert in such sports as climbing in the summer and ski-ing in the winter, which are quite unsuitable for the hyperpietic. Whereas the hyperpietic should be strictly moderate in his consumption of tobacco, alcohol, and coffee, and should even give them up entirely if previously taken in excess, such restrictions are rarely called for with the hypopietic; a cup of black coffee and a pipe after dinner and an occasional half-bottle of champagne will materially help him to enjoy work which would otherwise require an almost intolerable effort. Restriction in the quantity of food, which should be as largely vegetarian as possible, for the stout and plethoric hyperpietic is essential, whereas the thin hypopietic should be urged to eat plentifully without restrictions as to the consumption of meat. For both types any source of infection should be looked for and treated. I have seen several hyperpietic patients, who had more than the normal percentage of haemoglobin, benefit greatly from periodic bleeding, though it did not appear to lower their blood pressure; when well marked plethora is present the application of deep x rays to the long bones may throw out of action sufficient red marrow to reduce the number of blood corpuscles to normal limits, and at the same time cause a definite fall in blood pressure. In addition to outdoor exercise, physical drill, especially directed to the respiratory and abdominal muscles, is very useful for the hypopietic, who may also derive much comfort from the use of an abdominal support.

THE CONSTITUTIONAL FACTOR IN ASTHMA, EPILEPSY, AND MIGRAINE.

Several years ago²⁵ I defined asthma as a condition in which that part of the vagal nucleus which controls the motor and secretory activity of the bronchi is abnormally sensitive to chemical, reflex, and psychical stimuli. The importance of this definition lies in the recognition of the sensitive bronchial centre. In the first decade of the present century many rhinologists were so impressed with the results of the nasal treatment of asthma that they were inclined to regard an abnormal nose as the sole etiological factor. More recently the work of a number of investigators in England and America and on the Continent has directed attention to the importance of specific hypersensitivity to the proteins of bacteria, food, animal emanations, and pollens, and most of the recent literature of asthma would lead one to suppose that in this—the "toxic idiopathy" of Freeman—is to be found the whole explanation of asthma. Lastly, a few enthusiastic neurologists would regard asthma as always of psychological origin. Attacks of asthma may, in fact, be caused by a great variety of reflex and chemical stimuli, as well as occasionally by psychological stimuli, but only if the individual has the asthmatic constitution, which manifests itself in an irritable bronchial centre, this being the one essential factor in the pathogenesis of asthma. It was inherited in 49 per cent. of 1,129 cases collected from various sources, compared with only 7 per cent. of 115 controls, and it is interesting to note that an individual may inherit it and transmit it to his children, without ever having an attack of asthma himself owing to the absence of the three groups of exciting causes. Thus the paternal grandparent and uncle and maternal grandmother and aunt, but neither parent, of one of my asthmatic patients suffered from asthma.

The question of inheritance of asthma is complicated by the fact that a toxic idiopathy, though sometimes acquired, may also be inherited, either in the form of a general hypersensitiveness to proteins, or, much less frequently, in a specific form to a single protein. Asthma does not, however, necessarily occur in each individual

with a toxic idiopathy, as the asthmatic constitution may not be present. A toxic idiopathy will give rise to asthma, hay fever, urticaria, or angio-neurotic oedema, vomiting or diarrhoea, or vasomotor neuroses of various kinds, according to whether the individual affected has a bronchial centre, nose, skin, alimentary tract, or vasomotor centre which is abnormally irritable. Two of the conditions may be present together, or they may occur in different members of the same family; thus asthma is frequently associated with hay fever and sometimes with urticaria, and a family history of hay fever is common among asthmatics, and vice versa. Just as an inherited asthmatic centre may be present in an individual who never gets asthma, though he may transmit it to his children, so a toxic idiopathy may be transmitted by an individual who is otherwise so normal that he never suffers from its effects. As toxic idiopathies give rise more frequently to asthma than to any other condition, it seems probable that the asthmatic constitution is one which is particularly likely to develop such idiopathies.

The clinical picture presented by the other most important paroxysmal neuroses—epilepsy and migraine—resembles asthma so closely in certain respects that the question of their relation with each other requires consideration. Epilepsy depends upon the presence of a constitutional and often inherited excitability of some part of the nervous system, which responds to certain stimuli by the production of an epileptic attack. The nature of these stimuli is, however, quite unknown in the majority of cases; the most important is perhaps chemical in nature, but there is no evidence to support the theories that intestinal intoxication or toxic idiopathies play any part. Reflex and psychical stimuli also occasionally give rise to attacks, but they are of comparatively small importance. A family history of epilepsy in an asthmatic or of asthma in an epileptic is so uncommon that, when it occurs, it cannot be regarded as more than a coincidence, and I have only seen one case in which asthma and epilepsy occurred in the same individual.

Migraine also depends upon a constitutional and frequently inherited irritable focus in the brain, which gives rise to headache, disturbances in vision, and gastric symptoms; there was a family history of migraine in 30 out of Bramwell's²⁶ 54 cases (55.6 per cent.). In migraine the usual stimulus is ocular, and a very thorough investigation in numerous cases under my care has invariably failed to reveal anything in the nature of alimentary toxæmia, hepatic insufficiency or a toxic idiopathy, which could be held responsible, in spite of the fact that on theoretical grounds these have frequently been suggested as the exciting cause of attacks. The evidence of a psychological origin is also quite insufficient except in rare cases, in which, however, eye-strain also invariably plays a part. I have only met with one case in which migraine and asthma were associated in the same individual, and there is no evidence that they occur together in the same family more than would be expected from the frequent incidence of both conditions among the general population. The same is true with regard to the association of migraine and epilepsy, so that it may be concluded that the constitutional basis of asthma, epilepsy, and migraine, though somewhat similar in nature, is in each case specific, and that no one of these conditions in a parent predisposes to the development of either of the other two in the children.

Long ago, in discussing the treatment of the constitutional basis of asthma, I said that the only cure of asthma is not to have it. The same is true of epilepsy and migraine. The longer a patient can be kept free from attacks by any form of treatment, the less irritable his abnormal nerve centre becomes, though it is doubtful whether the constitutional hypersensitiveness is ever entirely lost in asthma or epilepsy, though with advancing years the complete cessation of migraine attacks is not uncommon. A patient of mine, who had been free from asthma during a residence of twenty-five years in South Africa, developed an exceedingly severe attack on his return to his home in England, where as a boy he had been almost constantly asthmatic. I have known many epileptics relapse directly they gave up taking bromide, which they had been told they could discontinue after they had been free from attacks for one, two, or three years.

It is true that the liability to attacks steadily diminishes as the period of freedom lengthens, but I am inclined to think that nobody who has once suffered from epilepsy should ever discontinue the use of small doses of bromide or luminal, even if he remains free from fits for five or ten years. Kinnier Wilson has recorded the case of a lady who had only two attacks in her life, the interval between them being no less than thirty years.

Conversely, the more attacks an individual with asthma, epilepsy, or migraine has, the more irritable his centre becomes. An asthmatic develops the status asthmaticus, in which the treatment he usually employs for an attack fails to help; nothing will then relieve him until he has moved to some more favourable surroundings, where rapid recovery will generally take place.

The *faiblesse irritable* of the nervous system, which is the ordinary sequel of mental and physical fatigue, increases the constitutional irritability of the nervous centre upon which the paroxysmal neurosis depends. Consequently it is of the utmost importance for individuals who are subject to asthma, migraine, or epilepsy that the work of each day should be limited in duration, that the week-end should be sufficiently restful, and that two annual holidays of adequate duration should be taken. This is particularly important in the case of asthma and migraine, both of which tend to occur in people whose mental capacity often leads them to adopt a career in which overwork is likely to occur.

Unfortunately there is no drug which exerts a favourable influence on the constitutional factor in asthma comparable with that of luminal in epilepsy and migraine and of bromide in epilepsy. Climate has, however, a remarkable effect, quite apart from the influence of vegetable and animal emanations which may render one place unsuitable to some asthmatics without having any effect on others. Thus asthma hardly ever occurs among the permanent residents of the Swiss mountains, and many asthmatics who, in spite of the greatest care with regard to diet, the avoidance of fatigue, and other exciting causes, have asthma more or less continually whilst at home and are unable to take any active exercise or even walk upstairs without dyspnoea, become entirely free within a day or two of their arrival in the mountains, where they can climb all day in summer and ski or s'ate in winter without respiratory distress. That the climate exerts a specific influence in diminishing the irritability of the bronchial centre is shown by the fact that chemical and reflex stimuli, which would cause violent attacks at home, no longer produce the slightest ill effect. This is perhaps one of the strongest arguments against those who regard nasal abnormalities or toxic idiopathies as the only factor worthy of consideration in the pathogenesis of asthma and entirely neglect the essential constitutional element in the disorder.

No child should be allowed to go to school or spend his holidays in a place where he is asthmatic. I knew an Eton boy whose home was in London and who was always in the status asthmaticus whilst at school; this could be interrupted by sending him to Paddington Station for a few hours, but returned as soon as he got back to Eton. If he had stayed at Eton the constitutional basis of the disorder would have been so firmly established that the prospects for the rest of his life would have been seriously affected. He was removed on my advice, and is now at a school where he has no asthma.

In the comparatively rare cases in which it is impossible to find a place in England where a child is free from asthma, and where rhinological, immunological, and other treatment has failed to give relief, a year's residence in the Swiss mountains is likely to save him from becoming a permanent invalid. The removal of chemical and reflex causes is likely to be futile if the constitutional element of the disease is neglected; such treatment is always most effective if carried out during a period of comparative or complete absence of symptoms.

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