the inspired air with oxygen usually, if not always, gives relief. On the other hand, when the symptoms are due primarily to a slowing of the whole circulation or a circulatory deficiency due to a local vascular lesion, the administration of oxygen may have little or no effect. The reasons for this would seem to be self-evident. In certain cases, however, the administration of oxygen may give relief when not expected to do so; on the contrary, its failure to be efficacious is sometimes experienced when a good result would be most expected. A more thorough examination of these cases usually indicates that a combination of these causes is operative. To what extent either factor predominates may, however, be difficult to ascertain.

If the partial pressure of oxygen in the alveoli is to be increased the inspired air must be enriched with oxygen by the time it enters the nasopharynx. This necessitates the administration of a sufficient quantity of oxygen a minute by some apparatus which will ensure its being inhaled. The placing of a funnel one inch from the patient's face will not accomplish this. In our experience only two methods are efficacious—by the use of a fairly tight-fitting mask, or by introducing a rubber catheter through the nose into the nasopharynx. Through this catheter there is passed an adequate supply of oxygen. The supply is frequently regulated by, in lieu of some better method, bubbling the gas through a Wolff bottle or other similar contrivance. In order that a sufficient quantity shall be administered it must enter the bottle through a tube of at least 1 cm. bore, and the bubbles must be so rapid as not to be countable.

The use of oxygen, of course, does not remove the necessity for adopting all other means of treating cardiac failure, and by no means the least important of these is physical and mental rest. It is remarkable how patients do improve by good nursing and general comfort. It would appear that the reason for this is the conservation of circulatory energy for those vital organs which of necessity require a good blood supply.

The employment of drugs which increase the cardiac power is not to be ignored. Of these there is, to my mind, only one which is of value, and that is digitalis. The indications for its use and the method of its administration must be left for consideration at another time.

Many of the observations upon which these conclusions have been based were undertaken in the Department of Therapeutics, Edinburgh University, in collaboration with Drs. Davies, Dautrebande, and Fetter.

THE EFFECT OF HEAT UPON OPERATIONS FOR EXOPHTHALMIC GOITRE.

BY

A. J. WALTON, M.S., F.R.C.S., M.B., B.Sc.,
LONDON HOSPITAL.

THAT the results of operative treatment in many cases of exophthalmic goitre are satisfactory is now generally admitted. Until some fifteen or twenty years ago the danger of such an operation was, however, so great that few physicians felt justified in advising it. To-day the results have been so enormously improved that the mortality is no higher than that of other major operations. At the discussion of the Royal Society of Medicine in 1921,⁶ and again at the meeting of the British Medical Association in Glasgow, it was generally agreed that the mortality was somewhere in the region of 5 per cent. In the hands of individual surgeons it has often been lessened considerably below this. Romanis⁵ was able to show a mortality of only 2.4 per cent. in a series of 250 cases, and the latest statistics from the Mayo Institute published by Pemberton⁴ record a series of 1,093 operations with 11 deaths—that is, a mortality of 1 per cent. All who have operated on large numbers of these cases feel, however, that in spite of their care and attention to detail there is an element of uncertainty in the result which is absent in other cases. My own experience has been that although these cases can be divided into definite groups, one of which has a higher death rate than the others, yet now and again a death will occur when least expected. This feeling of uncertainty and anxiety has been expressed also by Berry,² Dunhill,³ and

Romanis,⁵ and all are agreed that there is some factor which is at present not fully understood.

If the causes of danger in the operation be analysed, it is possible to appreciate not only what are the means by which so much improvement in the operative results has been obtained, but also which is the factor at present uncertain and to which attention must be given in future. Pemberton⁴ has well analysed these dangers. He classifies them into the three following groups:

1. Those directly resulting from the disease and the effects of the disease.
2. Those directly due to accidents such as haemorrhage, pulmonary embolism, etc.
3. Those the joint result of disease and accident.

Careful attention to the technique of operation, to the limitation of haemorrhage, to careful handling of the gland, etc., have done very much to lessen the dangers of groups 2 and 3; so that the risks arising therefrom are in no way specially applicable to operations of exophthalmic goitre. In the first group the dangers are twofold. If the hyperthyroidism has been present for a long period, secondary changes will have taken place in the heart and kidneys, and the patient will stand any operative measures badly. In the future it is probable that risks of this nature will be almost negligible, for the condition will not be allowed to progress too far before operation is undertaken. At present, however, but little can be done to reduce the mortality. The secondary conditions can be readily recognized, but the operation must be undertaken in spite of them, with a full knowledge of its danger, in order to give the patient her one chance. It is the inclusion of so many such cases that, in my own series of 140, has maintained the mortality at about 5 per cent. In fact, at the present time the reduction of the mortality much below this figure would, in my own hospital practice, made up as it is so largely of ignorant patients, lead to the suspicion that advanced cases were being unjustifiably refused the benefits of operation.

The second danger in this group is the presence of hyperthyroidism. If a patient dies unexpectedly after operation there are nearly always presented symptoms of profound post-operative hyperthyroidism, and hence it is to this danger that attention must in the main be directed. The importance of not operating in the first six months of the disease, when the symptoms can be most easily controlled and often, indeed, cured by medical treatment, I have previously laid stress upon. The fact that every case must be carefully watched in a nursing home or hospital until the hyperthyroidism is at its lowest ebb, the importance of the basal metabolic rate as an indication of the extent of the hyperthyroidism, and the value of medicinal measures in reducing the hyperthyroidism before operation, have been noted by many operators. In fact, more has been done by attention to such details to lower the mortality than by any other step. All surgeons have appreciated the fact that chloroform in such patients is a deadly poison and must be avoided. Some surgeons, indeed, advocate that all general anaesthetics should be abandoned, but here there is not so much unanimity of opinion, for many, and among them myself, have felt that the nervous upset of the patients which is produced when they are conscious at the time of the operation will more than balance the benefit gained by omitting a general anaesthetic. My own custom is to obtain unconsciousness by a minimal dose of rectal ether, and to continue the anaesthesia by means of ether administered on an open mask. Even with every care in the use of such methods, and in the administration of large doses of fluid before and after operation, it will be found that there is a post-operative reaction. In the more satisfactory cases this is slight, but in others the temperature may reach 103° for two or three days, and the pulse may rise to 160. The patient will sweat excessively, will suffer from dyspnoea, and will show a very considerable restlessness which is only controlled with difficulty by morphine. I have previously directed attention to the fact that two distinct groups of cases may be recognized, although there is every gradation between the two. The one occurs in young females who have a large soft, smooth thyroid, marked exophthalmos,

and a rapid pulse, and sweat freely. Such cases I have described as the "vascular group," and as a rule they show only a moderate reaction and rapid improvement after operation. The second group I have designated the "nervous type." Here the patient is more commonly between the ages of 40 and 45; the thyroid is smaller and more nodular, the pulse is less rapid, though often more irregular, and the nervous symptoms are much more prominent. These patients show considerably more reaction and make a slow post-operative recovery. Even when these two groups have been recognized and separated, a careful study of the immediate post-operative results will show a very considerable variation in the reaction, and it is to one cause of this variation that I wish to direct attention in this communication.

It has long been realized that the thyroid secretion has a very marked effect on the heat regulation. All cases of myxoedema feel the cold very severely, while those of hyperthyroidism are in a like degree affected by the heat, so that they are much more comfortable during the cold weather. In my own cases the post-operative distress in hot weather has been much accentuated, and special precautions, such as the use of electric fans, of ice, and of cold sponging, have long been used. In spite of all such precautions it has been my steadily increasing opinion that the mortality during the hot periods has been abnormally high. A careful analysis of my cases from this point of view shows very clearly that such is the case. In my own series there have been two deaths, occurring respectively in the months of January and December. Both of these were in patients with advanced degrees of the disease and were dependent upon secondary cardiac changes. All the others occurred during the hot months of June, July, and August, and all were what may be described as unexpected deaths in that they occurred in patients who by no means showed a pre-operative hyperthyroidism in excess of the others and in whom all the usual precautions had been taken. They also all showed extreme post-operative reaction passing on to acute hyperthyroidism and death. In the accompanying chart I have plotted out the percentage mortality among the total cases operated upon in the individual months of the year, and it is seen that whereas in February, March, April, May, September, October, and November there is no mortality, in the three months of June, July, and August it is in the region of 20 per cent. The effect upon the curve in January and December of the two deaths mentioned above is also shown.

Chart showing the percentage mortality among cases of exophthalmic goitre operated upon in the individual months of the year.

These figures have been collected over a period of ten years, and hence are of considerable value, for it is unlikely that any accidental factor should give so marked an alteration in the mortality which occurs for these three months. Moreover, a mortality of 20 per cent. which is present when the cases operated upon in June, July, and August are considered alone, is one that is much too high and must in fact be considered as an unjustifiable risk. These figures have made it manifest to me—and I publish them in the hope that they will warn others—that no operation on a case of exophthalmic goitre should be undertaken in extremely hot weather, for under such conditions the risk in spite of all precautions is too great and can be easily countered by awaiting more suitable conditions. Fortunately from this aspect the English climate is so variable

that seldom would it be necessary to postpone operation for more than two or three weeks.

REFERENCES.

- ¹ Berry, J.: Discussion on Exophthalmic Goitre, BRITISH MEDICAL JOURNAL, November 11th, 1922, p. 911.
- ² Berry, J.: Discussion on the Medical and Surgical Treatment of Graves's Disease, *Proc. Roy. Soc. Med.*, July, 1921, p. 4.
- ³ Dunhill, T. P.: Discussion on the Medical and Surgical Treatment of Graves's Disease, *Proc. Roy. Soc. Med.*, July, 1921, p. 9.
- ⁴ Pemberton, J. de J.: Mortality in Surgery of Exophthalmic Goitre, *Surg., Gyn., and Obstet.*, April, 1920, p. 458.
- ⁵ Romanis, W. H. C.: The Surgical Treatment of Exophthalmic Goitre, *Lancet*, March 11th, 1922, p. 471.
- ⁶ Walton, A. J.: Discussion on the Medical and Surgical Treatment of Graves's Disease, *Proc. Roy. Soc. Med.*, July, 1921, p. 42. A Consideration of Some Cases of Exophthalmic Goitre Treated by Operation, *London Hospital Gazette*, Clin. Supplement, April, 1914. A Consideration of Some Cases of Exophthalmic Goitre Treated by Operation, *Lancet*, May 16th, 1914. The Operative Treatment of Exophthalmic Goitre, *Practitioner*, October, 1914. Fifty Cases of Exophthalmic Goitre Treated by Operation, *Practitioner*, October, 1917.

INTRAVENOUS INJECTIONS OF PEPTONE AS AN AID TO VACCINE TREATMENT.*

(Abridged.)

BY

H. WARREN CROWE, M.D., B.Ch.Oxon.,

HARROGATE.

DURING the last eighteen months I have used intravenous injections of peptone in some seventy odd cases of patients who were very sensitive to vaccines, with satisfactory results. Patients to whom one could not give 100,000 streptococci or the same number of *M. deformans* without producing a reaction and general malaise, after peptone treatment were able to tolerate much larger doses.

For a good many years now Dr. Auld has given intravenous injections of peptone in cases of asthma, and claims a fair proportion of successful cases. It is fairly well established that most cases of asthma are due to an extreme sensibility on the part of certain cells of the body to a foreign protein. The slightest trace of this specific protein produces an attack of asthma. The disease, then, depends on a toxic idiopathy, and is strictly comparable with hay fever, urticaria, angioneurotic oedema, and possibly a large variety of other diseases.

Apparently the poison may be air-borne and conveyed directly to the cells, as we suppose it to be in hay fever; or it may be derived from the blood stream, as is the case when food or certain intestinal bacteria excite the attack. There are a great many different proteins which are poisonous in this way. Susceptible individuals may be affected by several of them widely differing in source (Freeman,¹ Chandler Walker²). Dr. Auld³ first brought forward peptone as a general non-specific immunizing substance, but its action in combating the cell sensibility is extremely obscure. There is no doubt that in some cases the effect is dramatic.

In Dr. Auld's present view, peptone acts by immunizing the system against any protein whatever, although itself incapable of acting as an antigen or producing any antibody, as he himself has shown by experiment. I cannot altogether subscribe to this view, because if peptone cannot function as an antigen, it does not seem to me possible that it should act as an immunizing agent.

It seemed a hopeful procedure to try the injection of peptone in other states of sensitiveness as well as in asthma. In my own experience the treatment of conditions like rheumatism, arthritis, and neuritis by streptococcal vaccine and *M. deformans* vaccine has frequently been rendered extremely difficult owing to sensitiveness—that is to say, that however small the dose given the patient gets a reaction and feels ill. Many cases have failed to benefit, or have obtained benefit only after very prolonged treatment with infinite patience and minute doses.

It is difficult to say why this condition of sensitiveness should arise; it may be that my method of giving frequent small doses excites sensitiveness, as some hold occurs in tuberculosis. On the other hand, patients are sometimes sensitive to the first dose. In a recent case half a million

*Read before the Leeds Medico-Chirurgical Society.