Phosphatase and the Diagnosis of Jaundice.

The enzyme, Phosphatase, originally described by Robison in bone, where it is concerned in the splitting of hexose mono-phosphate, an essential mechanism in the formation of bone, has been found to be a normal constituent of various viscera and is present in blood.

As early as 1930 Morrel Roberts drew attention to the fact that blood phosphatase —it is easily estimable colorimetrically—was appreciably increased in different pathological conditions, among which obstructive jaundice was a notable instance.

After the pursuance of further investigations into the phosphatase activity of blood, with particular reference to the various types of jaundice, he announced that an estimation of the enzyme in the blood constituted a far more reliable indication of the type of jaundice occurring than the conventional laboratory standby—the van den Bergh reaction. In fact, after subjection to rigorous experimental test, Roberts was convinced of the fallibility of the latter reaction.

In a series of experiments in 1933, in which the blood of jaundiced patients was subjected to a phosphatase estimation and a van den Bergh reaction, and in which diagnosis was subsequently confirmed, Roberts showed that in Haemolytic jaundice, no significant increase in blood phosphatase occurred, in toxic or infective jaundice the phosphatase was sometimes raised with occasional high figures, and that in obstructive jaundice, especially gross mechanical obstruction, the figure was always high, sometimes markedly. The van den Bergh reactions carried out at the same time proved to be, according to the author, far more variable and consequently less reliable as diagnostic aids than the former estimation.

Anderson and Herbert, in 1935, confirmed Roberts' results, although Anderson refuted the latter's statements of clear-cut lines of demarcation between the types of jaundice, whereas Herbert's work showed more definitely that values of blood phosphatase below a certain number of units was diagnostic indication against obstructive jaundice, and that values above a certain figure was in favour of a positive diagnosis of obstruction. Animal experimentation has yielded corroboratory evidence, although for some reason toxic jaundice, experimentally induced in dogs, has occasionally yielded as high a figure as that obtained in obstructive jaundice.

During the last two years this subject has continued to evince considerable interest, not only from the clinical side, but from the physiological and chemical aspect as well. The trend, however, has leaned appreciably towards the latter viewpoints. The mechanism of phosphatase action has been elucidated, and the existence of a complex system of enzyme, co-factors, oxidation and reduction potentials and substrate, demonstrated.

The clinical contributions that have appeared are apparently still somewhat conflicting, Rothman and Meranze, on the basis of their investigations, maintaining the value of a blood phosphatase estimation as an important aid in the differential diagnosis of jaundice, whereas Cantarow, Nelson and others declare that the overlap of figures between the two groups is too great to be of distinctive merit.

It is perhaps a little premature to judge the clinical importance of blood phosphatase, but no doubt the perfection and standardisation of technical methods of estimation, and the accumulation of sufficient clinical data, will shed more light on what is at the moment a somewhat controversial subject.

J. C. WILLIAM.

The Nasal Route as a Means of Medication.

Introduction of drugs into the body through the nose has been shown recently to be a most useful therapeutic method. Blumgart (Arch. Int. Med. 29, 508, 1922) first found in a case of diabetes insipidus that " extract of the posterior lobe (of the pituitary) applied intranasally checked both the polyuria and polydipsia as effectively as hypodermic injections." Similar results were obtained by Kintner and Greene (J.A.M.A. 91; 1370, 1928), while Hofbauer and Hoerner (Am. J. Obst. and Gyn. 14; 137, 1927) were able to induce labour by the nasal administration of pituitary extract on cotton swabs placed in the nostrils. Pratt and Smeltzer (Endocrinol, 13; 320, 1929) found that in addition to the pituitary extracts the administration of ovarian hormone could be effectively used by the intranasal route. Childrey and Essex (Arch. Otolaryng, 14; 564, 1931) proved the absorption, though delayed, of phenolsulphophthalein and snake venom in sufficient amounts to be detected in the urine.

These observations have been more recently applied to diabetes mellitus and diphtheria. Major (Am. J. Med. Sc., 192; 257, Aug., 1936) was able to keep hospital patients for periods of

two to eight weeks relatively sugar free by the intranasal instillation of insulin in ethylene glycol. The method, however, is still in the experimental stage; if it is practical for the ambulant case it promises to be a boon to diabetics.

A recent report by Jensen (Proc. Roy. Soc. Med., 30; 1117, July, 1937) indicates a valuable auxiliary method of anti-diphtheritic immunisation by means of the intranasal route. A single injection of purified toxoid produces an effective immunisation of about 80% in about four weeks. When the three intranasal instillations of this toxoid are then given at weekly intervals the effective immunisation reaches the figure of 95-100%. This method which dispenses with the giving of a second injection to the child and which is a valuable adjunct to the single subcutaneous injection is being used for routine prophylactic immunisation against diphtheria in Denmark.

The intranasal route as a means of medication thus appears to be a valuable method which is being gradually applied by the profession.

Chronic Inflammatory "Tumour" of the Intestine.

Since 1932, when Crohn, Ginzburg and Oppenheimer described a clinical entity, "Regional Ileitis," the medical literature has been inundated with articles supporting and supplementing their views.

This article makes no attempt to furnish new material in a subject already sufficiently complex, but its aim is to afford a concise and readily accessible resume of the current literature.

Definition of the Disease. Crohn in his first article described "a disease of the terminal ileum affecting mainly young adults, characterised by a subacute or chronic necrotizing and cicatrizing inflammation." However, in later reports, Crohn admits of the limitation of this definition, and the term "Regional Ileitis" has as a result fallen into disfavour.

Many definitions have since been formulated, all having as their bases a chronic inflammatory lesion of a segment of intestines. A definition which finds most favour is "a disease of diverse aetiology, characterised by the occurrence of infiltrating tumour-like masses in some or several segments of the intestinal tract."

Many authorities are of opinion that the disease is a new one, and Sir L. Barrington-Ward and R. E. Norrish claim that "a pathological condition of such a definite nature and so unlike any of the known diseases of the intestine could not have remained so long unrecognised."

Aetiology.

Age Incidence. Although young adults are more prone to attack, no age is exempt, cases in children below the age of ten and adults over the age of eighty having been reported.

Sex Incidence. Up to now males have been more commonly affected than females.

Site of Predilection. The terminal Ileum and the pelvic colon are most commonly affected, though no part of the gut is immune to the disease. Crohn has reported cases where multiple areas of the small and large intestine have been involved at the same time.

Relation of Appendicitis to Chronic Inflammatory Tumour. The appendix may be involved in the general disease. Lawen expressed the opinion that the majority of chronic inflammatory tumours of the caecum arise from a chronic fibroplastic inflammation of the appendix.

Other Aetiological Factors. The axiom that the more complex a subject, the more diverse are the factors of aetiology, more than applies in this instance.

Infective Theory. Jackman claims finding the streptococcus viridans in the floor of the ulcers in the ulcerative stage.

Direct extension of an inflammatory process from organs in the vicinity, *e.g.*, the uterine appendages, has been suggested by F. G. Ralphs. A low-grade lymphatic infection with subsequent obstruction has also been blamed. A further view is that of impaction of foreign bodies in the intestinal mucosa.

Crohn and Berg in a recent article express the view that the aetiology of "regional colitis" is essentially identical with that of non-specific ulcerative colitis.

Course of Disease. The disease may be spread over a period of a few months to two or three years. Spontaneous resolution following the acute stage is possible.

Symptoms of the Disease. In his description, Crohn describes the disease as occurring in four stages:—

1. Those giving a short history of acute symptoms simulating appendicitis, due to a peritoneal reaction.