Drug Treatment of Disease

PURGATIVES AND LAXATIVES

BY

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Until the days of specific and rational therapeutics one of the few procedures available to the physician which had a reasonably predictable and certain result was the prescription of a purge. The medicine could be shown to have a demonstrable effect, and any benefit accruing to the patient was credited to the wisdom of the doctor and the efficacy of the pill. The lay public has for generations believed in the doctrine that the bowels must be regularly evacuated, and the mythical evils attendant upon the presence of faeces in the colon are daily elaborated in the advertisement columns of newspapers and magazines. Continuous and insidious propaganda, the traditional habits acquired in childhood from over-conscientious parents, and a lack of full understanding of normal physiological mechanisms have led us to the situation where the efforts of doctors are far more likely to be directed to correcting faults caused by the abuse of purgatives than to prescribing them on valid indications.

Vicious Circle

Two motions daily may be normal for one individual, whereas two motions weekly may be equally normal and satisfactory for another. Yet countless bowels are conditioned to ritual purgation on Saturday nights, on no other indication, originally, than tradition. Normal bowel action is dependent on there being sufficient food residue to initiate peristalsis, and "constipation" which follows the adoption, for some reason, of a low-residue diet is to be expected and requires no treatment other than an increase if possible of the vegetable content of the diet. The injudicious use of a purgative without good reason may start a vicious circle. Normal defaecation usually empties the sigmoid and descending colon, but the complete colonic evacuation after a purge is followed by a gap of two or three days during which sufficient residue accumulates to initiate a further defaecation reflex. If, in the belief that he is still constipated, the patient takes a laxative again during this physiological lull, the stage is set for the development of what is, in fact, a form of drug-addiction.

Before discussing, therefore, the place of purgatives and laxatives in therapeutics, it is salutary to realize that the ill-effects of their abuse are far greater than the imagined ill-effects of constipation. The latter are chiefly those consequent upon the mechanical obstruction which may occur, but many of the subjective manifestations of constipation—previously blamed on "the absorption of colonic toxins"—can be reproduced by stuffing the rectum with cotton-wool, a procedure not surprisingly also associated with local discomfort. Many of the bowel disturbances for which purgatives have been taken have not been indications for the prescription of, but have rather been the result of maladroitness of use, laxative preparations.

Injudicious use may lead to complete loss of the spontaneous bowel rhythm on which normal evacuation depends. This rhythm may be broken by changes in

diet or environment, temporary illness or anal discomfort, a recent operation or confinement, or any factor which makes less easy the normal use of the muscle groups that contribute to defaecation. In such circumstances the temporary use of a laxative is justifiable, provided that the limitations of the procedure are acknowledged and reliance is not placed solely on its efficacy for future bowel movements. Retraining, redevelopment of the spontaneous bowel rhythm, and the use of a suitable roughage-rich diet may well be all that is necessary. For some patients it is well to remember that the primitive squatting position for defaecation is simpler and more physiological than the sedentary posture usually adopted in Great Britain. By such measures it should be possible to avoid the risk of inducing undue dependence on a group of remedies which, in their proper role, are very valuable.

Potassium Depletion

Apart from the proctitis and colitis which laxatives may produce, a very real risk is the development of profound potassium-depletion because of the abnormal loss of electrolytes which occurs during continued purging. The main presenting symptom is usually weakness, but it may be thought to be due to neurological or cerebrovascular disease, or the renal changes resulting from the potassium depletion may impair kidney function. All these changes are reversible with adequate potassium therapy, but replenishment of potassium stores may take a very long time, and it is unnecessary for them ever to become so depleted.

Indications

A purgative is justifiable if it is necessary to try to rid the gut of some actual or potential poison such as might be encountered in food- or drug-poisoning. Other drugs may be given as part of the therapy for intestinal worm infection, and most of them require a subsequent purge. Occasionally a lubricant, with possibly an additional irritant laxative, may be helpful in the presence of anal fissures or piles or when the abdominal musculature is weak after pregnancy or an abdominal operation. But otherwise a purge is only rarely indicated except as a temporary measure.

Contraindications

Purgatives should never be recommended when the patient has an undiagnosed abdominal pain, and seldom for an isolated missed bowel movement. If a full bowel action follows a purgative, the medicine should not be repeated for three days, provided the diet is such that normal bowel action can be expected and the patient is reasonably active.

Diet and Bulk Purgatives

Low-residue diets sometimes cause infrequency of bowel activity, and this of itself need not call for

action. If a higher bulk content is permissible, however, vegetable diets, with cereals and greenstuffs, are those most likely to increase faecal bulk and provide something for colonic peristalsis to grip upon. Alternatively, bulk can be added to the stool by the use of agar, which can be taken by itself in doses of 5 g. or 10 g., or as 10 g. scattered over food. It is commonly taken in a paraffin emulsion, but it should be noted that a number of agar-containing preparations also contain phenolphthalein, the latter being an irritant type of preparation which is better avoided. Preparations containing other hydrophilic colloids, such as psyllium seeds, are useful inasmuch as the peristaltic movements induced are essentially physiological responses rather than pharmacological effects, and this group of compounds is the preferable group to use when constipation is due to faecal bulk being too small.

Saline purges depend for their effect on the retention within the lumen of the gut of an appreciable volume of fluid. Magnesium sulphate, in doses of 8 g. with a tumbler of water, is an effective and rapid purge, and many less drastic and possibly more attractive effervescent saline purges can be equally useful. It must be admitted, however, that the efficacy of a "morning dose of salts" is at least in part due to the establishment of the habit of taking a glass of cold water on an empty stomach first thing in the morning, with the expectation of subsequent bowel action, and the consequent formation of regular and ritual times for defaecation.

Lubricant

The lubricant effect of liquid paraffin is of value when the stools are small in bulk and scybalous, when anal fissuring makes defaecation painful, and when minimal straining is desirable. It is not in its own right a purgative, but merely facilitates the passage of faeces by spontaneous peristalsis. It should never be taken in bulk doses, particularly not at night, and is most valuable when taken in doses of 8 ml. (one dessert-spoonful) after meals, thus ensuring that it is intimately mixed with all food residue.

Because of the degree to which it is absorbed it may cause reactive changes in mesenteric lymph nodes and elsewhere, and, because there is evidence that it affects the absorption of some fat-soluble materials, patients should always be discouraged from using it as a habitual aperient over long periods.

Irritant Purgatives

The most important drugs for inducing activity of the bowel are the anthracene group of purgatives, which comprise senna, cascara, rhubarb, and aloes. All derive their activity from the constituent emodin, which is combined in each with a sugar to form a glycoside. This is absorbed, releases emodin, and it is the effect of emodin on the large bowel which causes evacuation. These compounds are highly effective, widely used, and reasonably safe if not misused. They exert an effect in about 6–8 hours if taken by mouth, and emodin is also excreted in the milk, a fact that should be borne in mind by nursing mothers. In such circumstances, therefore, the anthracene group of purgatives should not be used, and preparations like bisacodyl (see below) are probably preferable when a mother is breast-feeding her infant.

Rhubarb and aloes cause more griping than the other two, and aloes is often combined with phenolphthalein,

also a constituent of other purges. It acts either by stimulation of motor nerves or by local irritation, but, being absorbed and re-excreted by the bile, has a repetitive action which may not be desirable. It is a constituent of very many proprietary preparations, and is usually the active component.

Preparations of compound syrup of figs, upon which so many children have been reared for generations, owe their activity to rhubarb, cascara, and senna; the syrup of fig as a vehicle bestows the name upon the group, but less objectionable senna and cascara preparations are now available.

The preferable preparations are the tablets of cascara sagrada, 130 mg., which are very effective in the morning when taken at night, and similarly 2 ml. of cascara elixir is a useful and homely remedy. Infusions of senna pods, the regular nightcap of many Victorian spinsters, cause much griping and discomfort, and modern standardized senna preparations, available as tablets or in granules, are safe, effective, and pleasant to take.

Bisacodyl

This compound, 4,4'-diacetoxydiphenyl (pyridyl-2)-methane, is of great value in the management of constipation due to surgical causes, and in many centres has replaced the need for enema evacuation for radiological preparation. This drug, ineffective and inactive in the small intestine, is not absorbed and produces peristalsis in the large bowel. It is also effective when given as a suppository, and the combination of two tablets (10 mg.) at bedtime, and a 10-mg. suppository first thing in the morning, is a routine which in many centres is replacing the ritual of the pre-operative enema.

Other Purgatives

The availability, therefore, of satisfactory and simple preparations which promote defaecation by a number of different pharmacological mechanisms makes it nowadays unnecessary to employ the drastic cathartic resins which used to be given so extensively—jalap, colocynth, and podophyllum are examples of the group, the latter being a constituent of some widely advertised proprietary laxatives. They are all profoundly irritant to the small intestine, cause watery stools and much colic, and are consequently usually prescribed combined with hyoscyamus to diminish the undesirable side-effects. With effective alternative drugs available, there can now be no place for this group in therapeutics, and it is the injudicious and long-continued use of purgatives of these types that has often been responsible for potassium depletion. The old adage that, "If you want a regular starter, use jalap, ginger, and cream of tartar," is no longer applicable.

Much ill-health has been caused, in adults and in children in the past, by the use of calomel and grey powder. The mercuric ion is extremely irritant, and absorbed mercury can create a number of pathological states much more serious than the constipation for which the drugs were given.

Castor oil is an unpleasant and objectionable purge which is nevertheless fairly safe and produces a copious stool in 2–6 hours, and is self-limiting in its action.

Conclusion

The management of a patient with constipation usually entails to a great extent the instruction and retraining

of the patient's bowels, and the correction of faulty dietary habits and the unconsidered use of laxatives. Bowel movements can be helped by hydrophilic colloids like agar or psyllium seeds, and the passage of scybalous faeces can be helped by a moderate use of liquid paraffin. If irritant purgatives are required, nothing more drastic is necessary than cascara or a standardized senna preparation. An enema of water or saline is occasionally necessary, but a bisacodyl suppository in the morning after bisacodyl tablets the night before usually achieves the required result. There is no place for cathartic resins, phenolphthalein is unnecessary, calomel is dangerous, and small morning doses of effervescent salts are usually unnecessary but have a beneficial effect on morale.

RESEARCH IN BRITISH CARIBBEAN ANNUAL SCIENTIFIC CONFERENCE

The fifth annual scientific conference organized by the Standing Advisory Committee for Medical Research in the British Caribbean was held at the University College of the West Indies, Jamaica, on April 2, 3, and 4. The topic for the meeting was the application of the laboratory to problems of clinical medicine. Doctors from the Caribbean islands, British Guiana, British Honduras, the Bahamas, Britain, and America attended. Thirty-five papers were read and discussed. Professor A. C. FRAZER, of Birmingham University, took the chair on the first day.

Patterns of Cardiac Illness

The first session was devoted to cardiovascular disorders. A number of hospital studies and field surveys were reported from Jamaica, Trinidad, British Guiana, and St. Kitts by Drs. J. A. TULLOCH (U.C.W.I.), G. WATTLEY (Trinidad), H. HAMILTON (British Guiana), and K. L. STUART (U.C.W.I.). Hypertensive heart disease was the most common cardiac cause for hospital admission, followed by luetic and then rheumatic heart disease. Acute rheumatic fever was common and in Trinidad affected the East Indian to a greater extent than the Negro. Cor pulmonale was uncommon in both Trinidad and Jamaica, but was seen with greater frequency in British Guiana. In British Guiana and Trinidad it occurred almost exclusively in the East Indian. No satisfactory explanation of this racial difference was forthcoming. Myocardial infarction was uncommon in all the territories. This was of interest, as aortic atheroma is as common in Jamaica as in the United States of America, although coronary artery atheroma is less severe in Jamaica than in America. The association of aortic and coronary atheroma with essential hypertension, diabetes, age, and sex was discussed by Dr. W. B. ROBERTSON (U.C.W.I.).

The importance of heart disease in the general population was illustrated by the report from Barbados of a chest x-ray survey of 3,000 subjects. This showed a 10.7% incidence of cardiovascular abnormality, and a considerable proportion of these had a positive serological test for syphilis. Yaws has not been recognized in Barbados for many years. This stressed the fact that symptomless cardiovascular syphilis may be more common than has been thought and therefore poses an important public-health problem. In the discussion of this paper the urgent need for a test, serological or otherwise, that will differentiate syphilis from yaws was stressed.

Pyelonephritis and Diabetes

Hypertension is common, and field surveys carried out in Jamaica and St. Kitts were reported by Dr. K. L. STUART (U.C.W.I.). The blood-pressure levels in St. Kitts were

slightly higher than those reported by the Medical Research Council team in South Wales, whereas in Jamaica the figures were comparable to those from South Wales. An investigation into the occurrence of significant bacilluria in the general population was also reported by Dr. STUART. There was a considerably higher incidence of bacilluria in the hypertensive female, and this increased with parity. The relationship of bacilluria to hypertension was discussed, and the possibility that pyelonephritis was responsible for the greater incidence of hypertension in the elderly female was suggested. A post-mortem study of hypertensive cases reported by Drs. J. A. LING and STUART (U.C.W.I.) did show that renal hypertension was responsible for 50% of the cases and that chronic pyelonephritis accounted for one-third of the renal cases.

Diabetes mellitus was discussed at the second session. It was pointed out by Dr. J. A. TULLOCH (U.C.W.I.) that the prevalence of diabetes in Jamaica was a little over 1% of the adult population, and that only about 40% of the cases were already known to have diabetes. The aetiology was reviewed and was considered to be very similar to that reported from temperate countries. An assessment of the J type cases by Drs. D. MACINTOSH and J. A. TULLOCH (U.C.W.I.) indicated that these were not a distinct type but simply a phase in the natural history of the badly treated type II patient. The results of treatment with chlorpropamide were reported from Trinidad by Dr. T. POON-KING. A considerable proportion of his cases responded satisfactorily. The distribution of blood groups in diabetic subjects was also reported from Trinidad. In both male and female cases there was a low incidence in group O. Males showed an excess of group B and females an excess of group A over that occurring in the local population. A study of liver enzymes in human diabetes was reported by Dr. S. J. PATRICK (U.C.W.I.). This largely confirmed animal experiments.

Malnutrition

On the second day Professor E. T. C. SPOONER (London School of Hygiene and Tropical Medicine) took the chair. Dr. R. D. MONTGOMERY, of the Medical Research Council Tropical Metabolism Unit, reported that the oxygen uptake per unit of body-weight was not reduced even in severe malnutrition. During recovery the increase became much greater, and evidence was given that this was related to thyroid activity. Drs. J. C. WATERLOW and D. I. M. PICOU reported preliminary observations from isotope studies that, in protein malnutrition, the economy of protein is achieved not by a decreased rate of katabolism but by an increased degree of re-utilization. Although the extent of protein synthesis might be reduced through shortage of supplies, the capacity for synthesis seemed in most cases to be unimpaired.

The occurrence of magnesium deficiency in malnutrition was reported by Dr. R. D. MONTGOMERY. This paralleled potassium deficiency and supported the concept of a primary loss of intracellular constituents. Further investigations into the megaloblastic anaemia noted in malnourished infants was reported by Drs. J. E. MACIVER and E. H. BACK (U.C.W.I.). They showed that the cause was a dietary deficiency of folic acid and that vitamin B₁₂ was not implicated. Dr. MACIVER also reported on the nature of the severe anaemic episodes in sickle-cell disease and showed that these were of two types. In one folic-acid deficiency was the aetiological factor and in the other there was an acute aplastic state. A possible relationship of this latter state to preceding infection was suggested. Non-Addisonian vitamin-B₁₂ deficiency in the adult was reported from Trinidad by Dr. G. HABIB. All the cases were Hindus, and with one exception they were strict vegetarians, eating no eggs, meat, fowl, or fish. It was considered that poverty and a vegetarian diet combined to produce this deficiency state.

A field survey of liver size in apparently healthy children was reported by Dr. C. G. MILLER (U.C.W.I.). Hepatomegaly