disease is furthermore often associated with chronic pancreatic damage. It is therefore interesting to find that patients with cirrhosis often have markedly increased iron absorption and that this can be reduced towards normal on giving the test dose with pancreatin (Callender, 1965).

In an attempt to elucidate further the part played by the pancreas in iron absorption, Helen Brown (unpublished), in our laboratory, produced pancreatic damage with ethionine in rats on a restricted protein intake. She investigated the absorption in two groups of rats, one given an iron supplement and one iron-deficient. These groups were further subdivided into those with and those without pancreatic damage. Iron absorption in the rats with the iron supplement was increased in those with pancreatic damage and addition of pancreatin restored absorption to normal, but in the iron-deficient rats the findings were reversed, i.e., pancreatic damage was accompanied by diminished iron absorption which was restored to control values by the addition of pancreatin. These contradictory findings emphasize the complexity of the problems of iron absorption.

In these few remarks I have only touched on some of the factors which affect iron absorption. Iron deficiency remains one of the world's greatest nutritional problems and until we learn a great deal more about the complex mechanisms and interactions of the many factors concerned in the control of iron absorption, it is likely to remain with us.

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Some aspects of the absorption and concentration of iodide by the alimentary tract in man

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Iodine is absorbed in some parts of the alimentary tract, and in other parts it is secreted into the lumen of the gut (Brown-Grant, 1961). Inorganic iodine is concentrated from the plasma by the stomach and the salivary glands and then secreted into the gastric juice and saliva. It is completely absorbed in the intestine so

that none appears in the faeces. Organic iodine (in the form of the thyroid hormones) is conjugated in the liver, and glucuronide and sulphate conjugates are secreted into the bile. Reabsorption is incomplete, and a significant amount of organic iodine is lost in the faeces. In human females the biliary clearance rate varied from 200 to 600 ml plasma/day, and thyroxine corresponding to 170–350 ml plasma was finally lost in the faeces—about 8–20 μg iodine at normal protein-bound iodine levels (Myant, 1956).

In rodents faecal losses are substantial. Albert & Keating (1952) found that an amount of thyroxine equal to that in the total circulation was excreted into the bile in less than 1 h, but about 97% was reabsorbed.

A factor which has received some attention as a possible cause of increased faecal iodine loss is consumption of soya bean and its products. Van Middlesworth (1957) and Beck (1958) reported increased faecal excretion of iodine in rats on a soya-flour diet. Beck also investigated the mechanism of action and found that soya flour did not increase the biliary clearance of thyroxine but decreased the proportion of thyroxine reabsorbed after biliary excretion, i.e. it increased faecal but not biliary clearance of thyroxine. Pinchera, MacGillivray, Crawford & Freeman (1965) have described a cretin who became resistant to thyroid medication when placed on a soya-bean diet. Studies using ^{131}I-labelled L-thyroxine showed that soya bean decreased the intestinal absorption of exogenous thyroxine. Goitre and hypothyroidism have occasionally been reported in infants fed on soya-bean diets (Shepard, Pyne, Kirschvink & McLean, 1960; Ripp, 1961) and when soya bean was discontinued both goitre and hypothyroidism have disappeared. Prolonged interference with intestinal thyroxine reabsorption presumably results in an iodine-deficiency state, and goitre formation. Since 1959 a widely used commercial brand of soya bean has been supplemented with iodide, and no further cases of soya bean-induced goitre have been observed (Pinchera *et al.* 1965).

Until recently no satisfactory methods of direct measurement of faecal iodine in man were available. With a method using bomb calorimetry (Mitchell, 1965) we have found that on a normal iodine intake the faecal iodine is virtually all derived from endogenous thyroid hormone. In thyrotoxicosis levels of faecal iodine are high, and in hypothyroidism they are low (Harrison, Harden, Alexander & Wayne, 1965).

Considerable effort has gone into the attempt to determine whether iodine-deficiency goitre is related to excessive loss of iodine in the faeces, which could result from either failure of absorption or excessive secretion by the intestine. It is well known that losses of iodide in the urine are reduced in iodine-deficiency states, although there is no renal homoeostatic mechanism (Wayne, Koutras & Alexander, 1964). We have carried out iodine balance studies in five patients with iodine-deficiency goitre and the faecal loss of iodine was within the normal range. There is, therefore, no evidence of either excessive loss of iodine, or of intestinal adaptation to iodine deficiency.

A high intake of calcium can potentiate the goitrogenic effect of an iodine-deficient diet in rats (Taylor, 1954), and it has been suggested that calcium may impede the intestinal absorption of iodine. We have carried out iodine balance

studies in three volunteers before, during and after a calcium supplement of 3 g/day. The intestinal absorption of iodine was unaffected by calcium ingestion, irrespective of the level of iodine intake.

The iodine in fish, an important source of dietary iodine, appears to be completely absorbed (Harrison, McFarlane, Harden & Wayne, 1965). Studies including trichloroacetic acid precipitation, resin chromatography and dialysis showed that the entire iodine content in the flesh of haddock and plaice was in inorganic form. Increased intake of inorganic iodine, at least within the physiological range, is not associated with increased faecal excretion.

Organic iodine compounds, on the other hand, may not be completely absorbed. Hays (1966) has studied the absorption of oral thyroxine using a double isotope technique. An oral dose of ^{125}I-labelled thyroxine and an intravenous dose of ^{131}I-labelled thyroxine were given simultaneously. In males about 50% of the oral thyroxine was absorbed. Absorption values calculated from faecal counts were variable, but uniformly higher than those obtained from the ratio of ^{125}I to ^{131}I in the plasma.

Iodide is concentrated by certain specific parts of the gastro-intestinal tract, and secreted into the lumen of the gut. In mammals the stomach and some salivary glands accumulate iodide, but organic iodine compounds are synthesized only in the thyroid and mammary glands. The iodide trapping mechanism can be studied by using pertechnetate 99m and isotope scanning procedures, and scans of the human stomach are shown in Fig. 1. The salivary glands can be examined in a similar
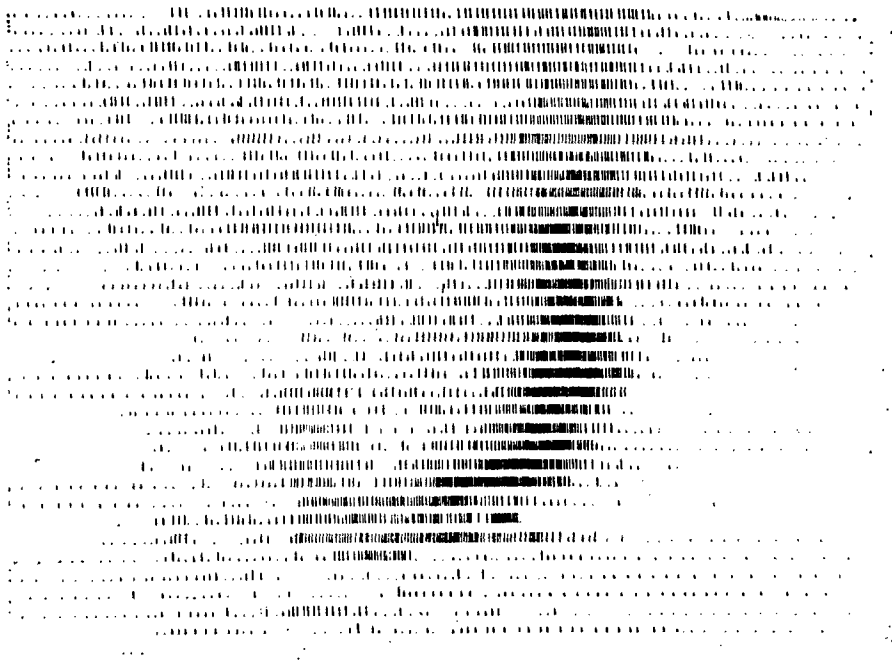

Fig. 1. Scan of the human stomach after intravenous injection of 800 μc pertechnetate 99m.

manner (Harden, Hilditch, Kennedy, Mason, Papadopoulos & Alexander, 1967). The salivary glands show marked interspecies variations as well as variation between different glands. The rat does not concentrate iodide, but the dog, cat, guinea-pig and hamster do. Salivary: plasma iodide ratios range from 10 to 50 in most species. Except for lack of response to thyroid-stimulating hormone the mechanism of concentration appears to be similar in the salivary and in the thyroid gland.

We have studied, in man, the affinity of the salivary glands for iodide and various other anions of the seventh periodic group. There have been no studies in man and these seem desirable since the iodide trap shows such marked species differences.

Table 1. *Parotid salivary clearance of iodide and pertechnetate in human subjects*

Parotid salivary clearance (ml/min)

Subject	Resting ^{132}I	Resting ^{99m}Tc	Fruit gum stimulation ^{132}I	Fruit gum stimulation ^{99m}Tc	Lemon juice stimulation ^{132}I	Lemon juice stimulation ^{99m}Tc
De	2·3	1·7	6·1	5·9	11·8	7·9
Ke	1·4	0·6	11·8	4·8	12·2	4·5
McE	7·7	4·7	7·6	5·2	27·4	16·8
Or	4·8	2·3	9·2	3·6	10·6	4·7
Ry	0·5	0·3	2·1	1·4	6·1	3·5
Sm	1·1	0·7	4·1	2·8	11·2	6·4
Mean	3·0	1·7	6·8	4·0	13·2	7·3
SE of mean	±1·2	±0·7	±1·5	±0·8	±3·3	±2·2

A solution containing a mixture of ^{82}Br, ^{132}I and $^{99m}TcO_4$ was injected intravenously. Parotid saliva was collected at three flow rates—resting, after fruit gum stimulation, and after lemon juice stimulation. At the mid-point of each salivary collection a plasma sample was obtained by venepuncture. Plasma and salivary samples were counted in an automatic well-type counter, and counts for each individual isotope were obtained (Alexander, Harden, Mason, Shimmins & Kostalag, 1966). The salivary clearance of ^{132}I and ^{99m}Tc are shown in Table 1. The salivary clearances of both isotopes increase when salivary flow is stimulated. At all flow rates the salivary clearance of ^{132}I approximates to twice that for ^{99m}Tc (Fig. 2). Saliva to plasma ratios under resting conditions for ^{132}I average 40 and for Tc 22. With lemon juice stimulation the figures are 10 and 6 respectively. These results contrast with those of in vitro studies in animals which have suggested a greater affinity of the salivary gland for technetium than for iodide (Wolff, 1964).

The stomach, too, has an active iodide trap. In one of our patients aspiration of gastric juice between 75 and 90 min after an intravenous tracer dose of ^{132}I showed a gastric iodide clearance of 18·7 ml/min. The gastric juice:plasma ^{132}I ratio was 20. Of the tracer dose, 12·2% was aspirated in the gastric juice during the first 90 min after injection.

Summary

Inorganic iodine is absorbed almost completely in the intestine: it is concentrated from the plasma and secreted into the lumen of the gut by the stomach and salivary glands.
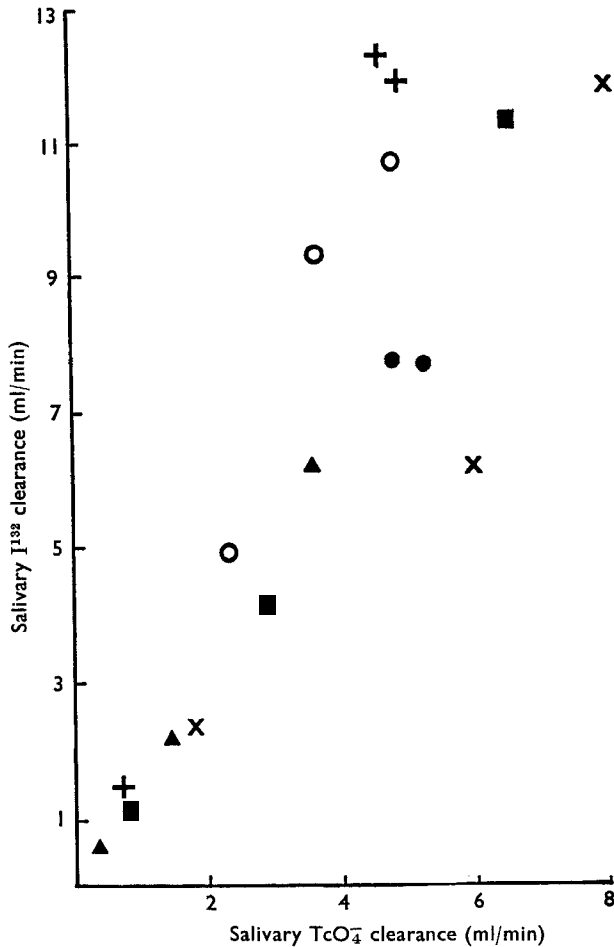
Fig. 2. Relation, in man, between the parotid salivary clearance of iodide 132 and pertechnetate 99m at varying salivary flow rates.

The iodide-concentrating mechanism of the stomach and salivary glands can be examined by using pertechnetate 99m and isotope scanning procedures. The parotid salivary clearance of pertechnetate was approximately half that of the simultaneously measured parotid iodide clearance.

The effect on faecal iodine excretion of an iodine-deficiency state, and of the ingestion of calcium, iodine, and soya flour is discussed.

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The absorption of calcium from the intestine

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From studies of loss of radiocalcium from the intestinal lumen of rats it was well known that the absorption of calcium occurs mainly in the proximal small intestine (Harrison & Harrison, 1951; Nicolaysen, 1951). A similar observation was made in the pig (Moore & Tyler, 1955). In the chick, according to Coates & Holdsworth (1961), however, calcium absorption appeared to occur over the whole length of the small intestine.

The recent advances in the use of everted sacs provided a useful tool to study the absorption of calcium. Thus Schachter & Rosen (1959), Rasmussen (1959) and others could show that active transport of calcium against a concentration gradient can be achieved in everted sacs of the rat duodenum, but not of ileum, and the capacity of this transport mechanism decreased with distance from the pylorus. Anaerobic conditions, low temperature, dinitrophenol or other enzyme poisons effectively inhibited the active transport (Schachter & Rosen, 1959; Schachter, Dowdle & Schenker, 1960; Wassermann, 1960). Additions of glucose or fructose improved greatly the active absorption, while mannose, galactose, amino acids or some fatty acids had no marked effect (Schachter & Rosen, 1959).

The age of the animals influenced the active transport in everted sacs; younger rats had a more efficient transport mechanism than older animals (Kimberg, Schachter & Schenker, 1961). These effects were more marked when a low-calcium diet was given (Kimberg *et al.* 1961).

When rats were given a vitamin D-deficient diet the active transport in everted sacs was significantly diminished and could be restored by in vivo dosing with vitamin D (Schachter & Rosen, 1959; Dowdle, Schachter & Schenker, 1960; Kimberg *et al.* 1961). The response to vitamin D had a certain lag period of about 8–10 h. A biological assay based on the technique of everted sacs has been suggested by Schachter, Kimberg & Schenker (1961). Addition of vitamin D in vitro did not restore the impaired absorption, but recently Schachter, Kowarski & Finklestein (1964) reported that cholecalciferol placed directly into in vivo loops of rat duodenum in vitamin D-deficient animals increased markedly the subsequent (5 h later) uptake