D-XYLOSE TEST IN ENTERIC FEVER, CIRRHOSIS, AND MALABSORPTIVE STATES

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Interest in the physiology of intestinal absorption has increased considerably during the last decade. This has been prompted by the availability of improved techniques of investigation of the function of the small intestine. It has become possible to demonstrate, categorize, and study the type and extent of deficient absorption in many clinical states. The available evidence emphasizes the multiplicity of factors capable of altering the physiology of the small intestine. These include metabolic disturbances in sprue, alterations in ground substance as seen in Whipple's disease (Puite and Tesluk, 1955), massive resection of the small intestine (Jackson and Linder, 1951), intestinal diverticulosis and fistulae (Baddenoch *et al.*, 1955), neoplastic involvement of the small intestine (Sleisenger *et al.*, 1953), ulcerogenic tumours of the pancreas (Maynard and Point, 1958), and ischaemia of the small-intestine tract (Joske *et al.*, 1958). The present study deals with the state and mechanism of intestinal absorption of carbohydrates in two unrelated conditions—enteric fever and cirrhosis of the liver—utilizing the D-xylose excretion test.

D-Xylose is among the naturally occurring pentoses, chiefly found in plant products. It has a molecular weight of 150. Its structural formula is:

$$CHO\text{–}HCOH\text{–}HOCH\text{–}HCOH\text{–}CH_2OH$$

It is not normally found in human blood. Like most sugars it is predominantly absorbed from the small intestine, more in the proximal than in the distal part. The transport of sugars across the intestinal mucosa involves more than diffusion. Despite the lower molecular weight of pentoses, which enhances diffusion, they have been shown to be absorbed more slowly than hexoses. Thus, Cori (1925) and McCance and Madders (1930) found the various absorption rates of sugars to be the following: galactose 110, glucose 100, fructose 43, mannose 19, xylose 15, arabinose 9. They also found that above a concentration range of 10–13% the rate of absorption is independent of concentration.

It has always been thought that active absorption involves phosphorylation of sugars. This hypothesis has been generally accepted, though direct evidence for it has been lacking. The phosphorylation of D-xylose is still debatable. Sols (1956) maintains that it is not phosphorylated *in vitro*. His quantitative data indicate that the normal role of mucosal hexokinase is to initiate glycolysis for the tissues' own needs and not for active absorption. The data of Hele (1953) prove the contrary, and Turner (1950) even suggested the probability of a xylokinase in the mucosa of the small intestine.

In normal individuals 65% of the xylose is absorbed (Christiansen *et al.*, 1959). It is unaltered by the liver (Fishberg and Friedfeld, 1932). Of the oral dose of 25 g., about 6 g. is excreted in the urine within the first five hours. Benson *et al.* (1957), studying two well-nourished subjects with ileostomies, found that no xylose was detected in the ileostomy discharge after the fifth hour and that 10% of the oral dose was excreted in the urine during the next 19 hours. About 50% of the dose appeared to be destroyed by the body.

Dominguez and Pomerene (1934) employed D-xylose as a renal-function test. Helmer and Fouts (1937) first reported on its use in intestinal absorption. They found no consistent abnormality in absorption of xylose in pernicious anaemia but noted defective absorption in three cases of non-tropical sprue. Fourman (1948) found decreased absorption of D-xylose in three patients with tropical sprue, in two with steatorrhoea, and in two with steatorrhoea due to healed tuberculous mesenteric adenitis. Since then many publications on the subject have appeared (Brien *et al.*, 1952; Gardner, 1956; Finlay and Wightman, 1958).

Methods and Materials

For at least eight hours prior to the examination food and fluids were withheld from the subjects to be tested. After voiding, each subject took 25 g. of D-xylose dissolved in 250 ml. of tap-water. Immediately thereafter another 250 ml. of water was given. The subject was then kept at rest, either in bed or on a chair, and given nothing by mouth for the next five hours. All the urine passed in that five-hour period was collected and was either directly examined or refrigerated.

The xylose content of the urine was determined by the colorimetric method of Roe and Rice (1948).

All the tested subjects had adequate renal function with a normal urine output, non-elevated urea nitrogen, and no clinical or laboratory evidence of renal disease.

Control Group.—The 11 subjects of the group consisted of medical students and a few patients in the hospital who had no evidence of organic disease of the renal or the gastro-intestinal tract. The range of five-hour D-xylose excretion was 5.9–8.9 g. (Table I). The calculated mean was 7.5 g. and the standard deviation of the mean, SD_M, was ± 0.27. These statistics are comparable to those of other series (Table II). The lowest normal recorded in the literature was 4.1 g. (Benson *et al.*, 1957).

TABLE I.—*Five-hour D-xylose Excretion in Our Control Group*

Case No.:	1	2	3	4	5	6	7	8	9	10	11
D-Xylose excreted (g.)	5·9	7·3	8·9	7·7	7·2	7·5	8·5	7·2	6·7	6·9	8·7

Mean = 7·5 g. $SD_M = 0{\cdot}27$ g. Range = 5·9–8·9 g.

TABLE II.—*Normal Range of Five-hour D-xylose Excretion*

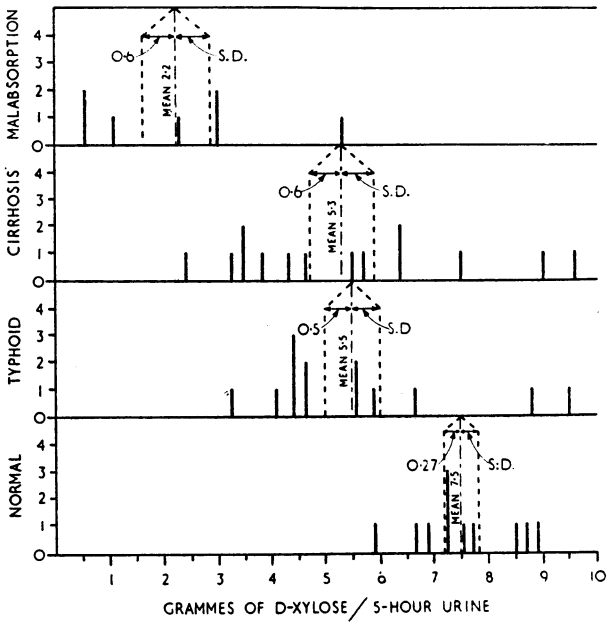
Authors	No. of Patients	G. Mean ± S.D.	Range G.
Dominguez and Pomerene (1934)	4	6·55	4·86–7·69
Helmer and Fouts (1937)	8	4·68	4·26–5·33
Brien *et al.* (1952)	12	6·14 ± 0·70	5 –7·2
Gardner (1956)	42	5·6 ± 0·6	
Benson *et al.* (1957)	25	6·5 ± 1·2	4·1–8·2
Christiansen *et al.* (1959)	10	6·76 ± 0·88	5·6–8·2
Present study	11	7·5 ± 0·27	5·9–8·9

Enteric Fever.—Thirteen cases with proved enteric fever were studied. The diagnosis was established by the isolation of the salmonella organism in blood culture in patients who had the clinical signs and symptoms of the disease. Eight of these patients had *Salmonella typhi*, three had *Salmonella paratyphi A*, and two had *Salmonella paratyphi B*. In all these cases the test was performed after the lapse of three to five days of normal

temperature. All these patients were taking chloramphenicol for their enteric infection. The results of five-hour D-xylose excretion are recorded in Table III and the Chart. The mean D-xylose excretion was 5.5 g.

TABLE III.—*Five-hour D-xylose Excretion in Enteric Fever, Cirrhosis, and Malabsorption*

Typhoid	Cirrhosis	Malabsorption
3·24 g.	3·25 g.	0·51 g.
4·1 ,,	3·8 ,,	2·96 ,,
4·4 ,,	9 ,,	0·62 ,,
4·4 ,,	9·6 ,,	5·33 ,,
4·4 ,,	6·3 ,,	2·88 ,,
4·6 ,,	4·65 ,,	1·11 ,,
4·7 ,,	7·5 ,,	2·26 ,,
5·5 ,,	6·4 ,,	
5·6 ,,	5·5 ,,	
5·9 ,,	3·5 ,,	
6·7 ,,	4·3 ,,	
8·8 ,,	5·7 ,,	
9·5 ,,	2·4 ,,	
	3·4 ,,	



Five-hour D-xylose excretion in normal subjects and in patients with typhoid, cirrhosis, and the malabsorptive syndrome.

The SD_M was 0.5 g. The values ranged from 3.24 to 9.5 g. Nine out of 13 patients (69%) had urinary levels lower than the lowest recorded in our control series. The difference between the means of the two groups was statistically significant at the 2/10,000 level of confidence. A significant reduction of xylose absorption occurs in the enteric fever group.

Cirrhosis.—Fourteen patients with cirrhosis of the liver were chosen for this study. The diagnosis of cirrhosis was established by clinical signs, tests for impairment of liver function, the presence of ascites, jaundice, and portal hypertension, and histological examination in nine patients. Except for one case which fits clinically and histologically with alcoholic cirrhosis, the cases were of the post-necrotic type. The mean D-xylose excretion was 5.3 g. (Table III and Chart). The SD_M was 0.5 g. and the values ranged from 2.4–9.6 g. Nine out of 14 patients (64%) had D-xylose excretion less than the lowest level recorded in our normal series. The hypothesis that the absorption of D-xylose in cirrhosis is not different from that in the normal had to be rejected at the 5/10,000 level of confidence. The absorption of D-xylose is significantly reduced in cirrhosis.

Malabsorptive Syndrome.—Seven cases with steatorrhoea were studied. These included three cases with lymphoma of the small bowel, one case with a presumptive diagnosis of tuberculosis enteritis, and three cases with idiopathic steatorrhoea. The mean was 2.2 g. with a SD_M of 0.6 g. The values ranged from 0.51 to 5.33 g. The reduction of D-xylose absorption in similar malabsorptive states has already been adequately established and needs no further emphasis.

Discussion

With the increasing awareness of disease of the small intestine and the availability of better techniques in the study of small-intestine function, deficiencies in absorption of various foodstuffs are no longer limited to idiopathic steatorrhoea—that is, sprue and coeliac disease—but may include many different pathological lesions. These include chronic pancreatitis, pancreatic cancer, lymphoma and other reticuloses, tuberculosis, Whipple's disease, intestinal diverticulosis and fistulae, and the results of major abdominal surgery, especially gastrectomy.

The D-xylose-excretion test has been found to be deficient in all of the above conditions with the exception of pancreatic disease. Joske *et al.* (1958) added a new member to the family of the malabsorption syndrome by describing two cases of temporary occlusion of the superior mesenteric artery which were followed by malabsorption. The D-xylose excretion in those two cases was 0.5 and 3.2 g. respectively. These two cases were of considerable interest in throwing light on the physiological mechanisms involved in malabsorption, with ischaemia as the underlying factor.

The above considerations have prompted us to study absorption in enteric fever, which may be regarded as a disease of the small intestine because of the particular involvement of the small intestine with inflammation and lymphatic swelling and hyperplasia. This is the first instance, to the best of our knowledge, that an absorptive study has been made on disease of the small intestine of infectious nature. The finding of a deficient absorption of D-xylose in this condition emphasizes the multifaceted nature of the factors involved in the pathogenesis of the malabsorption syndrome, and enhances the expectation that this state may well result from numerous factors which disturb the normal physiology of the small-intestine tract, by the gross involvement of the small intestine by neoplasm or an inflammatory process secondary to enteric infection.

It has already been stated that D-xylose is unaltered by the liver (Fishberg and Friedfeld, 1932). Finlay and Wightman (1958) have found a decrease in absorption of D-xylose in cirrhosis. Christiansen *et al.* (1959), however, found no abnormal results in patients with uncomplicated hepatic disease. In our group of cirrhotics the lowest values of D-xylose excretion were found in patients who had advanced liver disease with ascites, severe hypoalbuminaemia, and oedema. Patients with compensated cirrhosis showed minimal or no deficiency of absorption. Table IV shows the positive correlation between hypoalbuminaemia, ascites, and the degree of D-xylose malabsorption.

It is clear (Table IV) that the normal xylose levels in cirrhosis were seen in Case 3, 4, 5, 7, 8, 12. They all had albumin levels above 3 g./100 ml. except Case 5. All but one patient with ascites had low xylose levels. It is difficult to single out one factor producing malabsorp-

TABLE IV.—*Correlation Between Serum Albumin, Ascites, and Xylose Excretion in Cirrhosis*

Case No.	Albumin (g.)	Ascites	Xylose (g.)
1	2·6	+	3·25
2	2·4	+	3·8
3	3·9	−	9·0
4	3·4	−	9·6
5	1·7	−	6·3
6	2·2	+	4·6
7	3·4	−	7·5
8	3·3	+	6·4
9	1·7	+	5·5
10	2·0	+	3·5
11	2·3	+	4·3
12	4·1	−	5·7
13	2·4	+	2·4
14	4·1	−	3·4

tion of D-xylose in cirrhosis, but the above data may suggest that oedema of the small intestine secondary to chronic liver disease may be an important factor. This speculation has prompted us to initiate a study of other oedema states, such as are found in congestive heart failure, and their effects on the function of the small intestine.

The group of seven patients with malabsorptive syndrome support what has already been emphasized in previous publications. They demonstrate the utility of this test and its pronounced alteration in disease of the small intestine. D-Xylose, being a pentose normally absent in the human and relatively unaffected by various metabolic processes, is a better absorptive test of carbohydrates than is a ubiquitous and metabolically active substance such as glucose.

Summary

The D-xylose excretion test has been widely used in the study of the absorption of carbohydrates by the small intestine. This pentose is normally absent from the human and is relatively unaffected by the various metabolic processes of the body. A decrease in D-xylose absorption was noted in most of the diseases of the small intestine reported in the literature. These include sprue, intestinal diverticulosis and fistulae, tumours of the small intestine, and ischaemia that follows embolism of the superior mesenteric artery. The present study deals with the state and mechanism of absorption of carbohydrates in two unrelated conditions, enteric fever and cirrhosis of the liver, utilizing the D-xylose excretion test.

Enteric fevers may be regarded as diseases of the small intestine because of the particular involvement of that organ with inflammation, lymphatic swelling, and hyperplasia.

Thirteen cases with proved enteric fever were studied. There was a significant reduction of absorption of D-xylose in this group. Nine out of the 13 (69%) had urinary levels lower than the lowest recorded in our control group.

Fourteen patients with cirrhosis of the liver were studied. There was also a marked reduction of D-xylose absorption in this group. Nine out of 14 (64%) had D-xylose excretion less than the lowest recorded in the normals. Furthermore, there was a correlation between the serum albumin levels and the degree of absorption of D-xylose which suggested to us that, among other factors, oedema of the small intestine secondary to chronic liver diseases may influence intestinal absorption.

A third group of seven patients with malabsorptive syndrome was studied. The marked decrease in absorption of D-xylose in this group supports what has already been emphasized in previous publications.

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THE FUNCTIONAL EFFECT OF PULMONARY IRRADIATION*

BY

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When the lungs are irradiated by *x* rays to any degree an inflammatory reaction results which may lead to fibrosis (Whitfield, *et al.*, 1954). A number of workers have studied the effect of post-radiation pulmonary fibrosis on lung function (Leach, 1943 ; Baldwin, *et al.*, 1949). Little is known, however, about pulmonary function during the actual irradiation and in the period prior to the development of pulmonary fibrosis. It was decided to perform serial lung-function studies on patients receiving pulmonary irradiation. Accordingly a number of radiotherapy patients who were having their lungs irradiated either directly because of carcinoma of the bronchus or indirectly in cases of carcinoma of the breast were subjected to lung-function studies before, during, and after treatment.

The patients under study received either *x*-irradiation from the conventional 240-kV deep *x*-ray machines or supervoltage radiation from the 8-MeV linear accelerator. An attempt was made to show the difference in functional effect between the two forms of radiation.

Groups of Patients Studied

Carcinoma of bronchus treated radically on the 8-MeV linear accelerator.—These cases all had histologically proved tumours. The squamous-celled tumours were treated by a technique employing two non-opposed fields with wedges, and a tumour dose of 4,500 rads was given in one month. The anaplastic tumours were treated with two opposed fields without wedges, and a tumour dose of 4,000 rads was given in one month. The size of the fields and thus the volume of the lung irradiated depended upon the size of the tumour,

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