up of these patients may contribute to our understanding of the pathogenesis of atherosclerosis.

If one can assume a relation between raised blood-lipid levels and development of atherosclerosis, as many reports indicate, it would seem reasonable to expect that reduction of high blood-lipid levels would prevent or reduce the development of atherosclerosis, either in coronary arteries or in vein grafts. Such measures would seem to be especially applicable to patients with aortocoronary vein bypass, since most of them have abnormally high plasma-lipid levels.17,18

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REFERENCES

INTRODUCTION

The absorption of hexose sugars from the lumen of the jejunum incorporates two independent mechanisms. One is a diffusional process, which is non-saturable and non-electrogenic. The second is an active-transfer mechanism that displays saturation kinetics,1,3,4 and, because it is linked to sodium ion transfer, it is electrogenic5,6 (fig. 1).

The only direct methods of assessing the absorption of glucose from the jejunum in man are infusion techniques, in which the rate of disappearance from the lumen of increasing infused concentrations of glucose is measured. These techniques measure total absorption by both mechanisms. They are, however, time-consuming, poorly acceptable to the patient, and potentially inaccurate. Experiments on rats have shown that the active electrogenic component of glucose absorption can be assessed by measuring the changes in potential difference across the jejunum wall (transmural P.D.) during perfusion with increasing concentrations of glucose. Because this active mechanism exhibits saturation kinetics, the nature of the relationship between luminal glucose concentrations and the change in transmural potential difference can be quantitatively described by two kinetic indices. One is "V_{max}\), the theoretical maximum potential difference attainable, and as such is analogous to "V_{max}\), the maximum rate of glucose absorption determined chemically. The
second is the "apparent $K_m$", which is the concentration at which half the $P.D._{\text{max}}$ (or $V_{\text{max}}$) is attained. The apparent $K_m$ can be used as an index of the affinity of the carrier mechanism for glucose. The use of these indices allows us to characterise the absorption of glucose over a range of concentrations and hence study changes in absorption created by changes in the active transfer mechanism. In the rat, apparent $K_m$s determined electrically and chemically (after correction for diffusion) show a remarkable degree of correlation.\(^1\,2\)

We have now explored the possibility that kinetic indices for the active electrogenic absorption of glucose in the human jejunum can be determined by measurements in transmural potential difference.

**Volunteers and Methods**

The volunteers were four male and five female healthy young people, who were fully aware of the nature and implications of the study. One patient with jejunal amyloidosis secondary to rheumatoid arthritis was also studied.

After an overnight fast of approximately 12 hours, a radio-opaque tube, open at the distal end and weighted with a mercury balloon, was swallowed. One hour later the abdomen was examined radiologically by image intensification and television screening. When the tube was in position in the upper jejunum within 20 cm. of the duo-
denojejunal flexure, an intramuscular injection of 30 mg. propantheline bromide ('Pro-Banthine') was administered. This reduced the usual variation in the electrical record caused by jejunal motility. The proximal end of the tube was then attached to an infusion system, which incor-
porated a reservoir and a battery-powered constant-infu-
sion rotary pump (Holter Pump model 912).

The intestinal tube, which contained a solution of glu-
cose and saline, acted as a flowing intraluminal electrode. A plastic cannula, filled with 0.9% sodium-chloride solu-
tion and inserted subcutaneously on the dorsal aspect of the left forearm, was the reference electrode. These elec-
trodes were connected to paired calomel half-cells by means of agar/salt bridges, which consisted of plastic tubing 1 mm. in diameter containing 3% agar in 3M potassium chloride. The half-cells were in turn connected back-to-
back across the input terminals of a battery-powered elec-
trometer (Keithley model 602), the output of which was displayed on a battery-powered recorder (Smith's 'Servoscribe M' model RES01) to yield a permanent record. All the electrical equipment satisfied the safety requirements of the Department of Health and Social Security.\(^10\)

The asymmetry of the circuit was measured at the beginning and the end of the experiment by immersing the ends of the agar/salt bridges in a beaker of 0.9% sodium-chloride solution. The asymmetry potential difference never exceeded 1 mV and always remained constant throughout the experiment.

The solutions infused into the jejunal lumen are shown in table I.

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The solutions infused into the jejunal lumen are shown in table I.
Fig. 2—A plot of change in potential difference against glucose concentration in one volunteer (no. 5).

Fig. 3—Lineweaver-Burk plot of the data shown in fig. 2.

shape of a saturation-kinetics curve (fig. 2). The values of apparent $K_m$ and $P.D._{max}$ can be obtained from a double reciprocal plot (Lineweaver-Burk) of the same data as shown in fig. 3.

Most values for apparent $K_m$ in healthy volunteers fell between 50 and 77 mM (mean 61 ± 3.6 s.E.) while the $P.D._{max}$ ranged from 7 to 17 mV (mean 11.8 ± 1.1 s.E.). The results from the healthy volunteers contrasted strikingly with the very low apparent $K_m$ of 8 mM and $P.D._{max}$ of 5 mV found in a patient with malabsorption associated with infiltration of the jejunum with amyloid deposits.

Discussion

The existing work on transmural potential difference in the human jejunum has shown that the intraluminal presence of food or hexose sugars results in a change in potential difference, the lumen becoming more negative. In most studies, however, the instability of the record has precluded any attempt to characterise the absorption of glucose electrically over a range of concentrations.

The $P.D.$ across the human jejunum is very small compared to those recorded in the stomach or colon. Hence it is relatively more important that other causes of a change in potential difference, either physiological or environmental, are minimised. We found that a prior injection of propantheline bromide, which reduced intestinal motility and possibly secretion, proved most valuable in rendering the record sufficiently stable for the measurement of small changes in potential difference.

In the only other study where changes in potential difference were measured over a range of glucose concentrations, the $P.D.$s were so unstable that infusion of solutions for up to 15 hours through a transmural tube was necessary. In contrast, in our technique the total infusion-time never exceeded 90 minutes. Furthermore, a single-lumen tube was used, which could be swallowed with ease and usually reached the jejunum within an hour. This aspect of the technique also compares favourably with chemical methods of characterising absorption, which involve infusion of solutions for 6 hours or more through a much bulkier intestinal tube.

Computation of an apparent $K_m$ result for glucose from the data of Sachar et al. yielded a very low value of 5.5 mM. The discrepancy between this value and our own data can be explained in two ways. Firstly, the concentrations plotted were intraluminal concentrations, which would be lower than the infused concentrations used in our study owing to dilution and also absorption. Secondly, because no attempt was made to keep the osmolarity of the solutions constant, the changes in potential difference induced by increasing concentrations of glucose would be reduced by the increasing osmotically induced potential difference of opposite polarity.

This would have the effect of causing an apparent saturation of the system at a lower glucose concentration (i.e., reducing the apparent $K_m$). Because we took care to ensure that each of our solutions had the same osmolarity and ionic composition, it is unlikely that the changes in potential difference which we observed were due to mechanisms other than the active electrogenic transfer of glucose.

In the rat in vivo, it is possible to correct the chemical data on glucose absorption for diffusion, thereby obtaining a chemical estimate of the active transfer mechanism. This has enabled values of apparent $K_m$ for the active transfer of glucose to be determined both electrically and chemically under identical experimental conditions. The fact that these apparent $K_m$s show a remarkable degree of correlation encourages us to infer that both methods do indeed measure active electrogenic transfer of glucose. In man, however, all the existing estimates for the glucose apparent $K_m$ determined chemically by infusion techniques are uncorrected for diffusion. Therefore, it is not possible to compare these values directly with determinations of apparent $K_m$ for glucose from our electrical data. In any case, this would be difficult because values of chemical $K_m$ for glucose show a considerable degree of variation, being greatly influenced by differences in experimental method, particularly the rate of infusion.

It is interesting to compare the results from the healthy volunteers with those from the patient with jejunal amyloidosis and malabsorption. In this patient both the apparent $K_m$ and $P.D._{max}$ are significantly lower, reflecting an apparent increase in the affinity of the active transport mechanism for glucose as well as an apparent reduction in the $P.D._{max}$ generated. Clearly our technique provides a new method of assessing the active electrogenic component of glucose absorption in man, which is both rapid and clinically acceptable. There is no reason...
to suppose that the same technique cannot be applied to aminoacid absorption, for these compounds also generate electrical P.D.S when absorbed. The method will enable us to explore the changes in activelectrogenic absorption which may occur in health and in disease states.

Previous criticisms on the use of the electrical potential difference in man as an index of gut integrity and function were directed against its indiscriminate use as a direct measure of ion movement. We have made use of the changes in the transintestinal P.D. that occur with serially increasing hexose concentrations only as an index of the functioning of the active, electrogenic hexose-transfer mechanism and not of ionic secretion and absorption per se.

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References

Reviews of Books

Obstetric Therapeutics

This book brings together the therapeutic aspects of antenatal care, labour, and the puerperium, both normal and abnormal. That this has been achieved is a tribute to the editor and to the fourteen other contributors. There is certainly a need for such a book. As the editor points out, the Royal College of Obstetricians and Gynaecologists has instituted a part-I examination for its membership whose syllabus includes the physiological and pharmacological basis of obstetric therapeutics; to date there has been no one book which brings together this information. The specialist-in-training, however, may find it difficult to synthesise the data in this book, since in several instances descriptions of the same drug are found in different chapters, each chapter referring to the use of the substance in only one aspect of obstetrics. This is exemplified in the description of the ergot alkaloids which can be found in only one aspect of obstetrics. This is regrettable that, in a chapter on the pregnant uterus, no mention is made of the recent exciting advances in our understanding of the physiological control mechanisms of uterine activity. Again, in the chapter on induction of labour, there is no reference to publications, such as those of O'Driscoll in Dublin, advocating an active management of labour. The author of this chapter, G. W. Theobald, presents a highly personalised view of the subject rather than an unbiased review. He scarcely discusses the use of prostaglandins, which have now revolutionised induction of labour in anencephaly or intrauterine death. In this chapter, and in most other chapters in the book, there are few references beyond 1970, so that recent advances are excluded. In summary, although obstetricians will doubtless benefit from reading this book, candidates for the part-I F.R.C.O.G. may find the facts in its 600 pages are not easily digestible and not always in line with modern obstetric practice. Nevertheless, it deserves a place in the libraries of all obstetric departments, being the only book of its kind and a good reference manual.

Principles of Chemical Pathology

This is a serious attempt, by two young English pathologists who emigrated to Windsor, Ontario, to produce a new comprehensive textbook. Unlike shorter rival texts, the authors are able to include experimental evidence and full references to the literature. A second major difference from shorter works is that the authors hold that a knowledge of the "principles of methodology is essential in interpreting laboratory data"; consequently, terised by oxidation (instead of hydroxylation) at carbon atoms 3, 17, and 16. Later, progesterone is stated to be hydroxylated at C-17 and C-21. The appendix to this chapter gives a list of trivial and systematic names of steroids; the obstetrician-in-training would hardly be expected to be acquainted with these, especially since the systematic names given are out of date and would not be accepted by an international biochemical journal.

In several sections of the book there are notable omissions, particularly with reference to recent advances. It is regrettable that, in a chapter on the prenatal uterus, no mention is made of the recent exciting advances in our understanding of the physiological control mechanisms of uterine activity. Again, in the chapter on induction of labour, there is no reference to publications, such as those of O'Driscoll in Dublin, advocating an active management of labour. The author of this chapter, G. W. Theobald, presents a highly personalised view of the subject rather than an unbiased review. He scarcely discusses the use of prostaglandins, which have now revolutionised induction of labour in anencephaly or intrauterine death. In this chapter, and in most other chapters in the book, there are few references beyond 1970, so that recent advances are excluded. In summary, although obstetricians will doubtless benefit from reading this book, candidates for the part-I F.R.C.O.G. may find the facts in its 600 pages are not easily digestible and not always in line with modern obstetric practice. Nevertheless, it deserves a place in the libraries of all obstetric departments, being the only book of its kind and a good reference manual.