incorporated [U-¹⁴C]glucose, but this could be inhibited by adding *n*-decane or *n*-undecane either simultaneously with the glucose or 30 min later. Inhibition, with both types of cells, was directly proportional to the alkane concentration. Glucose, however, had no inhibitory effect on the incorporation of *n*-[1-¹⁴C]decane into the cells. The effect of *n*-decane on the rate of glucose assimilation was much greater at a given concentration of alkane with alkane-grown cells than with glucose-grown cells. Moreover, glucose-grown cells showed a maximum inhibition of the rate of ¹⁴C incorporation from [U-¹⁴C]glucose of about 75% at 3 μ l of decane/mg dry wt. of cells, but alkane-grown cells showed no such maximum, and at the same concentration of decane incorporation of ¹⁴C was 99% inhibited.

This inhibition of glucose assimilation could be due to alkanes or, less likely, because of the rapidity of this effect, to an oxidation product either inhibiting glucose transport directly or interrupting glucose catabolism with subsequent accumulation of glucose or a glucose metabolite that then inhibits glucose transport.

With *n*-alkane-grown cells, in which glucose assimilation was inhibited by *n*-decane to about 1% of the original rate, the rate of uptake of glucose was proportional to the density of cells but independent of glucose concentration. However, the apparent internal glucose concentration, although only reaching a maximum of about 5 mM, was still higher than the final external concentration. This low concentration suggests that only residual active transport was being observed under these inhibited conditions. As there are difficulties in interpreting these results because of the metabolism of glucose, we have also used [1-¹⁴C]sorbitol, which is not metabolized by this yeast but is actively accumulated by it, probably by the same porter system as glucose, reaching an internal concentration in excess of 1 M. Uptake of sorbitol was most effectively suppressed by *n*-decane, thus leading us to conclude that the process of glucose transport itself is being blocked by the alkane.

The functional differences between glucose- and alkane-grown cells with respect to the effect of alkanes on glucose uptake may possibly be connected with a structural difference between the two types of cells. Considerable differences in structures have already been reported with other species of *Candida* (Ludvik *et al.*, 1968; Bos & de Boer, 1968).

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Inhibition of the Utilization of Lactose and other Carbon Sources by 3-Deoxy-3-Fluoro-D-Glucose in *Escherichia coli*

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3-Deoxy-3-fluoro-D-glucose is an unnatural glucose analogue that was first synthesized by Buck *et al.* (1966). It has been shown to be metabolized to 3-deoxy-3-fluoro-D-gluconic acid and perhaps also to 3-deoxy-3-fluoro-2-oxo-D-gluconic acid in *Pseudomonas fluorescens* (White & Taylor, 1970), but it appears not to undergo any significant metabolism in *Saccharomyces cerevisiae* (Miles & Pirt, 1969).

In frozen and thawed cells of *Escherichia coli*, 3-deoxy-3-fluoro-D-glucose was rapidly phosphorylated by the phosphoenolpyruvate-dependent phosphotransferase system, and resting cells took up 3-deoxy-3-fluoro-D-glucose to the extent of 0.03 g/g dry wt. of cells. Uptake of 3-deoxy-3-fluoro-D-glucose was not lethal, though at concentrations in the range 0.1–10 mM it completely prevented or severely inhibited the utilization of all carbon sources other than glucose. It prevented lactose utilization by inhibition of the synthesis and activity of β -galactoside permease; its effects on the utilization of other carbon sources may also be interpreted as being due to specific inhibition of the synthesis and activity of enzymes and permeases involved in their utilization. 3-Deoxy-3-fluoro-D-glucose-resistant mutants were isolated that were deficient in the Enzyme II of the phosphoenolpyruvate-dependent phosphotransferase system specific for glucose and for 3-deoxy-3-fluoro-D-glucose.

In inhibiting the utilization of carbon sources other than glucose, 3-deoxy-3-fluoro-D-glucose presumably acts as an analogue of glucose, and the physiological significance of the inhibition that it causes may be related to the mechanism(s) whereby glucose brings about its own preferential utilization. 3-Deoxy-3-fluoro-D-glucose also inhibited the utilization of carbon sources other than glucose in *S. cerevisiae*.

The ability of 3-deoxy-3-fluoro-D-glucose to bring about effects analogous to those of glucose, which 2-deoxyglucose and α -methyl glucoside and other glucose analogues are either unable or only partially able to bring about, is presumably an indication of its close stereochemical similarity to glucose.

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Conditions Required to Maintain Linear Rates of Glucose Absorption and Transport by Rat Small Intestine

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In this and the following communication (Porteous & Pritchard, 1972) we report a quantitative study of the simultaneous absorption, accumulation, metabolism and transport of a single organic substrate by a single species of small intestine. D-Glucose was selected as substrate; it is the only sugar known to be both readily metabolized and actively transported by intestine. The everted-sac technique (Wilson & Wiseman, 1954) was used; glucose (10 mM) was placed initially in solutions bathing the mucosal and serosal aspects of each sac.

Rats were rendered docile by keeping them in the dark for 1 h. Intestines from such rats gave superior and consistent glucose absorption and transport rates; we postulate that intestines from excited rats give poor and erratic results because of an adrenalin-mediated partial anoxia of the intestine *in vivo* (see Folklow *et al.*, 1964; Robinson *et al.*, 1966).

Incubation of sacs for 20 min at 37°C under 100% O₂ in Krebs–Ringer phosphate medium, pH 7.2, gave maximum and linear rates of glucose absorption from the mucosal solution and transport to the serosal solution. Beyond 30 min at 37°C absorption rates diminished progressively to zero at 60 min; transport rates declined more slowly.

Glucose transport varied more markedly with position along the intestine than did absorption; Crane & Mandelstam (1960) reported changes in sugar absorption at different points in hamster intestine.

Water transport in rat intestine was glucose-dependent (see Fisher, 1955), reached a maximum at 10 mM-glucose and was most pronounced in the upper third of intestine.

Apparent saturation of the glucose absorption and transport mechanisms occurred at approx. 10 mM-glucose in the upper intestine (see Riklis & Quastel, 1958; Crane & Wilson, 1958; Crane, 1960). But in the lower intestine glucose absorption did not approach an apparent $V_{\max}$, even at 50 mM-glucose; glucose transport was inhibited in all parts of the intestine at 50 mM-glucose.

Maximum glucose absorption and transport rates in all parts of intestine occurred at 147 mequiv. of Na⁺/l; deviation from this optimum Na⁺ concentra-

tion affected absorption less markedly than transport. Bihler & Crane (1962) on the contrary found that tissue accumulation of deoxy and anhydro derivatives of glucose by hamster intestine increased with Na⁺ concentration up to 217 mequiv./l.

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Quantitative Fate of D-Glucose during its Absorption, Accumulation, Metabolism and Transport by Rat Small Intestine

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During glucose transport by intestine (Porteous & Pritchard, 1972a), glucose and lactate accumulate in mucosal tissue; the concentration of these solutes in the serosal solution exceeds that in the mucosal solution, but not that in mucosal tissue water. These results support the hypothesis (McDougal *et al.*, 1960) that (i) a hexose pump exists at the luminal pole of intestinal epithelial cells, and (ii) consequent intracellular accumulation of glucose from the mucosal solution, and subsequent diffusion towards the serosal solution, accounts for net transintestinal transport of glucose.

Lactate accumulation in mucosal tissue is due not to serosal muscle metabolism (J. W. Porteous & P. Pritchard, unpublished work) but to epithelial cell metabolism (Iemhoff *et al.* 1970; Kimmich, 1970) of accumulated glucose. Lactate is shown to diffuse preferentially towards the serosal solution, creating a transintestinal lactate gradient. A primary lactate pump need not be postulated.

We report a balance sheet for glucose absorption, accumulation, metabolism and transport at all points along rat small intestine: 8–27% of absorbed glucose was transported, 36–44% accumulated in mucosal tissue, and 27–41% was converted into lactate in