

yeast extract, KCl slants (Difco yeast extract 5 g/l, glucose 10 g/l, KCl 7.4 g/l, Difco agar 20 g/l). For quantitative growth tests, mutant and wild type cells were grown in 50 ml liquid, synthetic medium<sup>5</sup> in 200 ml Erlenmeyer flasks. Optical densities were measured with a Lumetron photometer using the filter 650. Flasks supplemented with varying amounts of KCl were all inoculated with the same number of viable cells ( $10^7$ ) and shaken at 30°C. Exponential growth rates were determined graphically from semilog plots of the optical density values. The relative exponential growth rates were computed, using the value of the growth rate of the wild type in synthetic medium as the standard.

Figures 1-3 summarize the data of the growth experiments. The potassium chloride concentration refers to the initial concentration of the potassium chloride supplement (the basal medium had a potassium ion concentration of

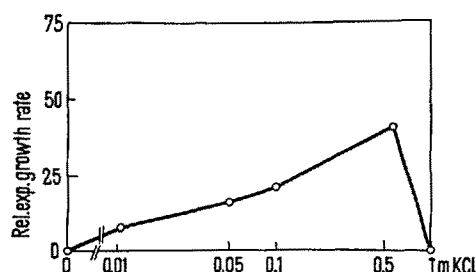


Fig. 3. Relative exponential growth rates of the potassium-requiring mutant 972-G-4.

$7.35 \cdot 10^{-3} M$ ). The mutants fall into at least two classes. One class, 972-G-1 and 972-G-5, grows optimally at 0.01 M KCl and is inhibited at higher concentrations. The second class with 972-G-4 grows best at 0.5 M KCl, a concentration at which both the wild type and the two other mutants are inhibited in growth.

The mutants 972-G-1 and 972-G-4 can grow at a KCl concentration (0.5 m) at which the wild type is inhibited. This observation suggests a simple method for the isolation of potassium-requiring mutants of *Sch. pombe*, which would involve plating of untreated or mutagenized cells on a medium containing KCl at a concentration of 0.5 m or higher. It is expected that only potassium-requiring mutants would grow on such a medium.

It is planned to determine the nature of the biochemical lesion as well as the genetics of the mutants described. These mutants might also be used as tools to study the mechanisms of potassium ion transport in yeast.

*Zusammenfassung.* Zwei Klassen von Mutanten der Hefe *Schizosaccharomyces pombe*, welche hohe Konzentrationen von Kaliumionen zum Wachstum benötigen, können auf Grund ihres Wachstumsverhaltens in mit Kaliumchlorid angereichertem Medium unterschieden werden.

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<sup>5</sup> R. MEGNET, Arch. Jul. Klaus-Stiftung 33, 299 (1959).

## The Rate of Biliary Secretion During Flow up Vertical Cannulas of Different Bore

Some time ago it was shown<sup>1</sup> that the perfused rat liver was able to force bile up a vertical tube at a constant rate until a head of about 12 cm was produced, after which the rate fell rapidly to zero. Recently, RICHARDS and THOMSON<sup>2,3</sup> reported a similar constant rate of bile flow up a wide bore tube attached to a biliary cannula in cholecystectomized dogs, but also showed that the initial rate of flow declined when tubes of narrow bore were used. They suggested that this difference was related to the failure of the hepatic cells to accumulate substrate fast enough to keep pace with the rapidly increasing intrabiliary pressure, and therefore put forward the interesting hypothesis that biliary secretory effort is dependent upon the substrate load until such time as the secretory mechanisms are fully engaged. This hypothesis clearly requires that the rate of secretion of bile is reduced in response to a rapid increase in intrabiliary pressure.

There is, however, another possible explanation of the observations made with tubes of narrow bore, since increased intrabiliary pressure produces distension of the biliary tree<sup>1,4</sup>. If the distension produced by each unit rise of pressure increases as the intrabiliary pressure rises, and the extra volume contained in the distended biliary tree is significantly large in relation to the volume of bile in the cannula, then the results seen with the narrow bore

tube would be not unexpected. The bile 'lost' from the vertical tube would, in fact, be present in the distended biliary tree and hence the postulated reduction in the rate of secretion of bile need not occur. RICHARDS and THOMSON state that this is not the case with dogs.

Measurement of the true secretory rate during the flow of bile up vertical tubes might be used to confirm or deny one of the above hypotheses. This measurement has been attempted in a series of 15 albino rats, whose common hepatic ducts were cannulated with a cannula having a side arm to which vertical tubes of different bore were attached. Obstruction of the main outflow resulted in bile passing up the vertical side tube. The rate of flow of the bile up tubes of narrow and wide bore (0.5 and 1.0 mm respectively) was measured and similar results obtained to those described by RICHARDS and THOMSON, i.e. the initial rate of flow was constant with the wider bore but declined when the narrow bore tube was used. The volume of the biliary tree was then measured at different pressures by the dye method described elsewhere<sup>5</sup>, and finally

<sup>1</sup> R. W. BRAUER, G. F. LEONG, and R. J. HOLLOWAY, Am. J. Physiol. 177, 103 (1954).

<sup>2</sup> T. G. RICHARDS and J. Y. THOMSON, J. Physiol. 154, 60 (1960).

<sup>3</sup> T. G. RICHARDS and J. Y. THOMSON, Gastroenterology 40, 705 (1961).

<sup>4</sup> G. BARBER-RILEY, Am. J. Physiol. 205, 1127 (1963).

<sup>5</sup> G. BARBER-RILEY, Am. J. Physiol. 205, 1122 (1963).

the volume per cm was calculated for each tube. A typical result is shown in Figure 1 from which the secretory rate may be calculated since:

$$V_0 + S = V_t + C + R$$

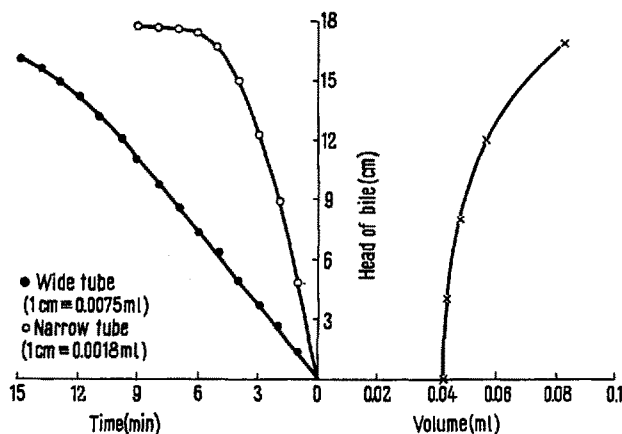


Fig. 1. The left-hand side of the graph shows the rate of bile flow up two vertical tubes of different bore. The right-hand side shows the volume of the biliary tree at different pressures. Single animal.

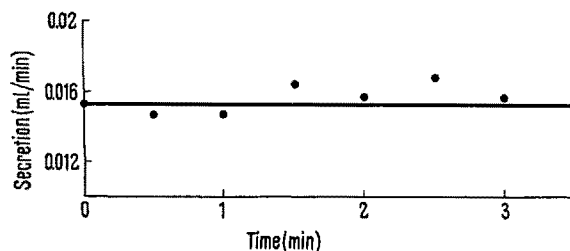


Fig. 2. The mean secretion rates calculated from the equation  $S = (V_t - V_0) / C$  at 30 sec intervals following the obstruction of the main outflow. The horizontal line represents the mean control flow rate measured before the experiments.

where  $V_0$  = the undistended volume of the biliary tree,  $S$  = the volume of bile secreted in  $t$  min,  $V_t$  = the distended volume of the biliary tree at time  $t$ ,  $C$  = the volume of bile in the cannula at time  $t$ , and  $R$  = the volume of bile reabsorbed in  $t$  min. Since back pressures of 0–12 cm of bile do not appear to reduce the rate of bile flow from the cannula in rats (apart from a brief temporary pause due to dilatation of the biliary tree), it is thought that  $R = 0$  over this range, and in these circumstances

$$S = \text{secretory rate} = (V_t - V_0) / C.$$

The mean values obtained for  $S$  with the narrow bore tube have been calculated at half minute intervals and are shown in Figure 2. Despite the decline in the rate of ascent of bile up the tube with the passage of time, the secretory rate measured in this way remained constant, and was approximately the same as the biliary outflow measured before the experimental procedure. The values for  $S$  found with wide bore tubes were also constant over the same range of back-pressure. The mean value for the ratio of the extra volume of bile in the distended tree, the volume of bile in the cannula ( $= V_t - V_0 / C$ ) when  $t = 15$  min was  $1.36$  ( $SE \pm 0.09$ ) with the narrow bore tubes, and  $0.27$  ( $SE \pm 0.03$ ) with the wide bore tubes. Finally, Figure 1 shows that the distension per unit rise of pressure was increased as the intrabiliary pressure was raised.

Therefore, these experiments do not support the hypothesis that the biliary secretory effort made against increasing back-pressure is dependent upon substrate accumulation in the case of rats, while the statement that 'the pressure-volume characteristics of the biliary tree play an insignificant part'<sup>2</sup> would appear to apply here only to the experiments with the relatively wide bore tube.

**Résumé.** La variation dans la vitesse de la montée de bile dans les vaisseaux biliaires verticaux de calibres différents semble, dans le rat, être expliquée d'une manière satisfaisante par une distension de l'arbre biliaire.

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## Variations of Plasma Cholesterol among South Indian Men in Relation to Economical Status and Diet

Results previously published in this journal<sup>1</sup> have shown that plasma cholesterol values, determined in 49 Tamil young men, follow a bimodal distribution. This finding was ascribed to the heterogeneity of the economic status of subjects. The present paper is a preliminary report of a larger survey done in this prospect.

Venous blood was taken before breakfast from 193 unskilled male workers or students living in Madras. All the subjects belonged to the Tamil ethnic group; they were young, 18 to 35 except 5 individuals of about 40, and reasonably healthy as assessed by routine medical examination. The workers constituted a rather heterogeneous

group which can be divided into four professional subgroups. In the order of decreasing economic status, they are the following: laboratory technicians, hospital servants, coolies and workers in sedentary professions, such as street sellers, weavers and unemployed. Total cholesterol expressed in mg per 100 ml of plasma was determined by CRAWFORD's modification of the method of Zak<sup>2</sup>. 'Student's'  $t$  test and the  $F$  ratio are computed for assessing the significance of results.

As indicated in Table I, the students have a much higher cholesterol level than the workers ( $P < 0.001$ ).

<sup>1</sup> J. G. HENROTTE, G. RANGANATHAN, and G. KRISHNAMURTHI, *Exper.* 16, 350 (1960).

<sup>2</sup> W. CRAWFORD, *Clin. chim. Acta* 3, 357 (1958).