note the appearance of biochemical structures not present in the pure cultures feeding into the mixture.

Summary. A continuous 2-stage system for investigations of interactions between 2 or more species of bacteria is described. The system employs 2 or more chemostatically limited stages of pure cultures feeding to a non-limited mixed continuous growth cell. This permits comparison at any point on the growth curve of numbers and products of organisms in pure culture with numbers and metabolic products resulting from interactions between the same organisms in growing in mixed culture. The systems are mathematically defined and the data can be expressed in generation time. Results obtained with a mixture of *S. salivarius* and *V. alcalescens* indicate a distinct interaction betwen the strains employed. Generation time of each of these species was noticeably increased while growing in context with the other.

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Liver Haemodynamics and Age.* (27056)

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Marked variations in the pattern of liver haemodynamics have been observed in normal rats of different weight and age, maintained under identical conditions.† When related to the metabolic processes of the liver and its capacity to react to various agents, these changes may be of considerable importance.

In the present communication, data are presented on the haemodynamic pattern of the liver of the rat in different age groups.

Technique and Materials. Three groups of white male rats of the Hebrew University strain maintained under identical conditions and fed a standard diet were used. The first group (20 animals) weighed between 80 to 150 g, the second group (100 animals) weighed between 200 and 300 g, and the third group (20 animals) weighed between 300 and 450 g. The parameters examined were hepatic blood flow per gram liver tissue and per 100 g body weight, vascular space of the liver and portal vein pressure values.

Hepatic Blood Flow Determination. Hepatic blood flow was estimated as rate of removal of radioactive colloid from the peripheral blood by the reticulo-endothelial system of the liver. Heat denaturated iodine^{131}-labeled, human serum albumin was used as described by Benacerraf *et al.*(1). The dose of radioactivity injected varied from 0.01-0.1 μc per 100 g body weight and contained 0.05 mg or less of iodinated albumin per ml of water solution. The radioactive albumin was injected into the vena dorsalis penis and samples of 0.2 ml of blood were taken from the tail at 1, 2 and 3 minute intervals. The gamma radioactivity of the blood samples was measured in an "Atomic" scintillation counter.

Liver blood flow was calculated by multi-

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plying the constant rate of liver clearance by the distribution of radioactivity. The results were corrected by the efficiency factor of every group of animals. This factor was determined by injecting directly into the portal vein 0.2 ml of an albumin solution containing 1/10 of the amount of radioactive protein used for blood flow determination. During the next 5-10 seconds the portal and hepatic veins were ligated and cut, the liver excised and total organ radioactivity determined. Liver clearance efficiency was calculated as the ratio between organ radioactivity found and amount of radioactivity originally injected.

The amount of radioactivity cleared by the liver (distribution) was determined by injecting into the vena dorsalis penis an identical quantity of radioactive albumin as was used for blood flow determination. After 6 minutes, the time needed by the normal liver to clear the entire amount of radioactive material from the peripheral blood, the animals were sacrificed, the liver excised and amount of radioactivity in the organ measured.

Distribution of radioactivity outside the liver was measured in the thyroid gland, lung, spleen, kidney, bone marrow and lymph nodes.

Vascular Space Determination. The vascular space was determined as described by Klein(2) and estimated as the amount of hemoglobin present in a gram of liver. The left paramedial lobe was always used after ligation of the afferent and efferent vessels, special care being taken not to cause tissue injury and blood loss. Amount of hemoglobin was determined as cyanmethemoglobin measured in a Klett Summerson electrophotometer, and vascular space calculated as the ratio between hepatic and peripheral blood hemoglobin.

Portal Blood Pressure. Portal vein pressures were measured by a water manometer. The needle was inserted directly in the portal vein or in one of the branches of the mesenteric vein. Zero pressure was based on the anatomical level of the portal vein.

Results. The liver clearance efficiency in the young group of animals was 80% while in the older groups 90% of the injected radioactive albumin was cleared during one passage through the liver. Distribution of radioactivity in the liver of the younger group of animals was not significantly different from that found in the older group and varied between 72% to 74% of the amount injected. No difference in amount of radioactivity was found in the various liver lobes or in different areas of the same lobe.

Hepatic Bloodflow. When calculated as ml/min/100 g body weight, hepatic blood flow was 8.52 ± 0.73 in the younger group; 6.62 ± 0.9 in the middle age group and 3.49 ± 0.49 in the old age group (Table I). When calculated per g of liver tissue, blood flow was 1.90 ± 0.16 in the young age group, 0.92 ± 0.16 in the middle age group and 0.99 ± 0.13 in the old age group. This parameter indicates that the older the animal the smaller the amount of blood flow per gram liver tissue as well as per 100 g/BW.

Vascular Space. The highest vascular space values were obtained in the middle age group, the smallest in the younger age group and somewhat higher values were obtained in the

TABLE I. Liver Haemodynamics in Rats of Different Age Groups.

Bodywt	120g-150g	200g-300g	>300g
Liverwt g/100g bodywt	4.07 ± .10 * (21)†	3.47 ± .04 (107)	3.33 ± .09 (12)
Portal Pressure units saline	66 ± 2 (17)	70 ± 2 (78)	71 ± 9 (12)
Vascular Space ml/g	.108 ± .006 (20)	.148 ± .004 (103)	.128 ± .010 (20)
Hepatic Blood Flow ml/min/100g bodywt	8.52 ± .73 (13)	6.62 ± .19 (85)	3.49 ± .49 (12)
Hepatic Blood Flow ml/min/g liver	1.90 ± .16 (13)	1.92 ± .16 (85)	.99 ± .13 (11)

* M ± S.E. † Figures in parentheses indicate the number of animals.

older age group. Vascular space in the young group was 0.108 ± 0.056, in the middle age group 0.148 ± 0.004, and in the older age group 0.128 ± 0.010. The P value of the last 2 groups was 0.05.

Portal Pressure. Portal pressure values were constant and did not show significant changes when related to age, although there was a slight tendency towards higher values in the older animals. Portal pressure values varied between 66 mm saline in the young group and 70 mm saline in the middle age groups.

Discussion. When related to age, the most pronounced changes in the pattern of liver haemodynamics were observed in the parameters related to intrahepatic circulation. Low vascular space values associated with the highest rate of liver blood flow were characteristic of young animals. Decrease in blood flow concomitant with an increase in vascular space was found in the middle age group, and a marked reduction in liver blood flow was consistently observed in the older animals. The parameters most affected were the liver blood flow per gram liver tissue and per 100 g body weight, both of which showed a gradual decrease as the weight and age of the animal increased. Portal vein blood pressure showed only slight variations in the different age groups.

The low vascular space values found in the younger group indicate that either vascularization of the liver is not sufficiently developed or that the functional pathways are shorter and centrally situated. This would agree with observations already reported on the liver circulation of the rat examined by serial X-ray films(3). The distribution of the vascular pathways suggests that the liver lobules are not being equally perfused and that conditions of tissue anemia prevail in the peripheral areas. Tissue anemia at an age when liver growth is still active may be of considerable importance when related to growth, repair and capacity of the organ to react to various injurious agents(4,5,6). The high liver blood flow found in this group, associated with the lowest portal pressures and vascular space values, indicates that flow-pressure and flow-vascular space relationships are different from those postulated by Poisseuille for pure liquids. The liver blood flow at this age is probably not dependent on the cross-sectional area of the vascular bed or on levels of portal vein blood pressures. In contrast, liver blood flow per gram liver tissue remained unchanged in the middle age group, although vascular space was increased and portal pressure values remained constant as compared to the younger group. More striking was the 60% decrease in liver blood flow associated with unchanged values in the rest of the parameters, found in the older animals. These data indicate that increased or decreased blood flow rates are possible when other haemodynamic parameters remain constant, and, conversely, variations in portal pressure and vascular space are compatible with constant liver blood flow values. In addition, variations in portal blood pressure do not always reflect changes in vascular space values or in rate of hepatic flow. This confirms previous reports on changed relationships between the parameters controlling blood flow(7) and suggests that age may be one of the factors which influence the pattern of liver circulation.

Summary. Variations in the pattern of liver circulation in the rat have been observed in different age groups. Hepatic blood flow decreased as age of the animal increased and was not dependent on vascular space and portal blood pressure. Vascular space values were higher in the middle age group but portal vein blood pressures were unaffected by variations in age.

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