

| | ICG clearance | |
|-----|---------------|-------------|
| | Plasma ml/min | Bile ml/min |
| 308 | 290 | |
| 139 | 58 | |
| 191 | 125 | |
| 171 | 70 | |
| 250 | 124 | |
| 220 | — | |
| 128 | 82 | |
| 57 | 13 | |
| 147 | 48 | |
| 66 | 30 | |
| 118 | 80 | |
| 176 | 217 | |
| 164 | 157 | |
| 66 | — | |
| 84 | 26 | |
| 113 | 57 | |
| 130 | 112 | |
| 149 | 99 | |
| 68 | 76 | |

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ed as HBF ([a]–[h]), symbols used as above. Hepatic plasma and bile clearance of ICG were calculated as above.

RESULTS

Table I gives the data of the isolated, perfused livers. Among the functional parameters the galactose elimination rate shows the smallest relative variation (21 per cent) and the ICG bile clearance the greatest (55 per cent). In the case of the in vivo pig livers shown in Table II, the smallest variations are seen regarding lactate/pyruvate ratio (32 per cent) and galactose elimination rate (35 per cent), and again the largest is ICG bile clearance (77 per cent).

The average pressures in the portal and hepatic veins were not significantly different in perfused and in vivo livers, but the mean arterial pressure was smaller in the perfused livers (81 mm Hg. vs. 105 mm Hg.).

The comparison between perfused and in vivo livers is summarized in Table III: the greater weight of the perfused livers may be due to an increase in tissue water during the perfusion (1). This may also account for the difference in total adenine nucleotide content (Fig. 2). The ATP/ADP ratio is identical in perfused and in vivo livers. The hepatic oxygen uptake of in vivo livers, requiring separate determinations of portal and hepatic arterial contributions, involves a greater error than in perfused livers, but the difference between the mean values is statistically significant. The

ADENINE NUCLEOTIDE IN PIG LIVER

□ in vivo (anaesthesia)
▨ perfused (after 3 hours)

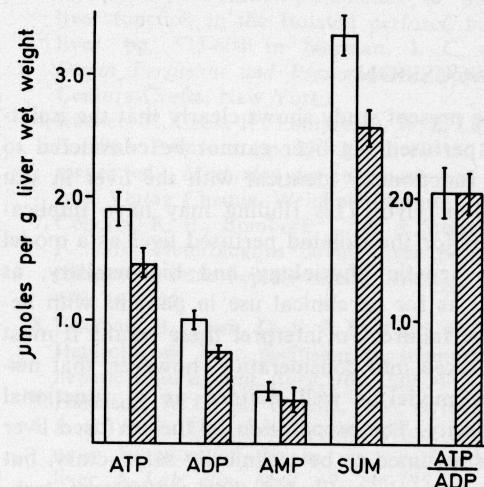


Fig. 2. Adenine nucleotides in perfused (N = 6) and in vivo (N = 6) pig liver. I = \pm SEM.

lactate/pyruvate ratio is lower in perfused than in vivo livers. The mean concentrations of neither lactate nor pyruvate are significantly different in the preparations. The galactose elimination rate of the perfused liver is 70 per cent of that of the in vivo liver, and due to the relatively small variations the difference is highly significant. Despite the reduced bile flow of the perfused liver, the ICG plasma clearance and bile clearance are almost two times greater in the perfused than in the in vivo liver. This

Table III. Comparison of functional data of perfused and in vivo pig livers by means of average values from Tables I and II

| | Liver weight Kg | Total liver flow litres/min | Oxygen uptake mmol/min | Lactate/pyruvate ratio | Galactose elimination hep. vein μmol/min | Bile flow μl/min | ICG clearance Plasma ml/min | ICG clearance Bile ml/min |
|---------------------|-----------------|-----------------------------|------------------------|------------------------|--|------------------|-----------------------------|---------------------------|
| Perfused liver* | 1.21 | 1.17 | 2.36 | 15.7 | 545 | 221 | 269 | 173 |
| In vivo liver** | 1.05 | 1.07 | 2.62 | 20.3 | 786 | 453 | 149 | 99 |
| Difference of means | + 0.16 | + 0.10 | - 1.26 | - 4.0 | - 241 | - 232 | + 120 | + 74 |
| P*** of difference | < 0.05 | n.s. | < 0.001 | n.s. | < 0.01 | < 0.01 | < 0.001 | < 0.05 |
| Perfused/in vivo | 1.15 | 1.09 | 0.52 | 0.77 | 0.69 | 0.49 | 1.81 | 1.75 |

* Mean values from Table I. ** Mean values from Table II. *** t-test.

could not be explained by differences as to infusion rate or plasma concentration. The relation between plasma clearance and bile clearance was about 3:2 in both preparations.

DISCUSSION

The present study shows clearly that the isolated perfused pig liver cannot be considered to be functionally identical with the liver *in situ* and *in vivo*. This finding may have implications for the isolated perfused liver as a model for hepatic physiology and biochemistry, as well as for its clinical use in patients with hepatic failure. To interpret these results it must be taken into consideration, however, that neither model is well defined as to functional capacity. The preparation of the perfused liver was assumed to be technically satisfactory, but it cannot be excluded that a different technique may result in better livers. On the other hand, the *in vivo* studies probably underestimate the function of the intact pig liver, since they were performed during anaesthesia and laparotomy. The difference between the isolated perfused and the intact pig liver therefore may be greater than found in the present study.

The relation between the functions of the perfused and the *in vivo* liver varies from one parameter to another, the *in vivo* liver being twice as 'good' as the perfused one from the point of view of bile flow and only half as 'good' as to ICG uptake and excretion. The low bile flow of the perfused liver is well explained by the lack of an enterohepatic recirculation of bile salts, since it has been shown that the perfused pig liver may react with almost as high a bile flow to a bile salt 'drive' as the intact liver (4). In preliminary experiments the bile acid excretion in perfused livers was found to be about 2 $\mu\text{mol}/\text{min}$, and in *in vivo* pigs 25 $\mu\text{mol}/\text{min}$ (unpublished observation). The ICG data are more difficult to explain, but it is remarkable that the *in vivo* clearance data are low when compared with values seen in normal man (mean 650 ml/min per kg \pm 2.5, data derived

from (20)). It is therefore possible that the experimental procedure involves inhibitory factors (anaesthesia, contrast medium). Other factors, as differences in capacity of the proteins for binding of ICG, or absence of 'normal' inhibitors from the perfusate must also be considered. Strelbel et al. (15) found that the BSP T_{max} was considerably higher *in vivo* than in perfused pig livers. No explanation for this difference can be given at present.

The striking difference between the oxygen uptake of the two models examined may be more significant, but again the high values *in vivo* are more remarkable than the low values of the perfused liver. Tauber et al. (16) found a lower oxygen uptake of the *in vivo* pig liver (1.1 $\text{mmol}/\text{min}/\text{kg}$). From our data the estimated hepatic oxygen uptake *in vivo* is 2.3 $\text{mmol}/\text{min}/\text{kg}$ liver weight. This may be compared with human data (17) of 1.9 $\text{mmol}/\text{min}/\text{kg}$ (estimated) liver weight. On the basis of body weight pig liver oxygen consumption is almost twice as high as that of human liver (0.07 and 0.04 $\text{mmol}/\text{min}/\text{kg}$ body weight, respectively). More observations are needed to decide if the present data can be accepted as normal and used as a reference basis, but if they can, the oxydative metabolism of the perfused liver is only a little more than 50 per cent of that of the intact liver:

There is good agreement between published observations of the oxygen uptake of the perfused liver. Data almost identical with ours were obtained by Hardison et al. (9), Pissidis et al. (14) and Abouna et al. (2), slightly lower values by v. Wyk et al. (21) and Hobbs et al. (11) and slightly higher values by Bombeck et al. (5) and Tauber et al. (16).

The oxygen uptake gives in itself little information about the metabolic efficiency of the organ, but the identical ATP/ADP ratios in perfused and *in vivo* livers, despite different oxygen uptake, point more to differences in oxygen demands than to differences in capacity of oxydative metabolism.

The only test which is presumably an indicator of the metabolic capacity of the organ is the galactose elimination rate (18). In the perfused liver it was measured as the amount of

galactose removed from, and *in vivo* as the concentration difference in blood flow. Extrahepatic consumption and oxygenated blood flow therefore causes of the difference, they cannot be quantified, likely that they can account for a minor part of the difference under different conditions. Sustained considerably higher *in vivo* pigs (about 1700 $\mu\text{g}/\text{min}$) data on perfused pig livers. The conclusion therefore is that the capacity of the perfused liver is about two-thirds of that of the intact liver.

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galactose removed from the perfusate per minute, and in vivo as the arterio-hepatic venous concentration difference multiplied by hepatic blood flow. Extrahepatic splanchnic galactose consumption and overestimation of hepatic blood flow therefore must be considered as causes of the difference between both models; they cannot be quantitated, but it is very unlikely that they can account for more than a minor part of the difference. Under slightly different conditions Strelbel et al. (15) found considerably higher galactose elimination in in vivo pigs (about $1700 \mu\text{mol}/\text{minute}$) whereas their data on perfused pig livers are similar to ours. The conclusion therefore is that the metabolic capacity of the perfused liver is at the most about two-thirds of that of the intact liver.

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