The first increment in dose caused a large increase ($P<0{\cdot}001$) in the initial distribution volume V_1 and in the rate of transfer C_t (ml/min) between the two compartments ($P<0{\cdot}10$). The increase in V_1 has been reproduced without increase in dose in subjects performing physical exercise or sucking glyceryltrinitrate tablets; it is attributed to peripheral vasodilatation. The increase in V_1 caused a reciprocal fall in k_{el} but there was no change in amylobarbitone elimination expressed as the plasma clearance rate C_a.

The second increment in dose caused no significant change in V_1, C_t, C_a or k_{el}.

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Preliminary observations on the elimination of amylobarbitone by patients with chronic liver disease

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Amylobarbitone (3·23 mg/kg) was given by intravenous injection over a 3 min period without loss of consciousness to seven patients with chronic liver disease. The serum amylobarbitone decay curves were determined and each was fitted by a two compartment mathematical model. The results were expressed as the half-time $T\frac{1}{2}$ (h) for the slow decay of serum amylobarbitone concentration, the plasma amylobarbitone clearance C_a (ml/min) and the steady state distribution volume V_{dss} (ml). Bromsulph alein retention and other conventional indices of liver function were measured. The purpose and nature of the experiments were fully explained and each patient, gave informed consent.

TABLE 1. *Amylobarbitone elimination and bromsulphalein (BSP) retention in patients with chronic liver disease*

Description of patient and long term drug therapy	Distribution volume (V_{dss}) (ml)	Plasma clearance rate (C_a) (ml/min)	Half time (slow phase) ($T\frac{1}{2}$) (h)	BSP retention (45 min) (%)	Age (years)	Weight (kg)
Juvenile hepatic fibrosis; portacaval anastomosis; frusemide, prednisolone, spironolactone	111,000	26	49		22	84
Alcoholic cirrhosis; portacaval anastomosis; no drugs	115,000	28	49	46	56	72
Post-necrotic cirrhosis; no drugs	69,000	36	22	48	33	70
Primary biliary cirrhosis; no drugs	46,000	33	17	39	43	38
Portal cirrhosis; isoniazid, rifampicin, ethambutol	43,000	22	23	47	42	59
Portal cirrhosis; diphenhydramine, methaqualone	83,000	53	20	7	51	76
Active chronic hepatitis: lincomycin, tetracycline	53,000	55	12	8	29	50
Healthy controls; mean	61,000	35	21	<5	29	63
No drugs (range) ($n=10$)	(36,000–84,000)	(23–51)	±4 (S.D.)		(20–43)	(53–85)

The two patients with portacaval anastomosis had greatly increased serum half times ($P<0{\cdot}001$) associated with low plasma clearance rates and high distribution volumes. Two patients with chronic liver disease who were not receiving drugs and one who was receiving antituberculous chemotherapy had normal values for $T_{\frac{1}{2}}$, C_a and V_{dss}. Two patients receiving long term drug therapy had plasma amylobarbitone clearance values at the upper limit of the normal range. One of these had a significantly shortened half-time ($P<0{\cdot}05$).

There was a strong and significant negative correlation ($r=-0{\cdot}93$, $P<0{\cdot}01$) between the plasma amylobarbitone clearance rate C_a and the bromsulphalein retention at 45 min. This is consistent with the suggestion that both measurements are directly related to the functional capacity of the liver.

There was a weak and insignificant positive correlation ($r=0{\cdot}52$, $P>0{\cdot}20$) between the serum concentration half-time $T_{\frac{1}{2}}$ and the bromsulphalein retention; the half-time is dependent not only on the plasma clearance rate but also on the distribution volume, and this is not directly related to liver function.

$$T_{\frac{1}{2}}=\log_e 2.\frac{V_{dss}}{C_a}$$

Increased half-life of antipyrine in women taking oral contraceptives (T)

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The absorption and elimination of cloxacillin in patients on chronic intermittent haemodialysis (T)

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The effects of steroid and of immunosuppressive drug therapy on lymphocyte stimulation by *Candida* antigens (T)

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