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Plasma ^{65}Zn kinetics in the rat

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The amount of ^{65}Zn in the plasma of rats after intravenous injection was found to decline following closely two-compartment kinetics over a period of 90 min. Comparative analysis of the amount of ^{65}Zn present in the two kinetic pools at various time-intervals post-injection with the actual physiological location of the ^{65}Zn, revealed that the initial pool (Qa) is primarily the blood plasma, while the second pool (Qb) is primarily within the liver. The plasma Zn concentration and Qa were both found to fall reproducibly during Zn depletion, whereas Qa and Qb increased following injection of *Escherichia coli* endotoxin in contrast to the decline in plasma Zn concentration. Further investigation of the nature of Qb indicates that it represents in part a metabolic pool within the liver which varies substantially in response to Zn status in a manner similar to metallothionein.

Metallothionein: Zinc: Rat

Zinc deficiency has been claimed to be associated with common pathological conditions such as Crohn's disease (Steinberg, 1985) and alcoholic liver cirrhosis (Keeling & Thompson, 1983), and it has also been claimed that certain large population groups may be at risk from Zn deficiency (Prasad *et al.* 1961; Lyon *et al.* 1979). In contrast to acute deficiency there are no universally recognized clinical symptoms in the marginally deficient state and there is debate as to whether the Zn contents of any accessible tissues provide a reliable index of Zn status (Solomons, 1979; Jones *et al.* 1981; Jackson *et al.* 1982).

Plasma Zn concentrations are frequently used as a measure of Zn status but stresses such as post-operative or endotoxin stress may cause a fall in plasma Zn levels unassociated with Zn deficiency (Hallbook & Hedelin, 1977).

There has been little use of kinetic techniques to analyse pool sizes and rates of Zn turnover as an aid to the diagnosis of deficiency, although Prasad *et al.* (1961) gave ^{65}Zn to subjects suspected of being Zn deficient. He found them to have a reduced loss of the isotope between 10 h and 10 d post-injection, while Jackson *et al.* (1988) showed an increased turnover of stable ^{67}Zn in a group of malnourished subjects with marginal Zn status.

In experimental animals Chesters & Will (1981*a*) studied the turnover of intravenously injected ^{65}Zn in pigs fed on diets of differing Zn content, or injected with endotoxin. They found that the injected ^{65}Zn followed predictable two-compartment kinetics, but made no attempt to correlate the predicted pools with physiological sites. Dunn & Cousins (1989) have also used data derived from ^{65}Zn kinetics to model the redistribution of tissue Zn which occurs following treatment of rats with dibutyryl cyclic AMP. They also reported that the decay of ^{65}Zn in rat plasma obeyed two-compartment kinetics.

In the present paper we report studies in rats designed to extend this approach by examining the likely physiological sites of the pools with which injected ^{65}Zn exchanged, and by further examining the response of these pools to variations in Zn status and endotoxin stress.

* For reprints.

MATERIALS AND METHODS

Female weanling Wistar rats were randomly allocated to groups fed on either a standard laboratory chow of Zn content 84 μg/g (Dio-Sure Lavender Mill, March, Cambridgeshire) or an albumin-based Zn-supplemented (Zn+) diet (Zn content 180 μg/g) or Zn-deficient (Zn−) diet (Zn content 5 μg/g). All groups were given free access to distilled water, housed in stainless-steel wire-bottom cages and fed on the diets for 6 weeks before study.

For studies of plasma ^{65}Zn turnover animals were anaesthetized with sodium pentobarbitone (60 mg/kg body-weight). A cannula (size 2FG; Portex Ltd, Hythe, Kent) was placed in the carotid artery and 2·5 μCi $^{65}ZnCl_2$ (specific activity 1·3 mCi/mg Zn, NEN, Stevenage, Herts) in 100 μl saline (9 g sodium chloride/l) were injected via the femoral vein. Blood samples (0·4 ml) were removed at specified time-intervals post-injection via the cannula. Blood volume was maintained by replacement with 0·4 ml saline. Heparin (Zn-free) was used to prevent blood clotting in the cannula.

Blood plasma was separated by centrifugation, the ^{65}Zn activity was determined by gamma counting (LKB 1275 minigamma) and total Zn by atomic absorption spectrometry (PYE Unicam SP 2900) following dilution with distilled, deionized water. The coefficient of variation of the assay of specific activity was approximately 5%.

In other experiments specified tissues were removed at certain time-intervals after the ^{65}Zn injection, weighed, freeze-dried and dissolved in concentrated hydrochloric acid (liver) or perchloric acid (600 ml/l) and concentrated nitric acid (1:1, v/v) before gamma counting for ^{65}Zn and atomic absorption analysis of the total Zn content. Liver metallothionein (MT) content was analysed by radioimmunoassay using a sheep antibody raised against rat MT1 (Mehra & Bremner, 1983). In this assay all samples were analysed for MT1 in the same batch with a coefficient of variation $< 10\%$.

Groups of female Wistar rats (150–200 g) fed on the normal laboratory chow were injected with either *Escherichia coli* endotoxin (3 mg/kg body-weight; Strain 0127:13% butanol extract; Sigma, Poole, Dorset) or an equivalent volume of sterile isotonic saline 24 h before injection of the ^{65}Zn.

Further groups were injected with either 25 μmol zinc sulphate in 0·5 ml sterile isotonic saline or an equal volume of sterile isotonic saline 6 or 24 h before injection of the ^{65}Zn.

Distribution of ^{65}Zn between different plasma proteins

The rate of distribution of added ^{65}Zn with endogenous Zn bound to plasma proteins was determined by incubation of 0·5 μCi ^{65}Zn with 2 ml rat plasma for various time-intervals up to 15 min. Albumin-bound Zn was then separated from other plasma proteins by precipitation with polyethylene glycol 6000 (Giroux, 1975; Chesters & Will, 1981*b*) and the ^{65}Zn and total Zn content of each fraction analysed.

Kinetic analysis of plasma ^{65}Zn specific activity

Decay curves of plasma ^{65}Zn specific activity were analysed using the techniques described by Shipley & Clark (1972). Over the time-course of the experiment (90 min) plasma ^{65}Zn kinetics were found to obey two-compartment kinetics and were analysed appropriately (Chesters & Will, 1981*a*). The fit of the data to predicted values from the derived two-component equation: general format

$$Y = ae^{-k_1 t} + be^{-k_2 t}$$

was always checked and re-analysis undertaken where necessary.

The sizes of the two exchangeable pools (Qa and Qb), their fractional turnover rates and the fluxes between these pools were calculated from the known amount of ^{65}Zn injected and

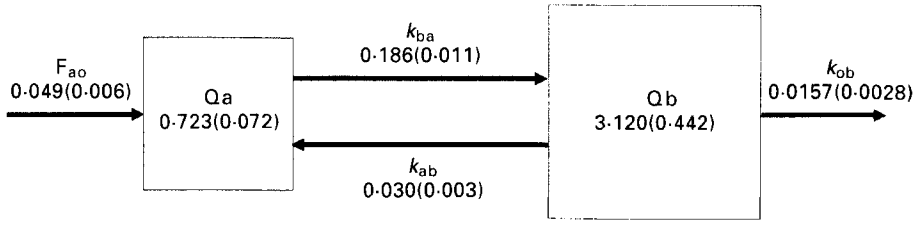

Fig. 1. Schematic representation of the two-compartment model of plasma zinc kinetics showing the calculated sizes of the initial (Qa) and second (Qb) pools (μmol/kg) with which intravenously injected ^{65}Zn equilibrates in control animals, the fractional rate of transfer of Zn from Qa to Qb (k_{ba}), from Qb to Qa (k_{ab}) and Qb and of the model system (k_{ob}), and the flux of Zn into Qa from outside of the model system (F_{ao}) (μmol/kg per min). Values are means, with their standard errors in parentheses.

the decay equation as described by Shipley & Clark (1972). It was assumed that on injection the ^{65}Zn could rapidly equilibrate with all the Zn present in plasma with no fractions within the plasma exchanging slowly.

Significance of results was assessed using Student's t test, $P < 0{\cdot}05$ being regarded as significant.

RESULTS

Distribution of ^{65}Zn between plasma proteins

No preferential distribution of ^{65}Zn between the albumin or non-albumin fractions of the plasma were seen at all time-points studied, ^{65}Zn apparently equilibrating rapidly between the various endogenous pools of the plasma. Results are not presented in detail but typical values were 70·7 (SE 1·3)% of ^{65}Zn in the supernatant fraction (albumin fraction) at 5 min after ^{65}Zn addition and 67·5 (SE 2·4)% at 15 min after ^{65}Zn addition.

Plasma ^{65}Zn kinetics in control animals

The calculated sizes of the initial pool with which the ^{65}Zn equilibrated (Qa) and the second 'exchangeable' pool (Qb) together with the fractional turnover rates between the pools for the control group of animals are shown in Fig. 1. These findings indicate that Qb was approximately 5-fold larger than Qa and that its fractional turnover was only approximately one-quarter of Qa. Plasma Zn concentrations did not vary significantly throughout the time-course of the ^{65}Zn turnover experiments.

Physiological location of the pools Qa and Qb

The values presented in Fig. 1 have been used to predict the proportion of an injected dose of ^{65}Zn present in the pools Qa and Qb and lost from the system (Fig. 2(*a*)) at various time-intervals post-injection. These are shown in comparison with the true distribution of an intravenous dose of ^{65}Zn found in tissues at various time-intervals post-injection (Fig. 2(*b*)). In addition to the tissues shown, the total amount of ^{65}Zn present in the bone, caecum, erythrocytes, hair, large intestine, lungs, skeletal muscle, spleen and stomach was also analysed. None of these tissues contained greater than 3·5% of the injected isotope at any time up to 90 min post-injection. Plasma was assumed to constitute 5% of body-weight for these calculations.

A comparison of the two series of curves shows the similar magnitude and rate of decline of the ^{65}Zn activity in the plasma and the predicted ^{65}Zn remaining in the pool Qa. This suggests that the Qa is likely to be primarily a reflection of the plasma 'pool' of Zn. The

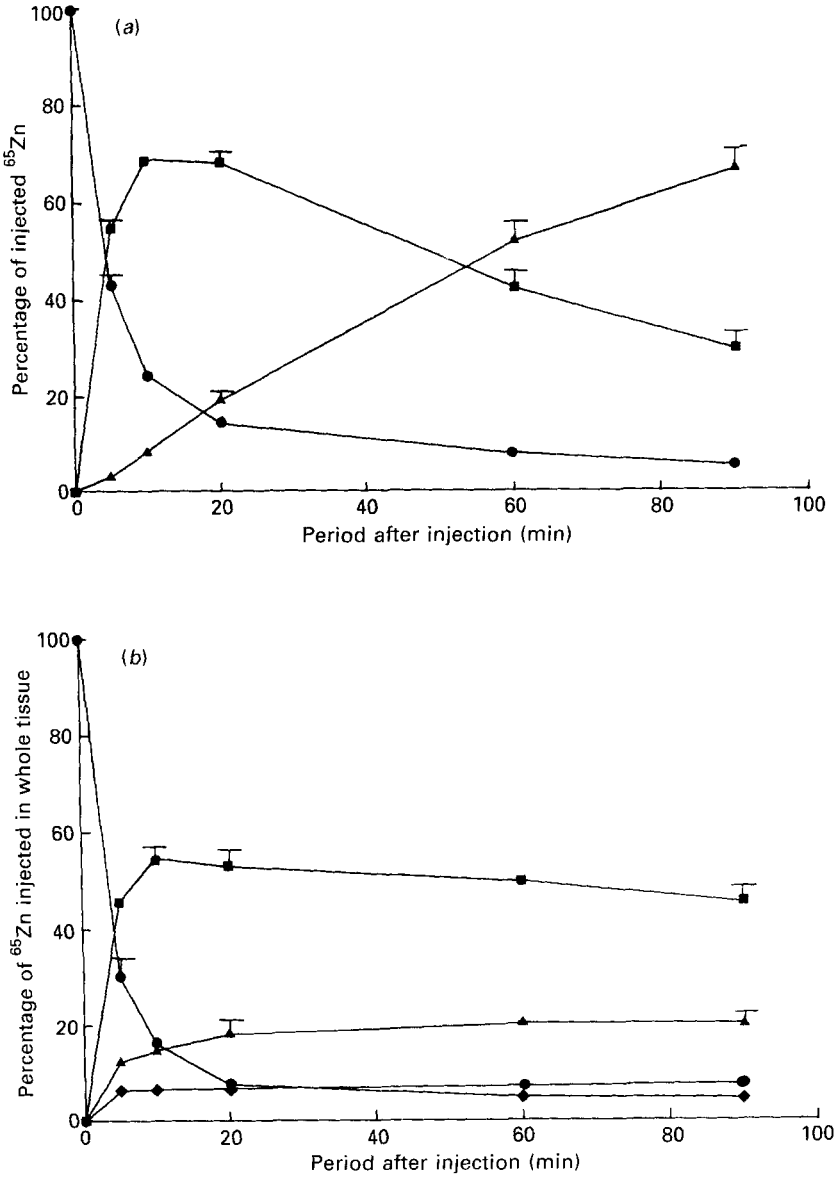

Fig. 2. (*a*) The predicted amounts of ^{65}Zn found in pools Qa (●) and Qb (■) and that lost from the system (▲) at various time-intervals after intravenous injection calculated from the values from control animals presented in Fig. 1. (*b*) Amounts of the ^{65}Zn found in various tissues of control rats at specified times after intravenous injection. Amounts in the blood plasma (●), liver (■), small intestine (▲) and kidney (◆) are shown. Values are means, with their standard errors represented by vertical bars. For details of procedures, see p. 446.

major proportion of the ^{65}Zn lost from the plasma was found in the liver (Fig. 2(*b*)), with a peak amount of activity being found at about 10 min post-injection. This time-course of accumulation is very close to that predicted for Qb (Fig. 2(*a*)), although the peak proportion predicted to appear in Qb is about 15% greater than that in the liver. All tissues other than the liver together only contributed 45% of the total body ^{65}Zn at the time when

Table 1. *Effect of zinc intake on tissue Zn content of rats*

(Mean values with their standard errors)

Dietary group†	*n*	Plasma Zn (μmol/l) Mean	SE	Liver Zn (μmol/g) Mean	SE	Bone Zn (μmol/g) Mean	SE	Liver wt (g/kg rat) Mean	SE	Body-wt (g) Mean	SE
Zn-supplemented animals	9	19·6	1·1	1·20	0·07	3·43	0·05	37·7	2·15	188·3	16·6
Zn-depleted animals	7	6·6***	1·2	1·14	0·11	0·53**	0·05	40·5	2·80	108·1***	25·5

Mean values were significantly different from those for Zn-supplemented animals (14 df): ** $P < 0·01$, *** $P < 0·001$.

† Albumin-based diet containing 180 and 5 μg Zn/g fed to Zn-supplemented and Zn-depleted rats respectively.

Table 2. *Calculated sizes of the two exchangeable pools (Qa and Qb) in zinc-depleted and control Zn-supplemented rats*

(Mean values with their standard errors)

Dietary group†	*n*	Qa (μmol/kg rat) Mean	SE	Qb (μmol/kg rat) Mean	SE
Zn-supplemented animals	9	0·620	0·106	2·512	0·577
Zn-depleted animals	7	0·269*	0·066	1·265	0·346

Mean values were significantly different from those for Zn-supplemented animals (14 df): * $P < 0·01$.

† Albumin-based diet containing 180 and 5 μg Zn/g fed to Zn-supplemented and Zn-depleted rats respectively.

Qb was predicted to contain 70% of the ^{65}Zn, with none singly contributing more than 15%. It therefore seems likely that the majority of the pool Qb is located within the liver.

Effect of Zn status on kinetics of ^{65}Zn

The effects of feeding the Zn− or Zn+ diets on tissue Zn contents are shown in Table 1. There was a significant decrease in the plasma and bone Zn contents in animals fed on the Zn− diet, although the liver Zn contents were not significantly different. The size of the pool Qa was also found to be significantly ($P < 0·01$) reduced in the Zn-depleted animals and the mean value for Qb was smaller, although there was no statistical significance between the groups (Table 2).

No significant changes in the fractional turnover rates between Qa and Qb were found in the two groups of rats, although the flux between Qb and Qa was found to be reduced in the Zn-deficient animals (0·032 (SE 0·01) *v.* 0·069 (SE 0·012) μmol/kg per min; $P < 0·03$).

Effect of endotoxin stress or acute elevation of body Zn content on kinetics of ^{65}Zn

In order to perturb acutely liver Zn homeostasis, groups of rats were given intraperitoneal injections of either *E. coli* endotoxin 24 h before injection of the tracer or $ZnSO_4$ 6 or 24 h before injection of the isotope. Control animals received intraperitoneal injections of isotonic saline.

Table 3. *Effect of endotoxin stress or acute elevation of body zinc content on tissue Zn levels of rats*

(Mean values with their standard errors)

Treatment group†...	Control		Endotoxin treated		6 h $ZnSO_4$ injected		24 h $ZnSO_4$ injected	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Plasma Zn content (μmol/l)	18·8	1·2	13·9**	5·3	179·1***	34·8	32·6***	12·3
Liver Zn content (μmol/g dry wt)	1·81	0·13	2·18††	0·12	3·40***	0·18	3·49***	0·14
Liver wt (g/kg rat)	36·8	1·6	41·0	2·2	37·5	1·1	43·3*	0·6
Body-wt (g)	183·8	32·3	177·8	30·0	205·3	10·7	228·2	27·3

Mean values were significantly different from those for control animals: * $P < 0·005$ (df 7), ** $P < 0·002$ (df 12), *** $P < 0·001$ (df 9), †† $P < 0·03$ (df 10).

† For details of treatments, see p. 449.

Table 4. *Calculated sizes of the two exchangeable pools (Qa and Qb) in control rats given injections of zinc sulphate,* Escherichia coli *endotoxin or saline (9 g sodium chloride/l)*

(Mean values with their standard errors)

Treatment group†	*n*	Qa (μmol/kg rat)		Qb (μmol/kg rat)	
		Mean	SE	Mean	SE
Saline injected	7	0·723	0·072	3·120	0·442
Endotoxin injected	7	0·943*	0·075	4·560*	0·442
$ZnSO_4$ injected					
(6 h)	4	8·472***	1·935	15·682***	1·494
(24 h)	4	1·748***	0·070	9·254***	0·454

Mean values were significantly different from those of saline-injected control animals: * $P < 0·05$ (df 12), *** $P < 0·001$ (df 9).

† For details of treatments, see p. 449.

Endotoxin injection induced a fall in the plasma Zn concentration and an increase in the size of the liver and liver Zn content (Table 3). This was associated with a rise in the size of both Qa and Qb in the endotoxin-treated animals (Table 4). Endotoxin treatment also induced a significant reduction in the fractional rate of movement of ^{65}Zn from Qb out of the system (i.e. k_{ob}, control 0·0157 (SE 0·0028) *v.* endotoxin 0·0100 (SE 0·0018); $P < 0·05$). No other significant differences in fractional turnover between pools were seen following endotoxin treatment.

Acute elevation of body Zn levels by intraperitoneal injection of $ZnSO_4$ (25 μmol) 6 h before injection of the ^{65}Zn caused a large elevation of both plasma and liver Zn contents (Table 3) associated with a gross expansion of both Qa and Qb. This was associated with a depression of the fractional rate of movement from Qa to Qb (k_{ba}, control 0·170 (SE 0·003) *v.* 6 h post-injection 0·113 (SE 0·016); $P < 0·04$) and an increase in the fluxes of ^{65}Zn between the pools (values not presented in detail).

Animals injected with $ZnSO_4$ 24 h before injection of the isotope have a smaller elevation of plasma Zn content but a high liver Zn content (Table 3), again associated with an expansion of Qa and Qb and a consequent increased flux of ^{65}Zn between the pools. Plots

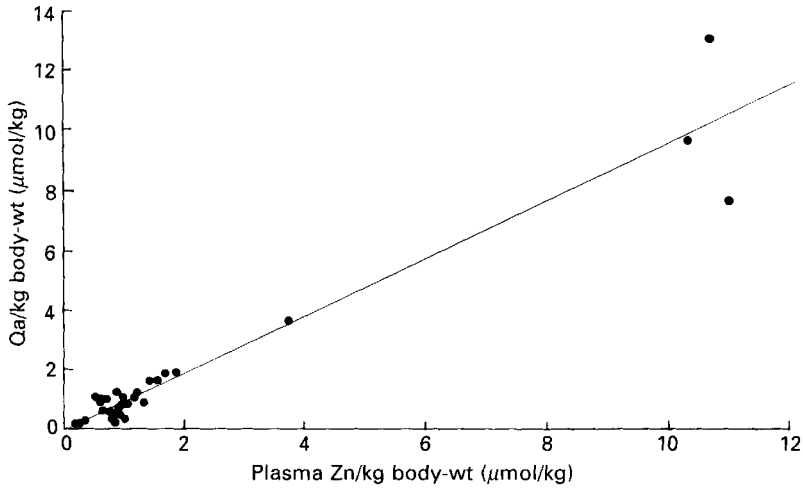

Fig. 3. The calculated size of exchangeable pool Qa *v.* the total plasma zinc content for all rats studied. The 'best fit' straight line through the data points has an equation of: $Y = 0{\cdot}944X - 0{\cdot}286$ (r 0·96).

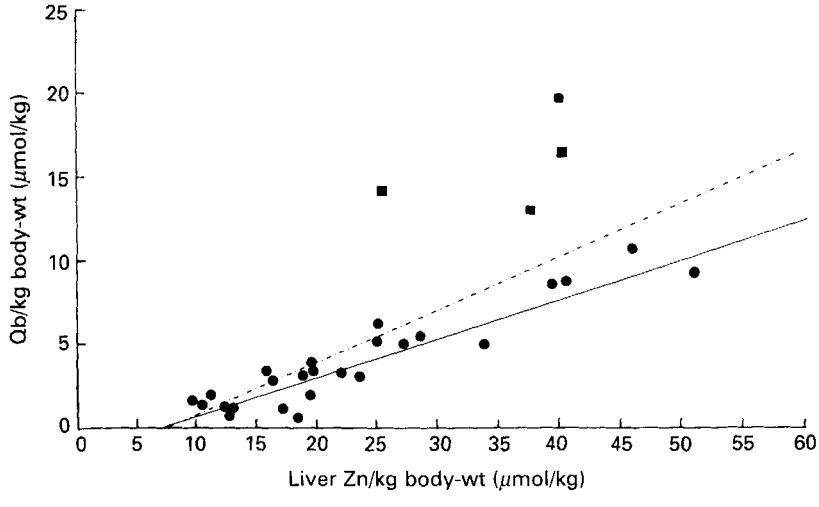

Fig. 4. The calculated size of exchangeable pool Qb *v.* the total liver zinc content for all rats studied. Animals injected with zinc sulphate (25 μmol) 6 h before the ^{65}Zn are shown separately (■) and lines of best fit and correlation coefficients are calculated with (–·–·–) and without (——) these points. The equations of the lines are $Y = 0{\cdot}336X - 2{\cdot}801$ (r 0·78) and $Y = 0{\cdot}235X - 1{\cdot}504$ (r 0·93) respectively.

of Qa *v.* plasma Zn content and Qb *v.* liver Zn content for these animals are presented in Figs. 3 and 4 respectively.

Relationship of Qb to liver MT content

A plot of Qb *v.* liver MT for all of the animals studied is shown in Fig. 5.

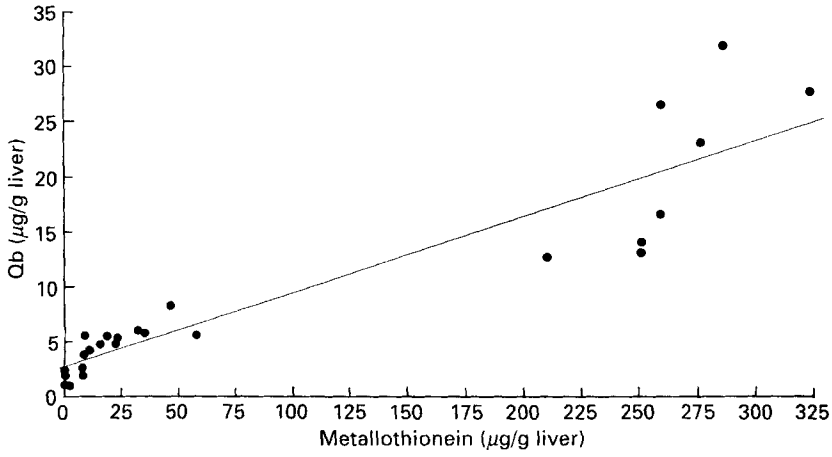

Fig. 5. The calculated size of exchangeable pool Qb *v.* the liver metallothionein content for all groups of rats studied. The 'best fit' straight line through the data points had an equation of: $Y = 7{\cdot}72X + 0{\cdot}0687$ (r 0·92).

DISCUSSION

Kinetic isotopic techniques offer the opportunity to obtain a picture of Zn metabolism which includes a time dimension but, with the exception of studies of Zn absorption rates, have been surprisingly little used in studies of Zn metabolism. The reasons for this are unclear, but it may be due to the unsuitability of available radioactive Zn isotopes to human studies and the technical difficulties of repeated tissue sampling from small laboratory animals. Chesters & Will (1981 *a*) have used a similar technique to that described here to study short-term ^{65}Zn kinetics in the pig. They found that over a period of 150 min the plasma ^{65}Zn kinetics closely followed a two-compartment model as did the values from rats over 90 min in the present study.

A comparison of the proportion of the ^{65}Zn dose found in various tissues to that predicted to occur from the two-compartment model using the values from normal animals (Fig. 1) is shown in Fig. 2. These findings suggest that the initial exchanging pool is primarily the plasma Zn. Further evidence for this comes from a plot of the size of Qa *v.* the total Zn found in plasma (Fig. 3) for all animals studied. This shows a correlation (correlation coefficient 0·96) between Qa and the Zn in plasma with a slope very close to unity (0·94) over a wide range of plasma Zn contents (without the four outlying points from animals given intraperitoneal injections 6 h previously, the correlation is still highly significant (r 0·81) with a slope of 0·94). There are two major assumptions which govern the actual values obtained for Qa; that plasma volume in rats approximates to 5% of body-weight (Constable, 1963) and that the injected ^{65}Zn rapidly equilibrates with all Zn within the plasma. This latter assumption is supported by our finding of no preferential retention of added ^{65}Zn with the albumin-bound fraction precipitated by polyethylene glycol. Chesters & Will (1981 *a*) assumed that their injected ^{65}Zn (which was bound to albumin before injection) would only rapidly equilibrate with albumin-bound Zn in the plasma which they took to be one-third of total plasma Zn. However, they were also unable to demonstrate any preferential retention or localization of the ^{65}Zn within the albumin fraction of the plasma in vitro.

The second slowly exchangeable pool appears to be largely present within the liver (Fig. 2), although there was approximately 15% of Qb unaccounted for by the ^{65}Zn in the liver

at the peak of ^{65}Zn accumulation. A plot of Qb *v.* liver Zn content for all animals studied is shown in Fig. 4. and demonstrates a significant correlation (r 0·78) between these two variables. However, it is apparent that Qb only constitutes a portion of the total liver Zn which is not constant, being a maximum of 6% of liver Zn in the Zn-depleted animals, but up to 40% of liver Zn in the animals injected with $ZnSO_4$ 6 h before study. The findings therefore suggest that Qb may represent, at least in part, some metabolic 'pool' within the liver which varies substantially with Zn status, both in terms of its absolute value and as a proportion of the total liver Zn.

Further examination of Fig. 2 also suggests that one of the further 'pools' to which ^{65}Zn is transferred from Qb may be within the liver, since Qb declined at a faster rate and to a lower level than the liver ^{65}Zn content (Fig. 2(*a*)) suggesting redistribution of ^{65}Zn within the liver.

Dunn & Cousins (1989) have also studied the sites of rapid redistribution of ^{65}Zn from blood plasma. They found that in normal animals only approximately one-third of the ^{65}Zn was rapidly transferred from the plasma to liver compared with approximately 60% described here (Fig. 2). Possible reasons for this discrepancy may include the considerably greater (i.e. 8-fold) amounts of ^{65}Zn injected by Dunn & Cousins (1989) or the different strains of rats used in their experiments.

Both Zn deficiency and injection of *E. coli* endotoxin reduced plasma Zn concentrations compared with control animals (Tables 1 and 3) but had differing effects on the size of Qa, Zn depletion reducing Qa but endotoxin stress increasing it (Tables 2 and 4). The reason for this expansion of Qa by endotoxin stress is difficult to interpret, but may reflect an increase in the extracellular space in these animals or an increased permeability of capillary membranes. Such an increased permeability has been described following injection of analogous cytokines into animals (Cousins & Leinart, 1988). Qb was also increased by endotoxin stress and reduced by Zn deficiency (Tables 2 and 4) which is in accord with the hypothesis that Qb represents part of liver Zn. Liver Zn concentration was also increased by endotoxin stress (Table 3).

The effects of dibutyryl cyclic AMP on Zn metabolism studied by Dunn & Cousins (1989) appear to be analogous to those produced by endotoxin, but in their kinetic model the initial exchangeable pool (Qa in the nomenclature used here) was fixed at half that found in control animals. In practise we found this pool to be expanded by endotoxin. These differences may partly explain why the rapidly exchangeable liver pool described by Dunn & Cousins (1989) was unchanged by dibutyryl cyclic AMP whereas Qb was increased by endotoxin in our experiments.

Injection of $ZnSO_4$ at 6 h before ^{65}Zn injection gave results which also support the idea that Qb primarily represents some discrete labile metabolic pool within the liver. At 6 h following the injection of $ZnSO_4$ the size of Qb was greatly increased (Table 4), but had fallen towards normal by 24 h, although it was still significantly elevated (Table 4). This was associated with a large rise in liver Zn content at both 6 and 24 h after $ZnSO_4$ injection (Table 3). Omission of values obtained from the rats injected with $ZnSO_4$ 6 h before ^{65}Zn injection (shown individually on Fig. 4) increases the correlation coefficient between Qb and liver Zn content to 0·93.

It therefore seems possible that following intraperitoneal injections of a large amount of Zn, Zn enters the plasma and is rapidly redistributed to the Qb pool within the liver. In the initial period after injection (i.e. 6 h after Zn injection) this influx is sufficient to saturate the processes by which Zn is transferred from both Qa and Qb to other pools (both within and outside the liver). By 24 h after Zn injection, however, this increased flux had decreased and the Qb:total liver Zn ratio had reverted towards normality (Fig. 4).

Some relationship between Qb and the MT-bound Zn in the liver is suggested by the

values shown in Fig. 5, although the true relationship may not be as strong as is suggested by this plot because of the uneven spread of the data. However, the findings do indicate that Zn will be present in Qb when MT is absent from the liver and that the relationship at high MT and Qb values is not linear. A lack of knowledge of the saturation of MT1 with Zn and of the contribution from the second isoform of MT (MT1 is known to represent approximately 40% of the total MT in rat liver; Sato *et al.* 1984) prevent any comparison of the sizes of the MT-bound Zn and Qb pools which could further support the likelihood of MT being, at least in part, the site of the Qb pool. Although it is commonly assumed that MT-bound Zn is difficult to remove, some evidence suggests that in the presence of certain binding agents Zn can be released from MT (Krezoski *et al.* 1988), but it seems unlikely that such a system would be present to permit the rapid recirculation of Zn from liver MT to plasma. It is therefore more likely that Qb and liver MT both generally respond in the same manner to changes in Zn status rather than constitute the same liver pool.

Of particular interest is the possibility that use of isotopic techniques will allow a differential diagnosis to be made between a low plasma Zn concentration due to Zn depletion or stresses such as endotoxin stress. The findings shown in Tables 3 and 4 suggest that analysis of the sizes of pools Qa and Qb will permit this. This is in direct contrast to the findings of Chesters & Will (1981*a*) who found no evidence for such a claim. We are unable to explain this difference, although it may be due to the different time-intervals after endotoxin injection at which animals were studied or a species difference related to the unusual plasma Zn-binding protein found in the pigs studied by Chesters & Will (1981*b*).

Comparisons of the time-course and pattern of plasma ^{65}Zn decay and liver accumulation shown in Fig. 2(*b*) for rats with that reported in man following intravenous ^{65}Zn injection (Wastney *et al.* 1986) suggest that over a short period of time similar kinetics may occur in both species, since the ^{65}Zn in human plasma reduces to less than 15% in 30 min after intravenous injection and liver ^{65}Zn increases to account for approximately 80% of the dose in that time. Plasma and liver 'pools', therefore, seem to predominate in the short-term in a similar manner to that reported here for rats.

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