A Multicompartment Model for Aluminium Biokinetics and Aluminium Speciation

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In pharmaco-, toxico- and biokinetics, metabolism processes can be described by compartment models. The transport between the compartments (boxes) is expressed by rate constants (inverse time constants). For the Aluminium metabolism, the central compartment is the blood. The organs are represented by peripheral compartments. Excretion is done via the kidneys into the urine. For oral administering, stomach and duodenum are needed as additional compartments. In case of intravenous (i.v.) administering, the dose is directly given to the central compartment, the blood. The analyses of the measured data show that 4 peripheral compartments are needed in order to describe ^{26}Al concentrations in blood and urine over such a long time period of 1/2 y. The results of calculations with this model for the volunteers of 24, 26 and 54 y are drawn in Figs. 1-3 on page 74. A "fast" peripheral compartment 1 with small time constants is needed in order to describe the fast decrease of the ^{26}Al content in the blood in case of i.v. administering and to reproduce consistently ^{26}Al contents in blood and urine after oral administering. This "fast" peripheral compartment 1 is tentatively considered to be the interstitium. The "slow" peripheral compartment 4 is tentatively considered to represent the skeleton. This interpretation is supported by ^{26}Al measurements in bones of rats. The rate and time constants of all measured volunteers and patients with renal failure and of a study performed by Day [1] are plotted in Fig. 2. It can be seen that in the case of the patients with renal failure the rate constants to and from the peripheral compartments 2 and 3 are different from those for the healthy volunteers. Aluminium in the blood can be bound to the large proteine molecules transferrine and albumine or to citrate which is soluble (see e.g. [1]). The measured creatinine clearances are by one to two orders of magnitude larger than the Al clearances. The clearance is given by the product of the rate constant for excretion times blood volume. If the creatinine clearance is used for the citrate bound aluminium in the blood, the ratio of Al bound to transferrine/albumine and citrate can be determined. This study is in progress.

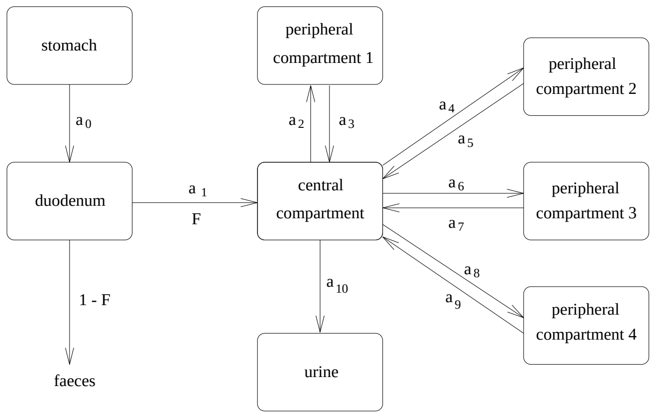

Fig. 1: Open multicompartment model used to describe measured ^{26}Al concentrations in blood and urine of humans

References

[1] J.P. Day et al. Nucl. Instr. and Meth. **B 92** (1994) 463

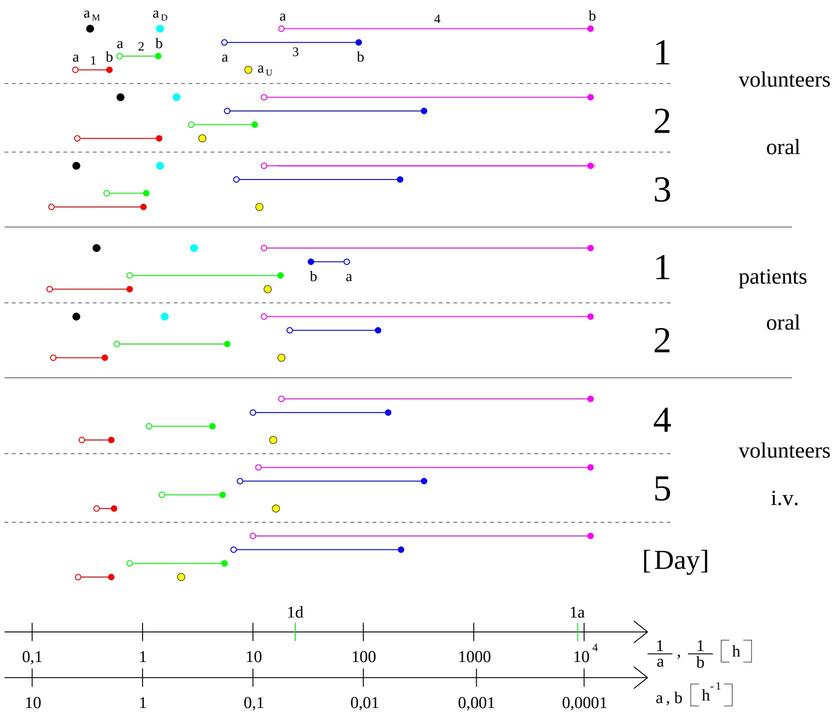

Fig. 2: Rate constants and time constants obtained in the analyses of ^{26}Al measurements in humans with the model of Fig. 1