# PRESENT STATE OF RADIO-STRONTIUM DECORPORATION RESEARCH WITH CRYPTAND (222) .

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Strontium-90 appears in high percentages in reactor burn-up as well as in nuclear fall-out . In animal experiments it has been demonstrated numerously that this bone-seeking element provokes skeletal malignancy . Therefore it is not only potentially hazardous to workers of nuclear power plants and related industries, but as an environmental contaminant to every body .

Prevention of intestinal uptake , removal during circulation , and removal of bone deposits are the three possibilities of therpeutic onset for decorporating remedies after Sr-90 incorporation .

Cryptating agent (222) is presented here as a potent means to remove radioactive strontium during the circulation of the latter . With (222) the strongest decorporation effects ever reached on the radionuclides Sr-85, Ba-133, and Ra-224 were obtained by us in rats (1,2, 3,4) . Our results were confirmed by Knajfl et al.(5) and Batsch et al.(6) . From recent experiments we extrapolate tentatively from rat to man , presenting here a probable treatment scheme, demonstrating the decorporation effect as function of the (222)-dose and the time interval between incorporation and treatment start .

Some toxicological aspects are also discussed.

## MATERIALS AND METHODS

The basic parameter in decorporation experiments is the effectiveness quotient (EQ), which permits to judge on the pure decorporation effect of an agent . In our experiments this quotient is defined as

$$EQ = 100 \times \frac{\text{TBR of radionuclide in (222)-treated rats}}{\text{TBR of radionuclide in untreated rats}}$$

(TBR = Total Body Retention) . One obtains this quotient with high significance, using two groups of 5-6 rats in general of about 300 g body weight, which were injected i.v. or i.p. with about 37 KBq Sr-85,(Ba-133 and Ra-224). One of these groups received additionally either together with, or after a time delay of the incorporation of the radionuclide, a constant or varying doses of cryptand (222) either i.v. or i.p. . The TBR was measured with a one-channal gamma-spectrometer immediately after the incorporation and consecutively after 24 hours .

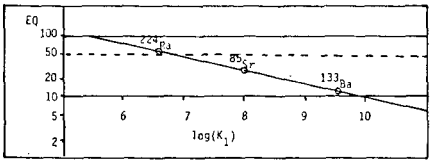
Two of the three questions , which had to be answered experimentally, are demanded by what we call Schubert - Catsch-Heller-Relationship (S-C-H) , valid within the re-

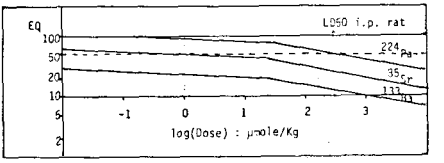
strictions for E and EQ given by Catsch (7) :

$$\frac{\log EQ_1}{\log EQ_2} = \frac{\log E_1}{\log E_2}; \quad \log E = \log K_{Sr(222)} - \log K_{K(222)} + \log A$$

A comprises the dose of (222). The S-C-H rules decorporation involving the EQ as dependent of two main physico - chemical parameters, 1) the stability constant $K_1$ of cryptand (222) towards the radionuclide (8), and 2) the concentration e.g. the dose of (222) (9), e.g. $EQ=f(K_1)$ and $EQ=f(Dose)$ . Third, the dependency of EQ from the start - ing point of treatment after incorporation of the nuclide e.g. EQ as a time-fuction $EQ=f(Time)$ .

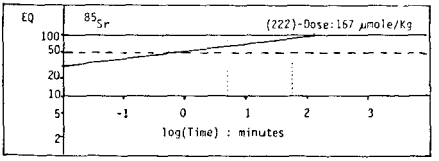
RESULTS

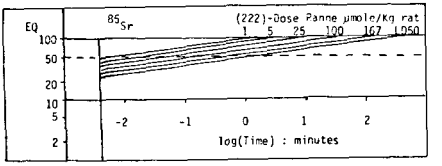



Graph 1 $EQ=f(K_1)$ Graph 2 $EQ=f(222\text{-Dose})$

The decorporation effect rises, e.g. the EQ drops with a rising stability constant $K_1$ strictly obeying the (S-C-H) (Graph 1) . It rises further with a rising dose, obeying also the S-C-H down to a dose of 25 µmole/Kg; further below it obeys again the S-C-H equations if one introduces instead of A, root of A (Graph 2)(9). The striking fact that EQ as time-function (Graph3)represents also a straight line in a log-log system is explained by the fact that decorporation with (222) follows the availability of strontium in the blood or extracellular space of rats(4). Graph 4, derived from the results of Graph 2 & 3, represents the EQ as function of the (222)-dose and a delayed treatment start (EQ=f(Dose & Time) ), which permited to extrapolate from rat to man(Table 1), using further : the Sr-retention in blood of rats (10) and men (11); and the following assumptions : 1) the extracellular space is as well reaction space as distribution space of (222) and Sr-85 ; 2) the Sr-retention in the extracellular space paralells the Sr-retention in the blood; 3) the blood volume of rats and men corresponds to 6% of the body weight; the extracellular space of rat and man corresponds to 16.6% of the body weight;4) the EQ-values obtained from experiments in rats do not essentially differ from those in men .




Graph 3 $EQ=f(Time)$ Graph 4 $EQ=f(Dose \& Time)$

## DISCUSSION

Though, a significant decorporation effect (EQ) in man (Table 1) may obviously be obtained , even after a few days of strontium incorporation , it seems hard to obtain an EQ lower than 50% with a single and relatively high (222)-dose even after a few minutes of treatment start . Further, in man the decorporation of strontium seems to slow much more down with the reduction of the (222)-dose than with an increasing delay of treatment . Consequently high doses of (222) are necessary in order to obtain a sufficient decorporation . High doses of (222) may approach acute toxicity . (LD-50 = 292 µmole/Kg rat i.p.(12)). If several protracted small (222)-doses given consecutively, may avoid toxicity of a single high dose, eventually producing the same or even a better decorporation effect must still be demonstrated. Table 1 permits to conclude finally : With a (222)-treatment one may obtain a decorporation effect of 50% after a very early start of therapy , accopainied by an additional significant percentage of naturally excreted strontium , but it seems inavoidable, that a certain rest of the nuclide will be trapped by bone . Decorporation of radiobarium will be more beneficial because of a higher $K_1$ (Graph 1 & 2) .

The therapeutic range of (222) deduced from Graph 2, varies from nuclide to nuclide along with its stability constant (8) . For Sr-90-89-85 it equals 100 , for Ba-140-133 even 146000 but for Ra-226-224 only 1.0 in the rat. If these ranges are large enough for man, even in the case of a steep mortality-dose function, cannot be answered at the moment .

If morphological and biochemical,e.g. enzymatical (5) disorders are limited to the lethal dose range of (222) or are reversible respectively not existent in the sub-lethal , therapeutic dose range, is not yet known .

Reversible side effects, such as impairment of protein- and DNA-synthesis (13) and urinary sodium/potassium retention (14) observed after single sub-lethal (222)-doses, may be accepted as those, because (222)- -treatment will always be an acute-treatment but never a chronical one .

Future studies will teach us, if (222) becomes an acceptable agent for the decorporation of radio-strontium barium and perhaps radium during their circulation in the blood and extracellular space of man .

| EXTRA-CELLUL Sr-85 % | MINUTES | | (222)-DOSE IN µ MOLE/Kg | | | | | |
|---|---|---|---|---|---|---|---|---|
| | BAT | MAN | .167 | 100 | 50 | 25 | 5 | 1 |
| 5 | 450 | - | - | - | - | - | - | - |
| 10 | 110 | - | - | - | - | - | - | - |
| 13.8 | 60 | 5000 | 88 | - | - | - | - | - |
| 15 | 48 | 3300 | 86 | 96 | - | - | | |
| 19.4 | 30 | 1050 | 82 | 91 | - | - | | |
| 20 | 27 | 1000 | 80 | 90 | 100 | - | | |
| 25 | 17 | 350 | 77 | 85 | 97 | - | | |
| 30 | 12 | 130 | 73 | 82 | 93 | - | | |
| 35 | 8,6 | 80 | 70 | 78 | 90 | 100 | | |
| 40 | 6,6 | 50 | 68 | 76 | 87 | 98 | | |
| 45 | 5,2 | 31 | 66 | 74 | 84 | 94 | | |
| 45,5 | 5 | 26 | 66 | 74 | 84 | 94 | | |
| 50 | 4,2 | 20 | 65 | 72 | 82 | 92 | | |
| 55 | 3,3 | 12 | 63 | 70 | 80 | 90 | | |
| 60 | 2,8 | 9 | 61 | 69 | 79 | 88 | | |
| 65 | 2,4 | 6 | 60 | 67 | 77 | 87 | | |
| 70 | 2,1 | 4,5 | 59 | 66 | 76 | 86 | | |

EQ-VALUES

TABLE 1

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