THE SIGNIFICANCE OF SERUM THYMIDINE CONCENTRATION AS BIOCHEMICAL INDICATOR OF RADIATION EXPOSURE

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In accidental cases of high level radiation exposure of persons, the actual exposure of the organism must be determined independent from physical dosimetric measurements. For suitable medical treatment, risk assessment and also for occupational legislative considerations, such determination is of primary concern. This requires a biochemical in vitro method (or combination of methods) which is specific, reproducible, significantly dosedependent and quickly and simply performed in the laboratory without undue burden to the patient from sample extraction. In addition, the method should allow for a dose assessment immediately as well as after a sufficiently long period of time following the exposure. Upon a comprehensive study of the available literature (1,2), a method was developed that may be suitable for dose assessment using biochemical indicators.

1. Determination of thymidine concentration in mice serum

Serum of whole-body irradiated mice inhibits the incorporation of 125-IUdR into the DNA of L929 cell cultures (3). The effect depends on dose and time and has its maximum at about 4 hours after acute exposure to 0.005 - 1 Gy. The corresponding humoral factor behaves identical to thymidine. Considering the possible use of higher levels of thymidine concentration as a biochemical indicator of radiation exposure, we reproduced Feinendegen's mice experiments (3) as an initial step (Fig.1).

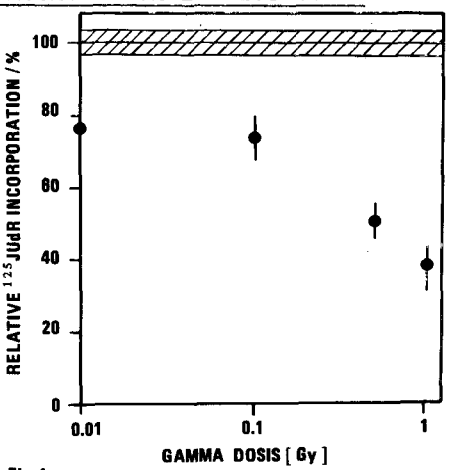

Fig. 1

2. Determination of thymidine concentration in human serum from healthy persons

The extrapolation of the results from mice to man is the objective of this study while considering the possible use of increased levels of thymidine concentration as a biological indicator of radiation exposure. In contrast to mice serum, human serum contains low levels of thymidine concentration - extremely low for a direct indication - and two factors that inhibit incorporation and differ in molecular weight: F_1 < MG 500, F_2 = MG 30.000 - 50.000 (3). All of the above renders an extrapolation to man more difficult.

2.1 Optimization of method, considering the low thymidine concentration in human serum and the interfering serum factors

2.2.1 Preliminary treatment of human serum

For separating the 125-IUdR incorporation inhibiting factor F_2, as well as further serum components of high molecular weight, the blood was ultra-filtrated (Diaflo-membrane, nominal separation limit 500 daltons). The yield was 70 - 80%.

2.2.2 Optimization of incubation time

It had to be clarified whether the assay system developed for mice serum requires the same incubation time for human serum. The incorporation kinetics of 125-IUdR in the DNA of L929 cells was examined after 15, 30, 45 and 60 min., respectively. Fig. 2 shows the results. The relative incorporation rate is fairly identical within these time spans. Therefore, we proceeded with an incubation time of 60 min, as was done in mice experiments.

2.2.3 Optimization of method in view of serum concentration

By increasing the serum concentration in the culture medium, the method can be adjusted to the lower thymidine concentration for improved sensitivity. For this purpose the assay system was tested for 10%, 20%, 40% and 60% serum, repectively. Results are shown in Fig.3.

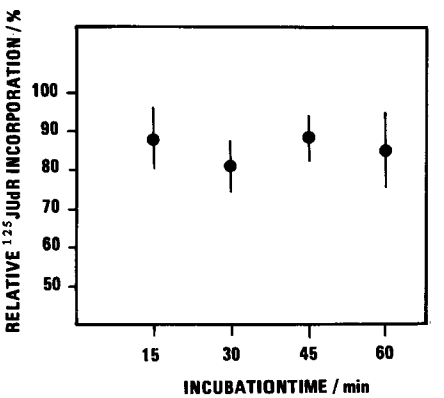

Fig. 2

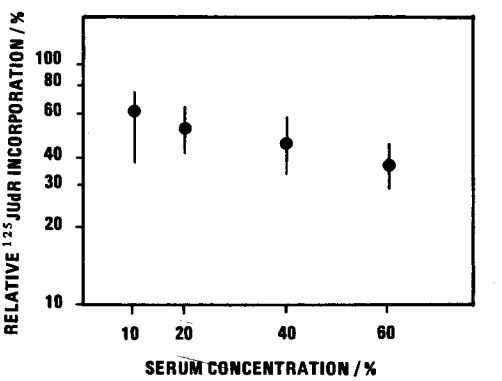

Fig. 3

3. Serum from patients receiving radiotherapy

First examinations on patients receiving radiotherapy (Tab. 1) yielded contradictory results. Therefore additional investigations are necessary.

Literature

1.) Stamm, A., Weitz, B., Bögl, W.
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3.) Feinendegen, L.E., Mühlensiepen, H., Porschen, W., Booz, J.
Acute non-stochastic effect of very low dose whole-body exposure, a thymidine equivalent serum factor
Int. J. Radiat. Biol. 41 (1982) 139-150

Table 1: Some results of examinations on radiotherapy-patients.

Case No. Sex Year of Birth	Diagnosis	Radiation Field	Field Size /cm/ Typ of Radiation	FHA/cm MD/Gy HD/Gy	Sampling (blood) h p.r.	125-IUdR-Incorporation⊕ before Irradiation %	125-IUdR Incorporation⊕ post Irradiation
10 male 1938	Kidney tumor T_2, N_x, M_x	1) Kidney tumor ventr., right 2) Kidney tumor dors. and lat., right	15x15 12 MeV X-rays	100 1) 2,92 2) 2,66 4,0	4	92	75 (Serum 10%, UF 25.000, Incubation Period 15 min)
						70	85 (Serum 20%, UF 25.000, Incubation Period 15 min)
12 male 1928	Metastases of Bronchial-Ca.	Skull lat, right	14x19 Co-60	80 2,92 2,0	5	100	60 (see above)
						50	54 (see above)
1 male 1913	Carcinoma of the Bladder pT_{2-3}, N_0, M_x	Pelvis	15x15 15 MeV X-rays	100 2,74 2,0	6	58	63 (Serum 10%, Heat Treatment, Incubation Period 60min)
						69	93 (Serum 10%, UF 50.000, Incubation Period 60 min)
						69	110 (Serum 10%, UF 25.000, Incubation Period 60 min)
2 female 1913	Rectum Ca.	Pelvis	14x12 X-rays	100 2,55 3,0	4	65	57 (see above)
						82	89 (see above)
						100	103 (see above)
5 female 1906	Cervix Ca. Stage IIb	Pelvis dorsal	15x16,5 15 MeV X-rays	100 2,68 2,0	2,25	83	66 (Serum 100%, UF 25.000)

6 female 1917	Ca. of Uterus, Bladder, Collum	Pelvis ventral dorsal	14,5x14,5 15 MeV X-rays	100 2,42 1,8	2,25	70 60	85(Serum 30%,UF 25.000) 85(Serum 50%,UF 25.000)
3 male 1908	Metasta- ses of Prostata	right Shoulder	14x8 Co-60	100 2,83 2,5	2	80 - 85	75(Serum 40%,UF 500,Incubation Period 60 min)
7 female 1925	Collum- Ca.	Pelvis dorsal	17x16 15 MeV X-rays	100 2,34 2,00	2,25	87	77(see above)
8 male 1913	Bladder- Ca.	Pelvis dorsal	15x15 15 MeV X-rays	100 2,74 2,00	2,25	95	87(see above)
11 female 1931	Met. Mamma-Ca.	Heart, Lungs, Stomach	16x7,5 Co-60	80 3,81 3,00	4	97	89(see above)

⊕The range of variation of the percentage values for incorporation is of 10 to 15 percent on the average

Abbreviations: FHA = distance between focus and tumor
MD = mean dose
HD = tumor dose
Ca. = carcinoma
UF = ultra-filtrate