Renal Function and Intra/Extravascular Distribution Spaces in the Rat after Supralethal Whole-Body X-Irradiation*

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Summary. Renal function and distribution of $^{51}$Cr-EDTA in intra/extravascular space has been studied in rats suffering from the gastro-intestinal syndrome after supralethal doses of X-irradiation. Urine excretion and glomerular filtration were found to decrease until 50 hr p.i. Urine excretion and, to a lesser degree, glomerular filtration rate increase then to a peak at 67 hrs before falling off to zero values before death. The extravascular space was found to be expanded in several organs from 60 hrs on (kidney, liver, stomach, intestine). Only in kidney where weight follows changes in extravascular space, a return to normal values is seen before death. An expansion in extravascular space due to a reduced re-extraction into intravascular space and diminished excretion constant can also be discerned beginning early after exposure on the basis of compartmental analysis of the blood activity-time curves. It is postulated that the changes observed reflect a state of shock developing slowly after irradiation and entering its irreversible stage 60 to 65 hrs after exposure.

Introduction

Animals exposed to supralethal doses of whole-body X-irradiation (3 kR) die 3 to 4 days later when the intestinal epithelium is denuded due to failure of the intestinal stem cells to divide (Bond et al., 1965). Several pathophysiological mechanisms participate in this death. Earlier, we had studied changes in intestinal absorption and electrolyte excretion (Gits and Gerber, 1973), in renin-aldosterone content (Gerber et al., 1975) and in blood flow (Watters and Gerber, 1975; Gerber and Watters, 1974). These results suggested that loss of electrolytes cannot be the exclusive mechanism responsible for death (Gits and Gerber, 1973). In the present investigation we have followed urinary excretion, glomerular filtration rate and relations between extra- and intravascular space as measured by distribution of Cr-EDTA and albumin, respectively.

Methods

Male rats of the Wistar strain weighing 230 to 280 g were exposed to 3 kR of whole-body X-irradiation under the conditions described earlier (Gerber et al., 1975). 200 μl of a mixture containing 78 μg of $^{51}$Cr-EDTA (obtained from the C.E.N. and having a specific activity of 0.59 to 1.2 mCi/mg) and 700 μg of $^{125}$I-albumin (from the C.E.N., specific activity 17 to 81 mCi/mg) were injected into the penis vein under nembutal anesthesia at different times after exposure.

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| Treatment                  | No. of animals | $k_{1.2}$ (min $\times 10^8$) Mean ± S.E. | $k_{2.1}$ (min $\times 10^8$) Mean ± S.E. | $k_{1.0}$ (min $\times 10^8$) Mean ± S.E. | Vascular space $V_1$ (ml/100 g B.W.) Mean ± S.E. | Ratio $V_2/V_1$ Extra/Intravasc. space Mean ± S.E. |
|---------------------------|----------------|------------------------------------------|------------------------------------------|------------------------------------------|-------------------------------------------------|-------------------------------------------------
| Control fed               | 5              | 2.10 ± 0.23                              | 4.68 ± 0.79                              | 3.74 ± 0.25                              | 7.12 ± 0.32                                     | 4.95 ± 0.63                                     |
| Control starved           | 8              | 2.11 ± 0.17                              | 3.95 ± 0.34                              | 6.62 ± 0.34                              | 7.62 ± 0.34                                     | 6.03 ± 0.78                                     |
| X-irrad. 3 kR 0 to 45 hrs | 8              | 2.16 ± 0.36                              | 2.25 ± 0.70                              | 7.71 ± 0.34                              | 7.71 ± 0.34                                     | 10.97 ± 1.77*                                   |
| X-irrad. 3 kR 45 to 60 hrs| 5              | 2.02 ± 0.37                              | 2.88 ± 0.20                              | 4.62 ± 0.29                              | 6.73 ± 0.48                                     | 8.67 ± 1.52*                                   |
| X-irrad. 3 kR 60 to 75 hrs| 4              | 1.77 ± 0.37                              | 1.94 ± 0.08                              | 0.81 ± 0.27                              | 8.64 ± 0.45                                     | 8.42 ± 1.28*                                   |

--- Values significantly different from fasted control; $p < 0.05$ and $< 0.01$, respectively
|| Values significantly different from preceding value; $p < 0.05$ and $< 0.01$, respectively
* Differences significant compared to fed controls at $p < 0.05$

The calculations are based on the model

$$
\begin{align*}
V_1 & \xrightarrow[k_{1.2}]{} V_2 \\
\text{intravasc.} & \leftarrow k_{2.1} \text{extravasc.} \\
\text{urine} & \downarrow k_{1.0}
\end{align*}
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