B19

RADIOLOGICAL PROTECTION AND THE BLOOD COUNT

by

[redacted].

Ionizing radiations produce blood changes in animals and man. At sufficiently high exposure rates, the blood changes are progressive and if exposure is continued a critical stage is reached, beyond which progression continues despite cessation of exposure. The process is then irreversible, progressive and leads to a fatal issue. Nor is it amenable to therapy. It is important in radiological protection of the individual to ensure that a progressive change is detected early so that a critical stage will not be reached. Whilst a similar picture is seen with acute exposure, only chronic occupational radiation exposure need be considered with regard to radiological protection and the blood count. Following an accidental acute high exposure, further blood counts of the individual may yield valuable prognostic aid - possibly serve as a therapeutic guide - but do not constitute a protective measure except insofar as they shed light for future guidance on the association between radiation dosage and blood count response. However great the engineering skill exercised; however complete the precautionary measures appear to be; human fallibility is such that complete intrinsic safety is difficult or impossible of achievement.

If the rate of occurrence and degree of change in blood count components in man could be linked with radiation exposure levels with some certainty; then it would be feasible to lay down some arbitrarily determined safety factor to take care of uncertainties in measurement and possible relatively small superadded accidental exposure. The standard of radiological protection required is that in which "a person will not receive appreciable bodily injury at any time during his life time". This requires study of the individual, that an appreciation of the presence or absence of effect should be made, and a judgment formed of whether the effect can be considered of no pathological significance at the time nor likely to develop into bodily injury at any time in the future during his life. If, with continuous exposure, at the maximum permissible rate it is impossible to detect any effect, then no such appreciation is called for. If the safety factor is such that no effect is seen with small additional accidental exposures, again no evaluation is required.

An assessment of the technical error in the blood count and coefficient of variation of white cells due to physiological causes has been made. If the expected variation due to radiation dosage is less than this, no information for protective measures can be gleaned from a white cell count. On this account, it is considered that the variation in the white cell count from radiation dosage is so small in the case of workers who receive a surface dose of less than 0.1 r. per week that the significance of a blood count is very doubtful at this exposure rate. There is now considerable human experience in support of this. Possibly this may be true for a higher dosage rate, but there is less human data linked with higher exposure rates, since in the large Atomic Energy plants, the average exposure has been less. It is opportune to see how much light can be thrown on the problem of the value of blood counts by examining the results of animal experimentation, despite the undoubted limitations of the method.

The most comprehensive animal experiments are those of Lorenz. He says "It is known that the blood picture of man responds to acute as well as long continued irradiation in a manner similar to that of the guinea pig although there are no data as to dose rate and total doses except in acute exposures", and he believes "The haemopoietic system of man may have a sensitivity to chronic irradiation similar to that of the guinea pig". The species variations are very great. Since the considered opinion of

Lorenz is that his guinea pig experiments throw most light on the human problem, it is only the guinea pig results that will be reviewed.

Five groups of guinea pigs were continuously irradiated throughout their life span, at exposure rates of 0.11 r., 1.1 r., 2.2r., 4.4 r., and 8.8 r./8 hr. day and the blood picture continuously observed.

Effect on leucocytes

A decrease in the total leucocyte count occurred a few weeks after the start of the experiment in each of the five irradiated groups. The degree of total leucocyte depression varied with the exposure level and was significant. In the two groups at lowest exposure rate, the reduction was caused by a decrease in lymphocytes: In the other three groups, at higher exposure rates, the reduction was partly from this cause but principally by a more significant reduction in heterophils.

In the two lowest exposure groups (0.11 r. and 1.1 r./day) the fall was not progressive. The initial lymphocyte depression persisted throughout the experiment; the pre-exposure level was not regained and once established the slightly lower lymphocyte count was sustained and thereafter remained constant. None of the animals died as a result of blood changes.

In the three groups, at higher exposure rate (2.2 r., 4.4 r., and 8.8 r./day) a steady state was not established, but the reduction progressively increased, until in each group fatalities occurred. Many of the animals exposed to 2.2 r./day, almost all exposed to 4.4 r./day, and all those exposed to 8.8 r./day developed a terminal pancytopenia.

Anaemia

In the two groups at lowest exposure rate (0.11 r. and 1.1 r./day) no anaemia of significance was produced, and there was no terminal anaemia.

In the 2.2 r./day group the males developed moderate anaemia; at approximately 79 weeks after the start of exposure. In five out of nine animals in this group, this progressed to a terminal anaemia. The females had a questionable reduction in haemoglobin: but five out of nine died of a terminal pancytopenia.

In the 4.4 r./day group, a moderate anaemia in both females and males developed: in this case, within a period of 49 weeks of exposure. In both sexes, the anaemia increased in severity; eight out of nine males and seven out of nine females succumbed with a terminal anaemia.

In the 8.8 r./day group, both females and males developed anaemia rapidly: within 19 weeks. Again this was progressive through 60 and 69 weeks, respectively, and all 18 animals died with a terminal anaemia.

Terminal stage

The terminal stage was short with an exceedingly rapid fall in red cell count; often a fall of a million cells within a few days during the final critical period. After the red cell count had decreased to approximately 2.5 to 2.8 million, the animals lived for one to two weeks.

Recovery processes

In order to study recovery processes, an experiment was planned to expose animals at the 8.8 r./day rate and to cease exposure when the red cell count fell to 2.8 million. This level was in a critical region. Despite the termination of exposure, 30 animals died within 9 weeks, 10

made a partial recovery but died within 24 weeks, and 10 made a permanent but slow recovery. The level was critical in that at this stage the fall in red cell count was so rapid that in 15 of the animals the count had already dropped below 2.4 millions before detection and hence termination of exposure. Thus for guinea pigs, a red cell count below the three million level, carries a poor prognosis and a high probability of a fatal outcome at this high exposure rate even when exposure is terminated.

Lorenz notes that except for the erythrocyte count of the non-recovery group, the other data on exposure time accumulated dose and mean blood cell counts show no correlation with the data of the partial recovery and permanent recovery groups. He states "This indicates that only the degree of the anaemia and not the degree of pancytopenia determines whether or not an animal is likely to recover."

Bone Marrow

The bone marrow of the guinea pigs developing terminal anaemia or pancytopenia showed moderate to severe atrophy: but the degree of this atrophy was not such, according to Lorenz, as to explain the fact of the sharp terminal decrease in red cells below the three million level. He advanced a theory to account for this dramatic phenomenon that an unknown agent is produced in sufficient amount in the blood stream to produce increased hemolysis.

Lorenz compared the effects of chronic exposures to guinea pigs at 8.8 r./8 hr. day with those for acute single exposures of 220, 260, 310, 360 and 420 r., and notes that the rapid decrease of red-cell counts is very similar. In contrast to the very gradual recovery after chronic exposure, there is rapid recovery after acute exposure.

Lorenz stresses the relatively much greater importance of the daily dosage rate than the total accumulated dose in the production of the terminal condition. In the 1.1 r./day group, no terminal anaemia was observed although total accumulated doses reached 2000 r. At this exposure rate, he considers that repair processes can balance the injury; but makes the proviso that this might not be the case in species with a similar sensitivity of the hemopoietic system but with a considerably longer life span.

It is of interest to compare these experimental results with those of human cases. Mole has cited three cases of fatal aplastic anaemia in radiation workers. These show a similar picture - in one case the R.B.C. count fell to 2.7 millions and death followed in $1\frac{1}{2}$ months; in another 3.8 millions with death 1 month later; in the third 2.2 millions $2\frac{1}{2}$ months before death. The critical stage had been reached when the condition had become progressive and irreversible. It would be of great value if regular routine blood counts of these cases from the beginning of exposure were available. From the animal data, a progressive fall in other blood count components would be expected before the onset of anaemia, and a fall in red cells and haemoglobin would be progressive also. The absolute values of any component are of less importance than the trend. Thus Hasterlik has noted in cases after acute accidental exposure that "it is only through repeated counts in comparison with previous base line studies that the trend toward diminution of the white count becomes apparent and indicative of the overexposure" and "a white cell count on any one day following irradiation was not strikingly significant."

Blood counts are not an alternative to physical monitoring procedures in radiation protection: there are different parameters in each case. In the one case an assessment of the action of an agent on an individual is made: in the other case, an assessment of the causative agent. The assessment of the causative agent does not necessarily tell the whole story.

To quote Lorenz "It has been pointed out that the experimental data suggest that an intensity factor in chronic irradiation exists. The intensity factor might cause more pronounced biological reaction when the same daily dose is given in a very short time (e.g. minutes) than when it is given over 8 hr.

The bulk of experience is with X and gamma radiation. There is little clinical experience with other ionizing radiation, or with the effect from combined external irradiation and that from internal emitters.

If blood changes occur in a proportion of individuals exposed at any particular exposure level, the individuals should be kept under review. If no change occurs at the maximum permissible level, only sufficient observations to establish the base line for the individual would be required, but further counts would yield no additional information.

- - - - - - - - -

Medical Division,
A.E.R.E. Harwell,
Didcot, Berks.

16th November, 1954.

H20050X.