Summary

This study is concerned with the role of biogenous amines in radiation processes as active compounds released, and as protectors applied against the effects of ionizing radiation. In both instances the compound action of multiple bio-amines received special attention. Stored in granules and vesicles bio-amines are liable to simultaneous release by the random action of irradiation. A number of consequences of this liberation have been considered.

In the irradiated hypophysectomized frog it may be the cause of the observed pigment expansion. This reaction has been analysed in isolated pieces of frog skin by building up a mixture of a few μg's of adrenaline, noradrenaline, serotonin and melatonin. In the presence of the energy providing components oxygen, glucose and ATP, a comparable expansion can be obtained. In the frog the X-ray induced release of serotonin has been demonstrated by the enhanced urinary excretion of this amine (chapter 4).

The isolated uterus of the rat reacts to X-irradiation by augmented release of serotonin, catecholamines and histamine. Simultaneously, evidence has been presented for participation of these bio-amines in spontaneous contractile activity of the suspended preparation. The mutual relations of the different amines rather than the absolute quantities may be of importance (chapter 5).

The toxicity of individual biogenous amines in mice is considerably potentiated by combined injections. The most active combination is formed by 10 mg of histamine, 1 mg of serotonin and 10 μg of adrenaline. Addition of acetylcholine causes a diminution of the toxic action; in this manner a combination is obtained which has strong protective properties against a dose of 1250 r of total body X-irradiation. The toxicity of this combination is lowered again by subsequent irradiation (chapter 6).

With regard to the mechanism of bio-amine protection in mice the role of hypoxia has been studied. Stagnant hypoxia of certain organs caused by bio-amine action can not be excluded. On the other hand the radioprotective effect of general hypoxia is thought to be mediated by the release of bio-amines. For, as shown, hypoxia still exerts a certain protective action if present up till 4 hours before exposure to irradiation. Since hypoxic conditions as well as bio-amine application after irradiation also have a favourable influence on radiative damage it ap-

pears likeley to ascribe the protective effect as being exerted on recovery processes (chapter 7).

The protective properties of bio-amines, increased by combined activity, could be of significance for the natural resistance of animals. Great variations in radioresistance exist, not only between different species but even between individuals originating from a same litter of intensively inbred animals. The presence of bio-amines might contribute to these sensitivity differences, particularly since combined activity of biogenous amines appears to be a natural situation, especially in reactions with defensive characters (chapter 1 and 4).

Regarding this, in our opinion, the release of biogenous amines must not be considered as specific. It is rather a general reaction to a variety of stimulants. Possibly, it is related to the general adaptation syndrome and represents a complex of peripheral reactions whereas the adaptation syndrome is of central origin.

The mechanism of bio-amine interaction, by which a combined effect is much more distinct, is obscure. In the described experiments the action of a combination of biogenous amines is quite distinct from that of the separate components. We, therefore, incline to the opinion of mutual interactions of the free bio-amines causing the organism to maintain a homeostatic state. To this balanced situation some of the amines might contribute in a positive and others, in a negative sense. Small quantitative alterations in one of the components will easily be corrected by the total system perhaps by means of minute shifts in the mutual relations. Sudden major changes in one of the participants will then bring the system out of balance and may trigger a specific reaction.

Although several indications are present for such interaction mechanisms, the manner of interaction is, as mentioned, unclear. It seems not unlikely that the study of ionizing radiation, by its pronounced influence on the amounts of free biogenous amines available, can contribute to the solution of this problem.