CXV. SOME METABOLIC DIFFERENCES, FOLLOWING X-RADIATION, BETWEEN NORMAL RATS AND RATS IMMUNE TO JENSEN'S RAT SARCOMA.

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WHEN rats are inoculated with Jensen's rat sarcoma, it often occurs that some of them fail to grow a tumour. If subsequently tested by re-inoculation from time to time, they are found to be always resistant and are spoken of as "immune" animals. Certain biological differences have been noted between these "immune" animals and normal animals, but up to the present no definite chemical difference has been demonstrated. It is not proposed in this preliminary communication to deal with the literature of the subject.

Since the response to X-radiation of normal animals and animals inoculated with sarcoma had not been worked out, it was thought that an investigation on these lines might yield interesting results.

Numerous analyses on the blood from these two types of animals, X-radiated and not X-radiated, were made for the following constituents: non-protein nitrogen, urea, creatinine, uric acid, amino-acid nitrogen and sugar. All the determinations were made by the colorimetric methods introduced by Folin.

In the first experiments the whole of the animal was exposed to the X-radiation. A galvanometric method of measuring the dose was employed, but it will suffice now to say that about an erythema dose was given in each case, the spark gap being 18 cm. and the screen being $\frac{1}{10}$ mm. aluminium and 3 mm. wood. The animals were killed at intervals of from 1 hour to 9 days after exposure, and the blood collected from the inferior vena cava into pipettes containing weighed quantities of powdered sodium citrate sufficient to produce 3 % citrate in the blood.

Tables I and II give the results obtained using normal animals. All the results are expressed as mg. per 100 cc. of blood.

An examination of these results shows that X-rays produce no effect upon the non-protein nitrogen and urea content of the blood of normal animals.

Table I. *Normal animals not X-rayed.*

	Non-protein N	Urea		Non-protein N	Urea
1.	54.0	—	7.	61.2	41.5
2.	55.9	—	8.	44.4	32.4
3.	57.4	—	9.	31.0	23.0
4.	61.5	—	10.	40.5	30.0
5.	60.0	33.5	11.	40.0	23.1
6.	58.9	34.2	12.	37.5	24.7

 Table II. *Normal animals X-rayed.*

	Time X-rayed	Mean galvo. reading in cm.	Killed after exposure	Non-protein N	Urea
1.	40 mins.	8.49	7 hours	57.0	37.5
2.	40 "	8.49	7 "	47.6	35.1
3.	40 "	10.72	31 "	43.8	24.1
4.	40 "	10.72	31 "	49.2	35.5
5.	30 "	5.46	9 days	61.8	31.3

NOTE. With the galvanometer reading 4.2 cm. an exposure of 1.2 hours gives a dose of one rad, which is the exposure required to kill Jensen's rat sarcoma *in vitro*.

Tables III and IV show the effect of radiation on the blood-constituents of the "immune" type of animal, *i.e.* animals previously inoculated with Jensen's rat sarcoma, in which no tumour resulted. The figures for uric acid, creatinine, sugar and amino-acid nitrogen content are not given, since no change was observed on irradiating normal and "immune" rats.

It will be observed that there is a reduction in the blood-urea content of these "immune" animals and that in many cases the non-protein nitrogen content is also slightly reduced.

 Table III. *"Immune" animals not X-rayed.*

	Interval between in- oculation and killing	Non-protein N	Urea
1.	12 days	60.7	33.8
2.	18 "	63.1	47.4
3.	—	57.2	41.2
4.	—	44.2	36.7
5.	41 days	45.0	—
6.	41 "	60.0	—

 Table IV. *"Immune" animals X-rayed.*

	Interval between inoculation and killing	Time X-rayed	Galvo. reading in cm.	Killed after experiment	Non- protein N	Urea
1.	35 days	35 mins.	9.28	1 hour	40.0	14.0
2.	35 "	35 "	9.28	1 "	43.0	12.9
3.	29 "	40 "	10.4	24 hours	48.3	8.5
4.	29 "	40 "	10.4	24 "	45.1	9.0
5.	32 "	30 "	8.87	3 days	57.2	27.7
6.	32 "	30 "	8.87	3 "	52.8	14.4
7.	32 "	30 "	5.1	3 "	44.9	23.6
8.	32 "	30 "	5.1	3 "	—	15.1
9.	44 "	30 "	6.8	3 "	32.2	9.6
10.	44 "	30 "	6.8	3 "	33.7	11.0
11.	44 "	30 "	6.8	3 "	35.7	10.4
12.	44 "	30 "	5.8	3 "	39.7	12.2
13.	44 "	30 "	5.8	3 "	42.8	12.5
14.	44 "	30 "	5.8	3 "	34.1	14.5
15.	57 "	30 "	5.46	9 "	57.2	32.1

On comparing Tables I and III it is seen that "immune" animals do not differ from normal animals in the non-protein nitrogen or urea blood content prior to X-radiation. A difference is, however, to be observed when these two kinds of animals are X-rayed (cp. Tables II and IV). In the "immune" animals there is a marked reduction in the blood-urea content and in many cases a slight reduction in the non-protein nitrogen content, whereas normal animals do not exhibit these changes after similar X-radiation.

These results suggested an inquiry into the behaviour of tumour-bearing animals under similar treatment.

Table V summarises these results.

Table V.

	Urea mg. %
1. Animal with growing tumour not X-rayed	32.7
2. Animal with growing tumour not X-rayed	45.4
3. Animal with growing tumour X-rayed	44.4
4. Animal with growing tumour X-rayed	43.5
5. Animal with disappearing tumour not X-rayed	31.9
6. Animal with disappearing tumour X-rayed	29.1
7. Animal with disappearing tumour X-rayed	64.4

It would appear therefore that tumour-bearing animals behave in the same manner as normal animals.

In all these experiments the whole animal was exposed to the rays. It was thought that the screening of certain organs might lead to information as to the cause of the fall in blood-urea content in "immune" animals, but the experiments showed that there is no particular organ which is especially acted on by the radiation so as to result in a reduced blood-urea content.

SUMMARY.

No difference in metabolism has hitherto been described between normal animals and animals immune to Jensen's rat sarcoma.

The observations described show that there must be some peculiarity in the metabolism of the "immune" animals, since an exposure to X-radiation causes an immediate fall in the blood-urea content, from a normal value of about 35 mg. per 100 cc., to about 14 mg. per 100 cc. This reaction to X-radiation appears to be a permanent property of "immune" animals.

At the present stage, it would be unwise to offer any explanation of these results, but it is hoped to extend the observations to animals rendered immune by artificial means.