Heating Characteristics of Laboratory Animals Exposed to Ten-Centimeter Microwaves. Research Report. Proj. NM 001 056.13.02, Mar 2, 1957. Ely/Goldman Hearon

APPENDIX A

Some Mathematical Considerations

Consider a body of heat capacity C (cal/degree) which is being heated by an internal source S (cal/sec.) and is cooling according to the law

$$\text{cal lost/sec.} = \lambda\, a(T - T_0)$$

where λ (cal/sec. cm.^{2} degree) is the loss per unit time per unit area for a unit temperature differential and a is the surface area of the body. Then

$$(\text{cal gained in dt}) = C\,dT = S\,dt - \lambda\, a(T - T_0)\,dt$$

where dT is the temperature change in dt. Or, T(t) is governed by,

$$\frac{dT}{dt} = \frac{S}{C} - k(T - T_0) \qquad [1]$$

where $k(\text{sec.}^{-1}) = \lambda a/C$. In the above it is assumed that S and T are *spatially uniform* and that T_0 is the external or environmental temperature. If spatial uniformity does not obtain, it can be shown that [1] still applies if T and S are replaced by their spatial or volume means and k has a different physical connotation (i.e., $k \neq \lambda a/C$) but still represents a formal "cooling constant" in terms of the (spatial) average or mean temperature.[1,2]

In the situation at hand, T and S are not uniform but we wish to show that T(t), measured at a fixed point in the body (e.g. point of maximum temperature) does in fact obey an equation of type [1] wherein moreover, a specific assumption is made relating S/C to a known external energy field, and T_0 is taken to be the "normal initial temperature" (i.e., the temperature in the absence of the external field).

In particular assume

$$S/C = K'I \qquad [2]$$

where I is the field intensity and K' is of the nature of a "pick up" or "dissipation" coefficient, and independent of T and of the explicit time t. Then [1] is

$$\frac{dT}{dt} = K'I - k(T - T_0) \qquad [3]$$

Denote the steady-state temperature by T_s, and define the temperature rise at any t by

$$\Delta T(t) = T(t) - T_0 \qquad [4]$$

and in the steady-state

$$\Delta T_s = T_s - T_0 \qquad [5]$$

Then [3] can be written

$$\frac{d\,\Delta T}{dt} = k(KI - \Delta T) \qquad [6]$$

where $K = K'/k$.

The general integral of [6] is

$$\Delta T(t) = KI(1 - e^{-kt}) + \Delta T(0)e^{-kt} \qquad [7]$$

It is clear from [7], and otherwise obvious from [6] with $d\Delta T/dt = 0$, that

$$\Delta T_s = KI \qquad [8]$$

Thus [7] may be written as

$$\Delta T(t) = \Delta T_s(1 - e^{-kt}) + \Delta T(0)e^{-kt} \qquad [9]$$

The assumptions embodied in [2] can be checked through [8] which predicts the steady-state rise in temperature to be proportional to I. In particular the slope of the line [8] estimates K. The result [8] depends, of course, upon the assumed form, $k(T - T_0)$, for the cooling law but this can be validated separately, and independently of assumption [2], as follows: If the body is heated, heating is stopped (i.e., I made zero), and time is reckoned from the instant of cessation of heating, then from that instant on, $\Delta T(t)$ obeys (from [7] with I = 0)

$$\Delta T(t) = \Delta T(0)e^{-kt} \qquad [10]$$

and under these conditions a semi-log plot of the temperature rise should be linear. The slope of this line estimates* -k. It is seen from [10] that beginning with any arbitrary initial temperature rise, $\Delta T(0)$, the time required for the temperature rise to fall to 1/e of this initial value is $\tau = 1/k$. Or, beginning with an initial rise, $\Delta T(0)$, of zero (i.e., $T(0) = T_0$, see [4]) it follows from [9] that at time $\tau = 1/k$ the temperature rise achieves the fraction $1 - 1/e \cong .67$ of its final value.** It is convenient to deal with this characteristic time τ. We consider now *only* situations in which $\Delta T(0) = 0$. Then [9] is

$$\frac{\Delta T(t)}{\Delta T_s} = 1 - e^{-t/\tau} = \frac{\Delta T(t)}{KI} \qquad [11]$$

Consider a system being heated under field intensity I, its temperature rise being given by [11]. Then for any t, and corresponding $\Delta T(t)$, there exists an intensity $I' \leq I$ which will produce a steady-state temperature rise equal to the observed temperature rise, $\Delta T(t)$, at that time. It is clear from [7] that the inequality $I' \leq I$ is not valid unless $\Delta T(0) \leq KI$. But the agreement to consider $\Delta T(0) = 0$ entitles us to speak of the *reduced intensity*, I', such that if the system is heated till time t under intensity I and at that time the intensity is instantaneously reduced to I', the temperature rise, $\Delta T(t)$, which obtained at that time will be maintained constantly and indefinitely. Plainly I' is a function of t and I but we do not display that fact in the notation. According to the argument leading to [8], I' is given by

$$KI' = \Delta T(t) \qquad [12]$$

and [12] into [11] yields

$$\frac{I'}{I} = 1 - e^{-t/\tau} \qquad [13]$$

or

$$\ln\left(1 - \frac{I'}{I}\right) = -t/\tau \qquad [14]$$

---

* Also, k can be estimated in a slightly different fashion, see equation [14] and cf. text.

** Stated otherwise, at time $\tau = 1/k$ the fractional displacement of the temperature rise from its steady-state value is 1/e, i.e.,

$$\frac{\Delta T_s - \Delta T(t)}{\Delta T_s} = 1/e$$

According to [11], if we prescribe a temperature rise, say $\Delta T(t) = A \leq KI$, then given A there is for each time t, an intensity I such that the temperature rise is precisely A at time t. These times and intensities are related by

$$A = KI\left(1 - e^{-t/\tau}\right) \qquad [15]$$

For small t, i.e., $t \ll \tau$,

$$A = \frac{K}{\tau} I\, t = K' I \cdot t \qquad [16]$$

Thus over the range of sufficiently small t (and large I) the hyperbolic relation [16] holds. The slope of the initial linear portion of the log I vs. log t plot is -1, the ordinate intercept log (A/K').

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APPENDIX B

Early Lesions In Dog Testes Due To Microwaves

INTRODUCTION

This study was limited to early lesions resulting from an elevation in testicular temperature by 10-cm. microwaves from a radar source.* Microscopic studies were conducted on 14 dogs following exposure confined to the gonadal region. Because of the mongrel population, numbers involved, and the period selected for observation, testicle weights were of no value in this study. Normal dog testicular temperatures ranged from 30.30° to 36.25° C.* Testicular temperatures in the treated animals varied from 36° to 44° C. The elevated temperature was maintained in all but one case for 60 minutes.

MATERIALS AND METHODS

Most of the dogs' testicles were removed surgically on the fourth day after exposure, the remainder on the third or fifth day after exposure. Immediately after orchiectomy the testicles were sectioned and placed in Bouin's solution. Following fixation, the sections were trimmed, processed and embedded in paraffin by the usual techniques, and cut at 6 microns. Hematoxylin and eosin, and Periodic Acid Schiff stains were employed.

Two known control sections and one section from a testicle in which a temperature of 44° C. was maintained for 60 minutes were first studied microscopically. Then the testicles from 13 dogs exposed to microwaves confined to the gonadal region were evaluated as unknowns. An attempt was made arbitrarily to assess the degree of injury in terms of 1, 2, and 3 plus. Those sections found to be indistinguishable from control sections were given a value of zero.

RESULTS

Control sections of dogs' testes are illustrated in figures 1 and 2. Minimal changes in the semeniferous tubules following exposure to microwaves were classified as 1 plus (fig. 3). In these, the tubular lining had a fenestrated appearance and the cells appeared to be grouped in columns, separated by clear areas. This appearance may have resulted from loss of adhesion between the cells, and was limited to those tubules immediately adjacent to the capsule. As can be seen in figure 4, the more centrally placed tubules in the same testis were indistinguishable from control sections. With one exception this change was not seen, *at the post-exposure time interval studied,* in testicles with a temperature below 39° C. (table 1).

The upper limit of exposure accompanied by a 1 plus reaction was approximately 41° C. for 60 minutes. One animal exhibited the 1 plus reaction after being exposed to 42° C. but the duration of exposure was only 5.5 minutes. The length of time as well as the extent to which the temperature is raised is known to affect the degree of injury produced in the testis (1).

The reaction arbitrarily classed as 2 plus is illustrated in figure 5. It is characterized by more marked dissociation of the tubular lining cells associated with focal areas of pyknosis and the appearance of giant cells in the lumina. As with the 1 plus reaction, the most severely involved areas were immediately adjacent to the capsule, and the more central areas, as illustrated in figure 6, either appeared unaltered or exhibited the 1 plus type reaction. No clear-cut relationship between this lesion and temperature and duration was established in the limited number of cases studied. In fact, one animal exhibited the 2 plus reaction with a testicular temperature of 37° C. following exposure which would be expected to yield either no change, or at most the 1 plus reaction.

*See main body of report.

TABLE 1

Animal No.	Degree of Histologic Injury (0-3 plus)	Temperature (°C.)	Duration (minutes)
128	0		control
134	0		control
118	0	36.0	60
124	0	37.0	60
110	0	38.0	60
114	0	38.0	60
116	0	38.0	60
126	1 plus	39.0	60
132	1 plus	40.0	60
104	1 plus	41.0	60
136	2 plus	37.0	60
130	2 plus	43.0	60
112	3 plus	41.0	60
119	3 plus	42.0	60
122	3 plus	44.0	60
101	1 plus	42.0	5.5

The lesion classed as 3 plus is illustrated in figure 7. It is characterized by necrosis, desquamation of cells, hemorrhage and lesser degrees of pyknosis and cellular degeneration. The 3 plus reaction occurred in testes exposed to 41°-44° C. for 60 minutes.

The differential sensitivity of even adjacent tubules can be seen in figure 8. Next to tubules lined chiefly by Sertoli cells, are others in which the lining appears to have been little, if at all, affected. An occasional degenerated tubule in control sections was not uncommon. On the other hand, the reaction to heat involved numerous tubules, either more or less confined to those adjacent to the capsule at lower temperatures, or scattered throughout the gland following higher temperatures.

Sertoli cells and mature sperm were least affected morphologically. Cells in all stages of spermatogenesis showed signs of degeneration and/or death in the most severely affected tubules (fig. 9). The interstitial cells of Leydig were not affected.

SUMMARY

Changes Associated with Testicular Hyperthermia

Testicular reactions to heat injury from a radar source appear to be basically the same as those due to hyperthermia associated with other conditions such as immersion in hot water (1), pyretotherapy (2) and cryptorchidism (3), to mention only a few. Similar changes have been produced by nutritional defects, including inanition and vitamin A or vitamin E deficiencies (4,5,6), by toxic substances, high oxygen tension, direct trauma, vascular changes following interruption of the blood or nerve supply, various acute and chronic diseases, and allergic reactions, periodic changes in seasonal breeding mammals (for instance the deer), alcoholism and mental depression (8), following the administration of certain hormones (9,10), and after exposure to ionizing radiation (12) both electromagnetic and particulate.

Problem of Recovery

While it seems probable that the semeniferous tubule illustrated in figure 9 might never recover, many tubules in the same section showed only minimal damage and this was taken from the animal exposed to 44° C. for 60 minutes, the most severe condition imposed. After such exposure a considerable decrease in spermatogenesis for varying periods of time would be expected. The loss of some tubules with a concomitant decrease in the size and weight of the testicle, and lower than average sperm counts might possibly persist. However, it is well known (11,12) that from 4 to 8 months or more are required to evaluate the degree of recovery that is possible after exposure of the rat's testicle to certain doses of ionizing radiation. Weight changes, numerous sections for histopathologic study, spermatozoa counts and fertility studies may all be required to assess the extent of residual injury. In addition, considerable biological variability even among litter mates exposed to the same conditions is a well recognized phenomenon. Such studies were not undertaken following exposure to microwaves, due to limitations in personnel and facilities. However, in view of the patchy distribution and paucity of seriously damaged tubules 5 days after exposure to the highest temperature-duration sequence tried, it appears unlikely that permanent sterilization would have resulted in any of the animals studied. In man it has been reported that elevation of the body temperature to points 0.5 C.° to 4 C.° above normal for periods of 2 to 3 hours resulted in a marked fall in spermatozoa production. The maximum body temperature attained (in a fever cabinet by electro-magnetic induction from a short wave apparatus, and the maintenance of humidity levels between 95 and 100 percent) was in most cases between 40.5° and 41° C. A fall in the number of spermatozoa did not become apparent for nearly 3 weeks with counts indicating impaired fertility (less than one-fourth the normal average) between 40 and 70 days after hyperpyrexia. This was followed by complete recovery based upon a return to normal levels of spermatozoa production (13).

Limitations of This Study

This initial study was confined to a single period of observation following a single exposure to microwaves, and does not indicate the degree of permanent injury to the testicle that might result from various combinations of temperature and durations of exposure. Neither were a sufficient number of animals or postexposure time intervals studied to establish a biological dosimeter. The problem of repeated exposure and the effect of dose fractionation, complicated as they are by biological recovery times, were also not within the scope of this investigation; nor were species differences in response from either the physical or biological standpoint. Such studies would require years for critical evaluation.

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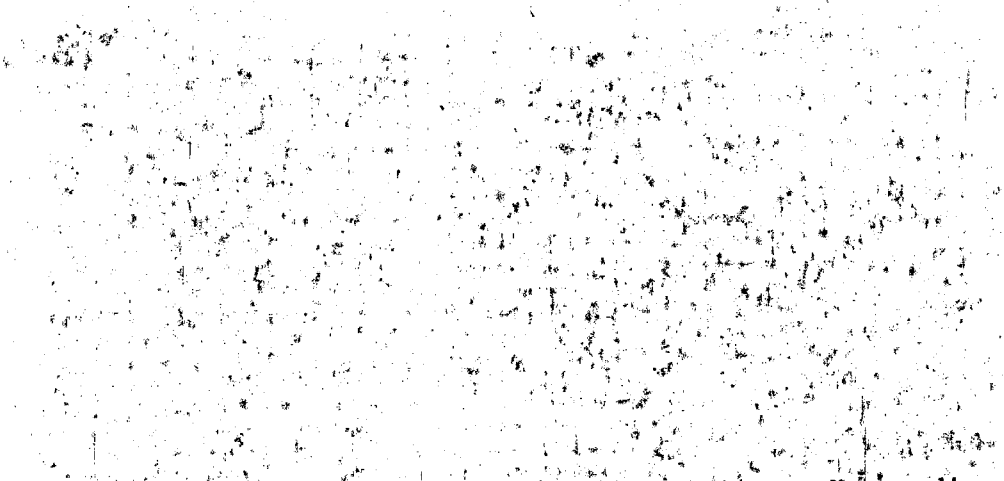
FIGURES 1 THROUGH 9

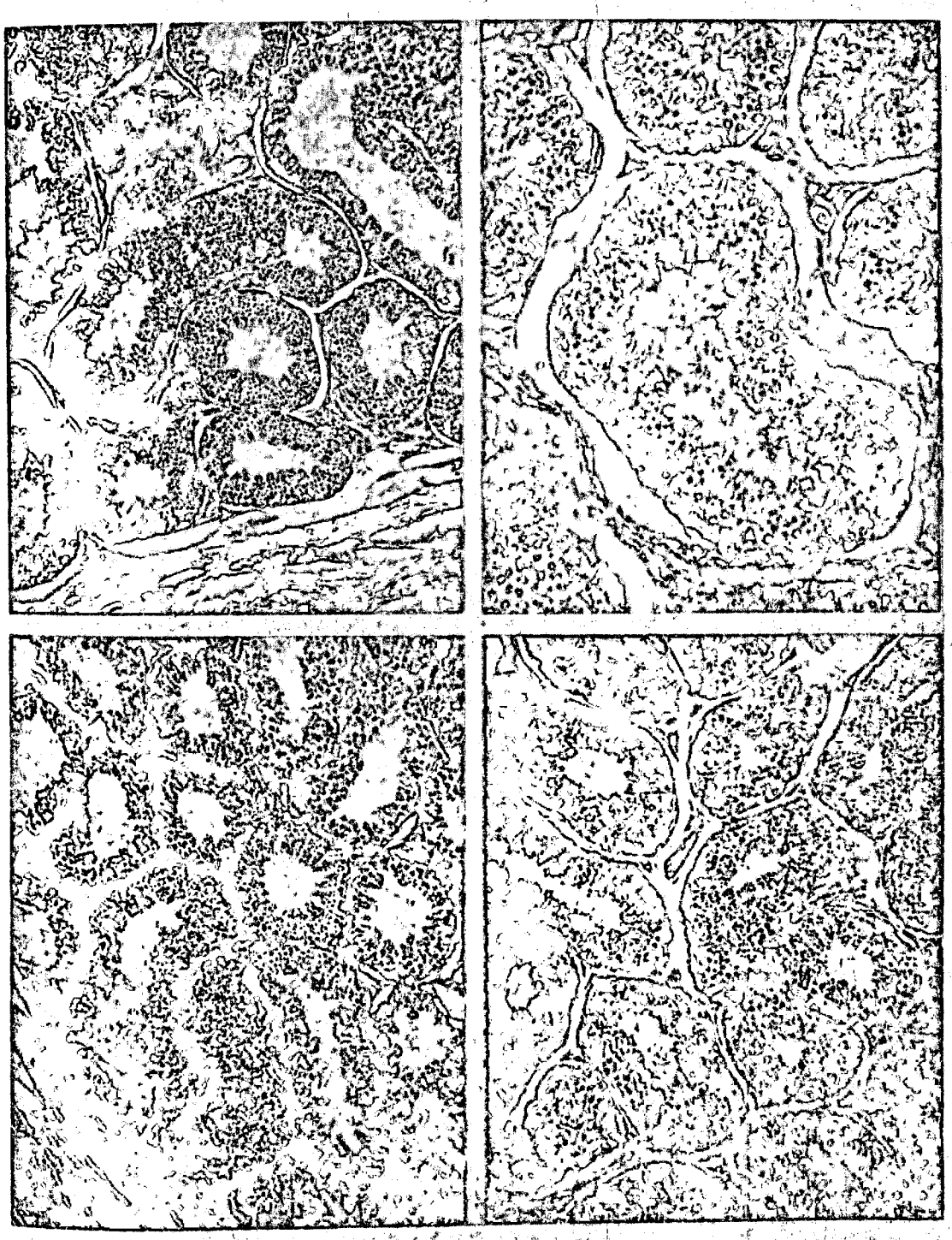


Figures 1 — 4. Testicle, Dog. Paraffin Sections Stained With Hematoxylin and Eosin.

Figure 1. and 2. Control sections. Figure 1 X 125, figure 2 X 250.

Figure 3. The minimal, detectable, morphologic change due to exposure to microwaves, arbitrarily called 1 plus is illustrated. It consists of a loss of adhesion between groups of cells in tubules just below the capsule. Except in a single case, this and the following reaction termed 2 plus, at the postexposure time intervals studied, were not noted in testicles with temperatures below 39° C. X 125.

Figure 4. From a section of the same testicle illustrated in figure 3. The more centrally located tubules are indistinguishable from control sections. X 125.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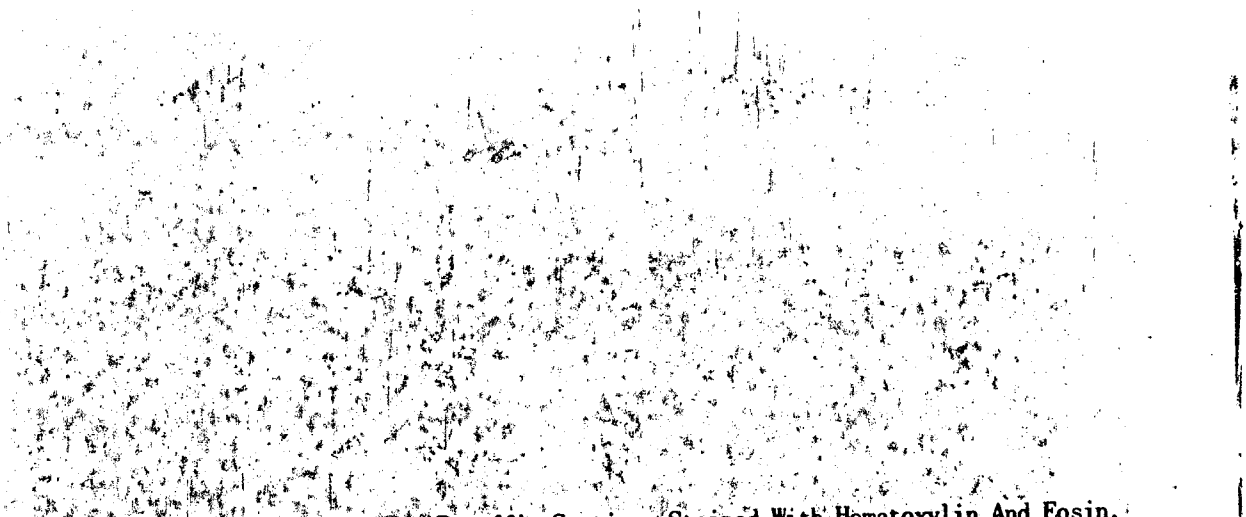

Figures 5 — 8. Testicle, Dog. Paraffin Sections Stained With Hematoxylin And Eosin.

Figure 5. The reaction classed as 2 plus is illustrated. It is characterized by a more marked dissociation of the tubular lining cells, associated with pyknosis in focal areas, and the appearance of giant cells in the lumina. Again this change in animals classed as 2 plus is limited to tubules just below the capsule. X 125.

Figure 6. Centrally placed tubules in the same testicle illustrated in figure 5. Some semeniferous tubules appear unaltered while others show only 1 plus reaction, consisting of a loss of adhesion between cells. X 125.

Figure 7. The reaction classed as 3 plus is illustrated. Cells lining some tubules have undergone necrosis and desquamation, with hemorrhage present in the lumens. X 125.

Figure 8. In testis showing the 3 plus reaction marked individual variation in the reaction of adjacent tubules to the same environment also was noted. The tubule in the center of the photomicrograph is lined chiefly by Sertoli cells. Adjacent tubules appear to be little, if at all, affected. X 175.

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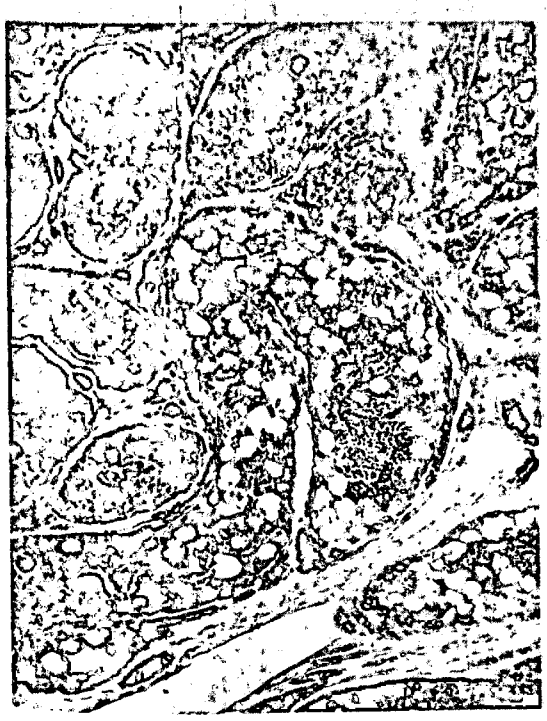

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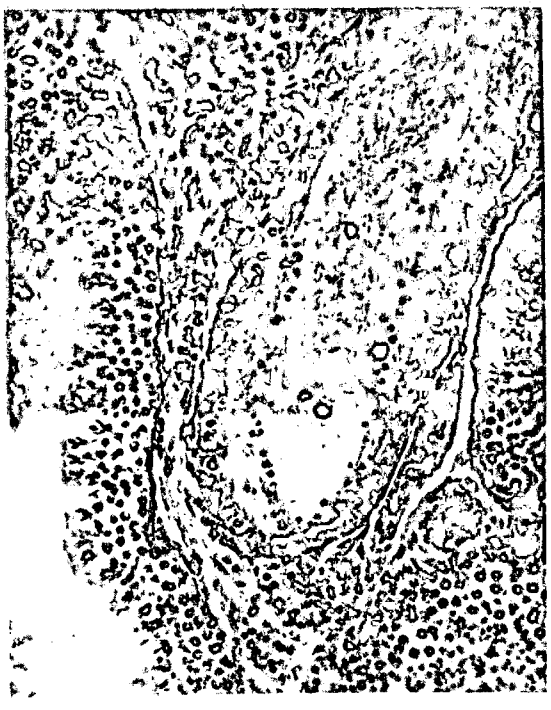

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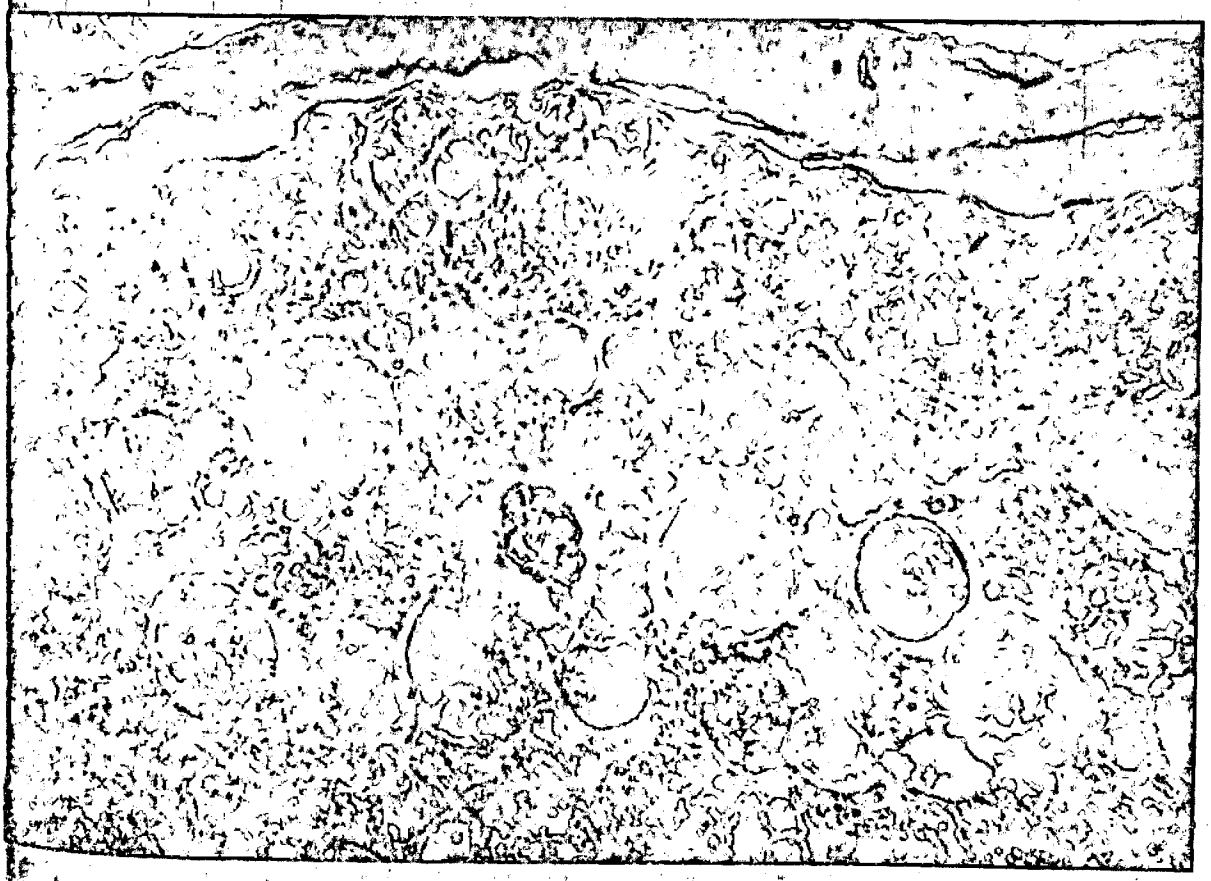
Figure 9. Testicle, Dog. Animal No. 122.

The nature of the giant cells is illustrated at higher magnification. The majority are multinucleated and are composed chiefly of spermatids. Some contain irregular shaped masses of deeply staining chromatin, from the fusion of degenerated nuclei. All cells lining the tubules, except sertoli cells and mature sperm may contribute to the formation of such giant cells. They are shed into the lumens leaving the most severely damaged tubules lined only by Sertoli cells. X 450.



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