

A MICROANGIOGRAPHIC STUDY OF THE EFFECT OF HYPERTHERMIA ON THE
RABBIT BLADDER

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Hyperthermia is now an accepted mode of treatment with radiation therapy and chemotherapy. Its use has been very restricted, and a wider use will encounter the same limitation as radiation therapy; namely, the tolerance level of normal tissue.

It is therefore worthwhile to devise a model to study the effect of hyperthermia on a normal tissue. The model selected was the rabbit bladder and the end point measured was the changes in the micro-vasculature of the bladder wall. It has already been demonstrated clinically that hot water bladder infusions will produce regression in bladder tumours (ref.1).

Material and Method

New Zealand white rabbits (male) weighing approximately 4 kg were catheterized and infused with sterile water heated to $43^{\circ}\text{C} + \frac{1}{2}^{\circ}\text{C}$. The water was heated in a coil in a heating bath and the bladder temperature was monitored with a thermistor threaded through the catheter. The water bath temperature was controlled by an automatic heating coil and cold water pump. An attempt was made to maintain sterility and the animals were anaesthetized with pentobarbital during the 15 minutes infusion time.

The animals were kept for periods varying from 7 days to 3 months, when microangiography was performed on the animals (ref 2).

The rabbits were anaesthetized and the abdomen opened to reveal the abdominal aorta which was then catheterized, and a 7% suspension of micro-opaque (barium sulphate) infused from a height of about 80 cm.

When the bladder vasculature was filled with contrast medium (about 2 hours), the bladder (which has been distended by filling with water) was dissected out and fixed.

The bladders are then cut into two halves and stretched. They are then set in a thin layer of paraffin and 30 Kvp radiographs taken of them on high resolution plates (Kodak).

Measurements

The normal bladders were used as a standard to establish three measurement criteria:

1. The number of vessels crossing a 1 mm line in the most vascular area.
2. The width of the vessels in the same area.
3. The tortuosity of the 5 most tortuous vessels between two terminal points separated by 5 mm .

It was in fact found that there was a close correlation between the scored results and a simple visual assessment based on experience in observing the samples.

It is important to avoid infection in the bladder because the appearance of the microangiogram of an infected bladder can closely resemble that of a bladder which has sustained some other injury such as radiation damage (fig 1).

Results

There is no evidence of any immediate change in the vasculature following the hyperthermic treatment. However, after 7 days, there was a noticeable slowing down in the rate of filling of the vessels with micro-opaque, and the vasculature is very sparse compared with normal samples.

In the case of the animals who were kept for 1 to 3 months post hyperthermic treatment, the appearance of the bladders was perhaps slightly hypervascular but not seriously abnormal, indicating that the immediate damage was repaired and that no medium term damage appears to result from a short hyperthermic treatment at a temperature which is sufficient to produce an enhancement of the effect of radiation on normal cells.

A present modification is that the anaesthetic has been changed to sodium brevital, which produces a shorter and shallow anaesthetized state and reduces the possibility of induced hypothermia, a condition which could possibly influence the results.

Figure 2 shows a normal bladder and figure 3 shows a slightly hypervascular post 3 months bladder.

REFERENCES

1. R.R. Hall, et al: Effects of hyperthermia on bladder cancer. British Medical Journal , vol. 2, 1977, pp. 593-594.
2. O. Hassler, S-O Hietala: Angiographic abnormalities in the urinary bladder wall after irradiation. Acta Radiologica Supplement 328, 1973.

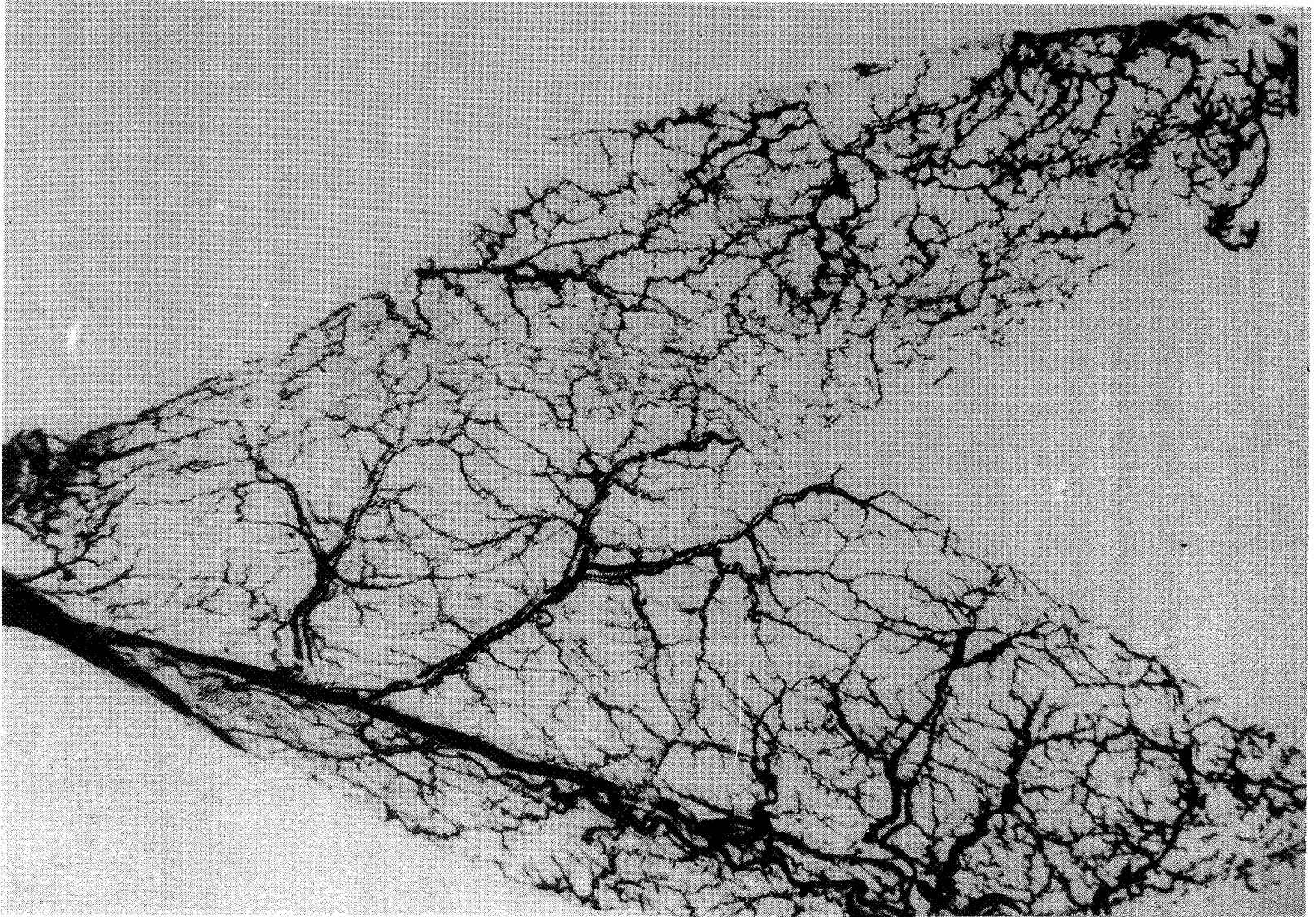


Figure 1.- An infected bladder.



Figure 2.- Normal bladder.

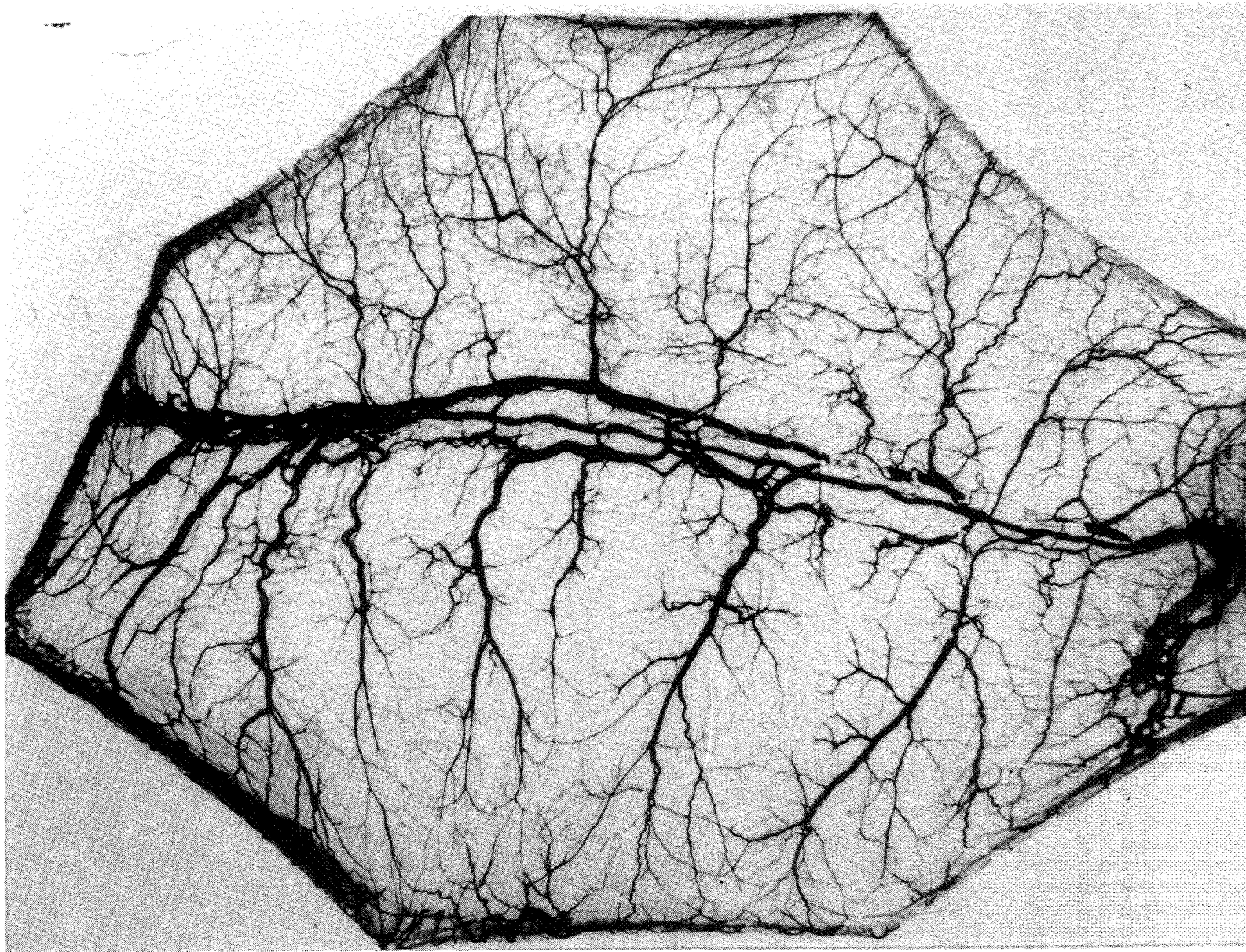


Figure 3.- Hypervascular post - 3 months hyperthermic treated bladder.

Questions and Answers Following Paper by Hietala, Howells, and Hazra

D. Cone: What was the composition of the so-called water that you infused with? Was it plain water, distilled water, or what?

Howells: It was sterile water.

D. Cone: Did it have a specific gravity, or pH control, or osmotic control?

Howells: It was plain, sterile water.

D. Cone: Could that have an effect?

Howells: I do not know. We were thinking of using saline, but we did not. We discussed this, but we did not really think that it had any significant effect.