Evaluation of Ioduron B in Bronchography

I. A Preliminary Study on Animal Tissues*

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The effects of a water soluble contrast medium (Ioduron B) upon tissues of the body have not been sufficiently investigated and reported in the literature. Fischer, discussed briefly the effect of Ioduron B on the peritoneum of guinea pigs. A statement is also made that blood counts on patients subjected to Ioduron B bronchography show no material changes.

We have undertaken a more intensified and detailed study of the possible effects of this bronchographic medium, not only upon our patients but also upon test animals which have been subjected to Ioduron B bronchography.

The chemical evaluations on patients prior to and after bronchography have been reported in a separate paper. Our results indicate slight transitory changes in chemical values shortly after bronchography with rapid return to normal values. Two of our patients and two of eight patients of Sheft, complained of substernal pain immediately following bronchial instillation of Ioduron B and lasting for approximately 12 hours.

This paper is confined to evaluation of any morphologic changes in the tissues of test animals. Such changes, if present, combined with the previous chemical studies on humans, should offer conclusive evidence regarding the possible toxic effect of Ioduron B.

Materials and Methods Used:

Guinea pigs were utilized as the test animals. Each animal was anesthetized with ether and subjected to surgical exposure of the trachea, with injection of 0.3 cc. Ioduron B directly into the trachea and bronchial tree. The guinea pigs were anesthetized with ether. A midline incision was made over the trachea so it was exposed. A small 26 gauge needle was inserted into the trachea between the cartilaginous rings and the predetermined amount of Ioduron B was delivered from a tuberculin syringe. The syringe and needle

*Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.
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Ioduron B was supplied by “Wyeth, Incorporated, Philadelphia, Pa.
were then withdrawn and the wound closed. Three tenth cubic centimeters of Ioduron B in a 450 gram guinea pig was calculated to be the amount equivalent to 40 cc. in a 70 kilogram man. X-ray films taken shortly after direct instillation of the contrast medium demonstrate filling of the bronchial tree (Figures 1 and 2). Control animals were subjected to anesthesia without exposure of the trachea. Each animal was numbered and caged in pairs to avoid confusion and discrepancies in numbers.

Five groups of animals were studied. Each group consisted of four test and two control animals from the same litter. The total number of animals studied was 30, 10 of which constituted control animals. Group I consisted of test animals 1, 2, 3 and 5. These animals were sacrificed 48 hours after injection of Ioduron B into the bronchial tree. Control animals A and B were sacrificed 48 hours after anesthesia for comparison with the test animals. Group II consisted of test animals 6, 7, 8 and 9. These animals were sacrificed two weeks after administration of Ioduron B. Control animals C and D were sacrificed two weeks after anesthesia. Group III consisted of test animals 10, 11, 13 and 14. These animals were sacrificed three weeks after administration of Ioduron B. Control animals E and F were sacrificed three weeks after anesthesia. Group IV consisted of test animals 16, 19, 20 and 21. These animals were sacrificed six weeks after administration of Ioduron B. Control animals G and H were sacrificed six

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**FIGURE 1**

*Figure 1*: Roentgenogram of Guinea pig demonstrating Ioduron B in Bronchial tree.

**FIGURE 2**

*Figure 2*: Roentgenogram of Guinea pig demonstrating Ioduron B in Bronchial tree.
Figure 3: Photomicrograph demonstrating perivascular lymphocytic infiltrate of lung. (X170).

Figure 4: Photomicrograph demonstrating peribronchial lymphocytic infiltrate. (X170).

Figure 5: Photomicrograph demonstrating lymphocytic infiltrate in cortical zone of the kidney. (X170).
weeks after anesthesia. Group V consisted of test animals 22, 24, 25 and 26. These animals were sacrificed 12 weeks after administration of Ioduron B. Control animals I and J were sacrificed 12 weeks after anesthesia.

Inasmuch as the material was administered by means of the bronchial tree, absorbed by the blood, and excreted by the kidneys, it was deemed necessary to study microscopic sections of the following structures: (1) trachea, (2) both lungs, (3) heart, (4) liver, (5) both kidneys, (6) bladder. Each set of tissue studies was compared with those of the same group and tissues of all other groups. All changes were noted.

Guinea pigs 4, 17 and 18 died within 24 hours following intervention as a result of atelectasis, believed to be secondary to anesthesia. Guinea pig 23 died within 12 hours following surgical intervention as a result of exsanguination. Guinea pigs 12 and 15 died within two days following intervention. These animals showed evidences of having been attacked by other guinea pigs. The actual cause of death is not known, but pathologic studies of the tissues, grossly and microscopically, presented no variation from the normal.

Results

Group I: In these animals, microscopic examination of the lungs demonstrated a distinct perivascular (Figure 3) and peribronchial round cell infiltrate (Figure 4). The peritracheal lymph nodes showed slight hyperplasia. No other microscopic abnormality was noted in any other portion of the lungs. All other organs of the test animals were microscopically within normal limits. Sections from the two control animals did not present any features suggestive of a perivascular or peribronchial pulmonary infiltrate.

Group II: The lung sections showed complete disappearance of the perivascular and peribronchial round cell infiltrate. The tracheal lymph nodes were considered normal when compared with those of control animals. With the exception of the kidneys, all organs studied demonstrated no change over the control animals. Both kidneys of each test animal presented small, scattered, isolated foci of lymphocytes in the cortical zone (Figure 5). No such abnormality was noted in the control animals.

Groups III, IV and V: None of the organs presented any microscopic change when compared with control animals.

Discussion

Our preliminary investigation leads us to believe that Ioduron B, utilized as a new medium for bronchography, produces slight transitory tissue changes in test animals. The peribronchial and perivascular infiltrate seen 48 hours after instillation of Ioduron.
B is explainable on a local reaction which probably takes place during transfer of the dye from the bronchial tree to the vascular system. This feature is transitory since it cannot be seen in sections of the lungs taken from test animals that have lived for two weeks or more. The renal involvement is also transitory and is probably caused by excretion of Ioduron B from the kidneys. This feature, although not present 48 hours after instillation of the dye, is seen within two weeks and then regresses to normal.

At present, test animals studied up to periods of 12 weeks following instillation of Ioduron B, show no evidence of permanent tissue damage or suggest the possibility of delayed toxic effects. We have a series of test animals which we will continue to study at frequent intervals until at least one year following instillation of this new water soluble bronchographic medium.

The deaths which occurred in this series could not be attributed to Ioduron B. In guinea pigs numbered 14, 17, 18 and 23, death was related to a known cause, unrelated to Ioduron B. However, in guinea pigs numbered 12 and 15, no actual cause of death was determined. It is possible that Ioduron B may have played some role, although we feel that this possibility is remote, since tissue studies revealed only normal findings.

Addendum: Our series of five test animals, which were permitted to live for one year following installation of Ioduron B, demonstrated no abnormal features either clinically or on microscopic examination of the vital organs.

SUMMARY

1) Ioduron B is not permanently damaging to tissues of test animals up to 12 weeks after intratracheal instillation of the dye.
2) Transitory inflammatory reactions are seen in the lungs and kidneys of test animals with complete disappearance within a short period of time.

RESUMEN

1) Ioduron B no daña permanentemente los tejidos de los animales en experiencia hasta 12 semanas después de la instilación intratraqueal del material.
2) En los pulmones y en los riñones de los animales de experiencia hay reacciones transitorias que desaparecen completamente dentro de corto tiempo.

RESUME

1) L'Ioduron B ne cause pas de lésions permanentes aux tissus d'animaux témoins observés douze semaines après instillation intratrachéale du produit.
2) Des réactions inflammatoires peuvent être observées au niveau des poumons et des reins des animaux témoins mais elles disparaissent complètement dans un court laps de temps.

REFERENCES
3 Shefts, L. M., Civilian Thoracic Surgical Consultant, Veterans Administration Hospital, Legion Branch, Kerrville, Texas: "Personal Communication."