Acta vet. scand. 1985, *26*, 428—430.

Brief Communication

THE DISTRIBUTION OF 3H-TETRACYCLINE AFTER A SINGLE, ORAL DOSE IN THE RAINBOW TROUT (SALMO GAIRDNERI) AS OBSERVED BY WHOLE BODY AUTORADIOGRAPHY

The tetracyclines are widely used in the treatment of bacterial diseases in Norwegian aquaculture. The fate of these compounds, however, is incompletely investigated; therefore the present study was undertaken in order to add some knowledge about the kinetics of tetracyclines in the rainbow trout. Rainbow trouts (Salmo gairdneri) weighing 200 ± 20 g were kept in 400 l fiber glass tanks supplied with running fresh water (1 l/min) at + 6°C. They were fed a pelleted fish diet containing 17.5 % fat, 51 % protein and 21 % carbohydrates (Ewos, Södertälje, Sweden) throughout the experiment. Before the experiment was carried out the fishes were allowed to adapt to the test conditions for 2 weeks.

Tetracycline, (7-3H (N))-free base, code NET-141, with specific activity of 635.4 mCi/mmol and chemical purity > 97 % was obtained from New England Nuclear (Boston, U.S.A.). The test substances was dissolved in 96 % ethyl alcohol and mixed with powdered feed. After evaporation of the alcohol at room temperature the feed was divided in gelatine capsules No. 2 (Parke Davis & Co., G.B.), with 200 μCi in 0.5 g feed in each capsule. One capsule was administered intragastrically to each of 6 fishes as described by *Bergsjø et al.* (1979). In addition, 2 fishes were administered the same amount of unlabelled tetracycline with the same procedure to serve as controls. After 2, 7, and 21 days pairs of 2 fishes were killed by benzocaine euthanasia, embedded immediately in 1 % carboxymethylcellulose in distilled water and frozen in a bath of n-hexane cooled with solid CO_2 to about —75°C. Sagital whole-body sections (40 μm) were cut from different levels and collected at —20°C on tape No. 821 (3M Co., St. Paul, Minn., U.S.A.) in a PMV cryomicrotome (PMV 450 MP, Stockholm, Sweden). After freeze-drying at —20°C for 24 h the sections were exposed to X-ray films (LKB ultrofilm LKB, Sweden) (*Ullberg* 1954). The control fishes were submitted to the same procedure 7 days after administration. After 3 months exposure at —20°C the films were developed and fixed.

At 2 days after administration only a negligible absorption had taken place and radioactivity was limited almost exclusively to the gastrointestinal content. At 7 days radiolabelled material was distributed throughout the body (Fig. 1) with the highest amount of radioactivity in the bile, the liver, the skin, the bone tissue and the uveal tract of the eye. Moderate degrees of radioactivity were present in the kidney, the blood and the muscle.

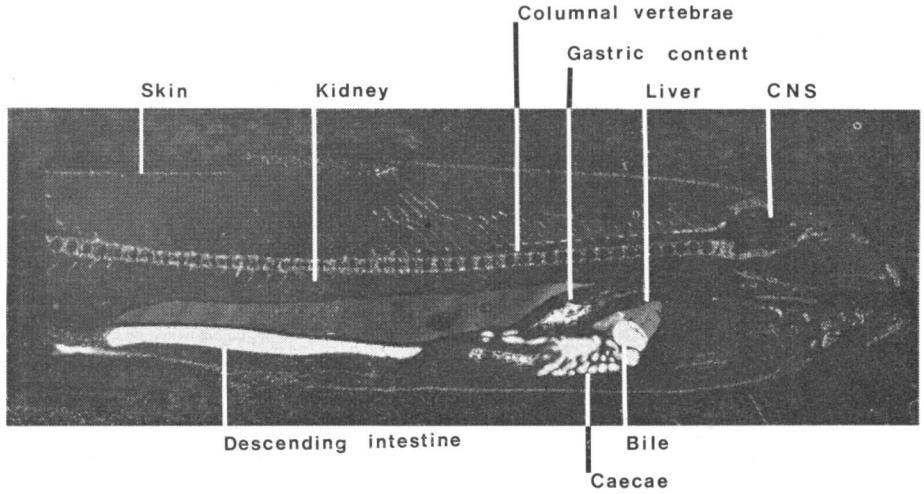

Figure 1. Whole-body autoradiogram of a rainbow trout 7 days after a single oral dose of 3-H-tetracycline. Light areas correspond to high concentrations of radioactivity.

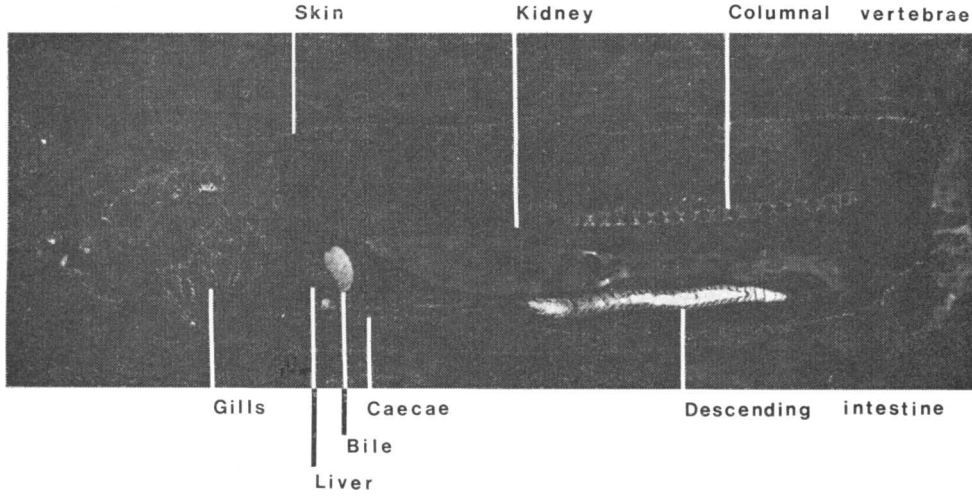

Figure 2. Whole-body autoradiogram of a rainbow trout 21 days after a single oral dose of 3-H-tetracycline.

Traces of radioactivity still remained in the stomach content, while considerable amounts were present in the content and mucosal lining of the caecae and the descending intestine.

At 21 days the bile and the content and mucosal lining of the intestinal tract showed a high degree of radiolabelling (Fig. 2). Radioactivity was still present in the skin, the skeleton and the uveal tract of the eye, while only traces of radiolabelled material remained in the liver and the kidney.

Whole-body autoradiography is a most useful technique for obtaining a view of the general distribution pattern of xenobiotic compounds. When this method is applied to examine the distribution pattern over prolonged time intervals, indications about other aspects of a compound's kinetics may as well be suggested. Although the administered dose in the present study was far below the recommended therapeutic dose level, and bearing in mind the possibility of dose dependent kinetics, we are of the opinion that the present results justify the qualitative kinetic considerations to follow. Firstly, the radiolabelling in the skeleton throughout the experimental period obviously reflects the affinity of tetracyclines for bone tissue which is a well documented feature. Furthermore, the radioactivity in the skin and the uveal tract of the eye could represent the association of the compound and/or metabolites to tissue macromolecules. Finally, the strong radiolabelling in the bile and in the content and mucosal lining of the intestinal tract throughout the experimental period probably indicates enterohepatic circulation of the drug and/or metabolites, a feature which may contribute considerable to prolongation of the excretory phase.

Kristian Ingebrigtsen, Inger Nafstad and *Alice Maritim*
The Department of Pharmacology and Toxicology, Norwegian College of Veterinary Medicine, Oslo, Norway.

REFERENCES

Bergsjø, T., I. Nafstad & K. Ingebrigtsen: The distribution of 35-S-sulfadiazine and 14-C-trimethoprim in rainbow trout (Salmo gairdneri). Acta vet. scand. 1979, *20*, 25—37.

Ullberg, S.: Studies on the distribution and fate of 35-S-labelled benzylpenicillin in the body. Acta radiol. (Stockh.) 1954, *118*, 1—110.

(Received July 1, 1985).

Reprints may be requested from: Kr. Ingebrigtsen, the Department of Pharmacology and Toxicology, Norwegian College of Veterinary Medicine, P. O. Box 8146, Dep., N-0033 Oslo 1, Norway.