Dr. W. H. Dudok van Heel, Zoological Director, Dolfinarium Group, Harderwijk, Netherlands.

Summary

In an earlier paper (POELMA et al., 1974) the observation of a case of Lobomycosis (Lobo's Disease) in the Dolfinarium, Harderwijk, was described. The animal, an old male *Tursiops truncatus*, was treated succesfully with the fairly new drug Miconazole (Jansen Pharmaceutica, Belgium). The treatment lasted from September 17, 1974 until April 28, 1975. At the time of conclusion of this report (December 1976) no recurrence of the infection has been observed.

Introduction.

For the purpose of forming a breeding colony, Youri, an old male *Tursiops truncatus*, was caught off Marco Island, Fla. The catching spot happened to be just south of the place of capture of a dolphin (*Tursiops truncatus*) which, according to MIGAKI et al., 1971, suffered from Lobomycosis. Other cases were reported by CALDWELL et al., 1975, GOLDSTON et al., 1974, DE VRIES et al., 1973 and WOODARD, 1972. Youri joined the Dolfinarium breeding group in March 1970 (DUDOK VAN HEEL, 1972). Upon arrival he was observed to have one round discoloured open lesion of two centimeters diameter above the left eye and a similar irregularly shaped lesion of two by three centimeters on the leading edge of his left flipper at its insertion. Samples were taken and studied then and at later times, but never organisms were observed or isolated until August 1974. In the mean time, however, fundamental changes in the environment of the animal had taken place.

The Dolfinarium has always laid much emphasis on the environmental conditions of its animals. During the period 1972-1975 in particular, a number of experiments were carried out with respect to watercomposition (DUDOK VAN HEEL, 1975) and water-treatment.

The outcome of these experiments was that, apart from changes in the techniques of chlorination, we raised the pH from the usual level of 7.4 - 7.6 to 8.1 - 8.3 in the

spring of 1974. In late July and early August 1974 we changed the composition of our artificial seawater to one much closer to natural seawater (DUDOK VAN HEEL, 1975). The general improvement in the health of the dolphins, which became decidedly apparent about six weeks after the change in the composition of the water, was also reflected in the growth of lower organisms. From late spring onwards the lesions of Youri increased in size and numbers, sharply in August, which brought us to renewed investigations as to their origin.

Scrapings, taken on August 15, at last showed organisms, which appeared to be Lobomycosis (POELMA, 1974). Mamma, an old female *Tursiops truncatus* imported in July 1965 (DUDOK VAN HEEL, 1972), also started to show the verrucoid lesions, but samples taken on September 9 turned out to be negative. WIERSEMA and NIEMEL, 1965, report, that there is no evidence of infection from man to man, rather infection occurs from the environment in a superficial wound of the skin. WIERSEMA, 1971, also states, that the occurrence of Lobo's disease is predominantly in adult males after middle age (38 years plus).

WIERSEMA and NIEMEL, 1965, describe wide excision of the lesions as the most successful treatment in human patients, but they caution against the use of toxic drugs. WIERSEMA, 1971, reports recurrence of skin lesions on surgical scars as well as disappointing results from use of fungal drugs. Not a bright picture indeed.

Treatment first stage.

Before contemplating the drastic action of a surgical approach with a doubtful outcome we decided to a treatment with Ectimar first. On the morning of August 20 Youri was placed in a sling for approximately one hour. Samples were collected from the various lesions, the one on the right hand tip of the fluke being the worst, the lesions dried and bleeding stopped. The patches felt markedly warmer and showed a temperature of 31°C against the remaining part of the body surface about 23°C. Then a solution of etisazol ("Ectimar", Bayer) was applied and allowed to act for three quarters of an hour, after which the animal was returned to the water. The treatment was repeated two more times that day. The next day the treatment was given four times, but at the end of the day Youri developed pressure marks on his pectoral girdle. Therefore on the third day, August 22, the lesions were treated with Ectimar after which a mixture of Ectimar and lanoline was applied in a thick layer. After this single treatment in the morning Youri was returned to his pool and a three week period of observation, planning and research followed. By the end of this period the lesions had increased markedly and the right hand tip of the fluke had become a foul, spongy mass and amputation was under serious consideration.

During the two days of treatment Youri's food intake dropped from 4-5 kgs to 3 kgs per day, but jumped to $9\frac{1}{2}$ kgs on the third day and stayed at 6-7 kgs daily for the next couple of weeks. The animal was sexually very active first with Lara, but later with Mamma, who encouraged him greatly.

Treatment second stage.

Discussions with our medical team suggested the use of a new drug "Miconazole" produced by Janssen Pharmaceutica, Belgium. During a thorough discussion with Pro-

fessor Dr. D. C. Thienpont of this concern we decided to treat both Youri and Mamma with this drug, since no toxic effects in either animals or human beings had been reported to date. Based on earlier weights of both animals we assumed a bodyweight of 200 kgs and used the recommended dose of 40 mg/kg bodyweight. Each tablet contained 250 mg of miconazole and it was suggested that treatment be started with 6 tablets /day gradually building up to 32 tablets /day in four doses. Figure 1 shows the food intake compared with the number of tablets from September 3 until October 6. As mentioned earlier Youri and Mamma were sexually extremely active during this period as is usual in our establishment in the autumn. Very often both animals, the male in particular, are irregular in their feeding, skipping meals, as they are more interested in each other than in food. Due to this irregular feeding the intended dosage of miconazole could not be properly maintained.

About 16.30 hrs on October 5 one of the trainers found Youri in great distress and pulled the animal, which was close to drowning, to the side of the pool. The animal was placed in a sling suspended in a frame on the bottom of our circular shallow pool of 6m diameter (DUDOK VAN HEEL, 1970). The waterlevel was raised so that the animal could just float. A permanent watchman was put on guard and 5 mg valium was administered to calm down the very nervous animal. The bloodpicture showed low levels in K, Ca and Fe. The animal was forcefed $1\frac{1}{2}$ kgs of mackerelmash, 1 L of RINGERS solution, 10 gr of KCl, double multivitamin dosage and Supradyn. To boost iron levels 10 cc of Fermin 100 was given intramuscular. At 14.30 hrs another 11/2 kgs of mackerel was forcefed upon which Youri lightly vomited and spilled about half the feed. As he was much quieter and showed no distress he was lowered into the water. He immediately turned towards the trainer and accepted ½ kg fish from the hand. The gate into the larger pool with Mamma was opened, but Youri preferred the smaller pool until later the following day. The myconazole treatment was suspended in both animals. After a week the bloodpicture had returned to the normal level. Figur 2 shows the foodintake from October 4 until November 6.

On November 4 Youri and Mamma were inspected again. Mamma's lesions were small, clean and about to close, Lobomycosis once more negative. Youri was positive on Lobomycosis. His lesions were open and foul, the lesion on the fluke was at least one centimeter deep. However, the situation had not worsened as quickly as before. The behaviour of both animals was very good. We decided to continue myconazole treatment in Youri four times a day in the manner as shown in Figure 3.

Bearing in mind the environmental considerations mentioned earlier, we lowered the pH to around 7.5 and changed the composition of the artificial seawater back to a solution with NaCl as the only salt constituent.

Inspection on November 12 shows a little improvement in Youri's lesions. On November 25 his lesion on the inside of the flipper was still raw and covered with pus. The serious lesion on the fluke had decreased in size and had clean and healthy edges. Both Youri and Mamma continued to be lively and ate well. Inspection on January 6, 1975, showed a further steady improvement. Mamma negative, Youri still positive on Lobomycosis. During this long second period of treatment Youri produced a "medical" smell from blowhole.

In the first week of February and the second week of March a lower intake of food and myconazole was due to a short intestinal infection, but without any detrimental effect on the treatment for Lobomycosis. Inspection in the end of March showed closed lesions and no fungal cells could be found. As inspection on April 28 was also negative the myconazole treatment was ended at that date.

X-X-X NUMBER OF MICONAZOLE TABLETS.

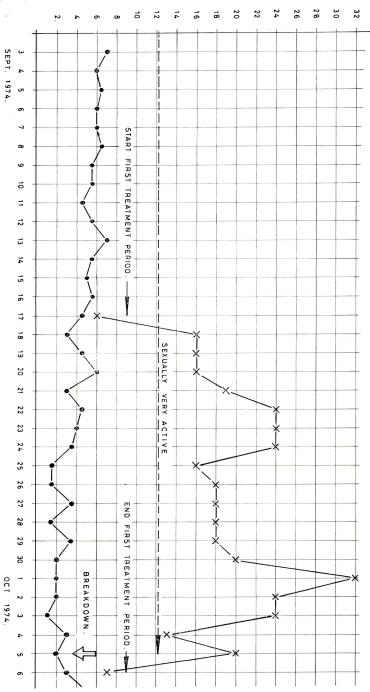
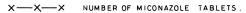


Figure 1. Foodintake of Youri against the administration of miconazole September 3 - October 6, 1974.



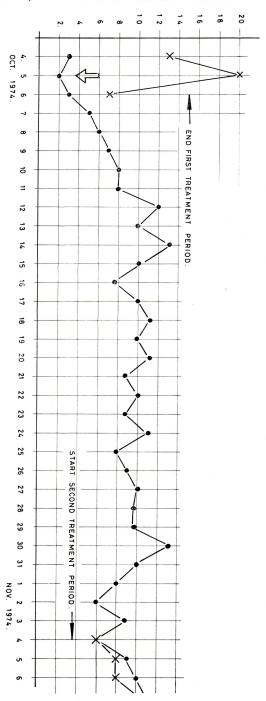
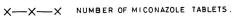


Figure 2. Foodintake of Youri during the suspensionperiod after his breakdown, October 6 - November 4.



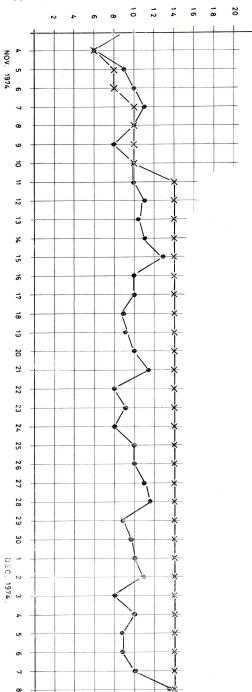


Figure 3. Foodintake of Youri against renewed miconazole treatment, November 4 - December 8. The treatment lasted at the same level until April 28, 1975.

There is no doubt, that in the drug miconazole we have found a very good fungicide against a fungus which so far defied a proper cure. This is in line with the experiences of the manufacturers, which point to wide spectrum capacities of the drug. At the conclusion of this report (December 1976) no recurrence of the disease has been observed, but we are alert to it. However, euthanasie in dolphins suffering from Lobo's Disease is certainly unnecessary.

A second point of interest is that the dosage that proved to be effective -18 mg of miconazole/kg of bodyweight- was very much less than originally suggested by Prof. Thienpont and his staff on the grounds of their earlier experiences.

The question has been raised whether the sudden breakdown of the animal on October 5 was due to the use of the drug or not. Of course we suspended treatment, but we came to the conclusion that the cause of the breakdown probably lay elsewhere (Mamma did not suffer) and as soon as Youri was in good health again we resumed treatment. In our opinion the cause of the breakdown was rather to be found in the very intense mating behaviour accompanied by a low intake of food on top of which leakage of minerals through open tissue could lead to deficiencies. We were able to raise the mineral level quickly and lateron, during the second stage of the treatment with miconazole, no ill effects could be attributed to the use of the drug. Apart from two mild intestinal infections and the Lobo Disease as such, Youri was in very good condition.

Acknowledgments

We want to thank Dr F. G. Poelma D.V.M., Faculty of Veterinary Medicine of the University of Utrecht, and Dr G. A. de Vries of the Institute for Mycology, Baarn, for their work in determining the Lobomycosis and their advice which lead us to the use of miconazole.

We are much obliged to Jansen Pharmaceutica, Prof. Dr D. C. Thienpont and his staff in particular, for the very thorough interest they displayed in this case of Lobo's Disease. Generously they took upon themselves to supply us with the drug for the full period of the treatment. We are happy that what looks to be a full recovery of a serious Lobomycosis victim can be attributed to the credit of this fungicide. We thank Mr V. J. A. Manton for his critical perusal of the text and Mr W. Paster-

References.

kamp for preparing the figures.

- CALDWELL, D. K., M. C. CALDWELL, J. C. WOODARD, L. AJELLO, W. KAP-LAN and H. M. McCLURE, 1975: Lobomycosis as a disease of the atlantic bottle-nosed dolphin (Tursiops truncatus Montagu, 1821). Am. Journ. Trop. Med. and Hyg., Vol. 24, no. 1.Jan.
- DUDOK VAN HEEL, W. H., 1970: The Dolfinarium at Harderwijk. Int. Zoo Yearb., Vol. 10, pp 49-51.
- DUDOK VAN HEEL, W. H., 1972: Raised levels of mercury and chlorinated hydrocarbons in newly captured Tursiops truncatus (Mont.) from Florida waters. Aq. Mam. Vol. 1, no. 2, pp. 24-36.

- DUDOK VAN HEEL, W. H., 1975: Remarks on the composition of water for dolphins in inland dolphinariums. Aq. Mam. Vol. 3, no. 2, p. 4-9.
- GOLDSTON, R. T., R. A. WHITMAN and TH. E. HASLETT, 1974: Lobo's Disease in the atlantic bottle-nosed dolphin (Tursiops truncatus). Annual Proc., 1974. Am. Assoc. Zoo Vet., Atlanta, Georgia, U.S.A.
- MIGAKI, G., M. G. VALERIO, B. IRVINE, F. M. GARNER, 1970: Lobo's Disease in an atlantic bottle-nosed dolphin. Journ. Am. Vet. Med. Assoc., Vol. 159, no. 5, pp 478-582.
- POELMA, F. G., G. A. DE VRIES, E.A. BLYTHE-RUSSELL and M. H. F. LUYKX, 1974: Lobomycosis in an Atlantic bottlenosed dolphin in the Dolfinarium, Harderwijk. Aq. Mam. Vol. 2, no. 3.
- VRIES, G. A. de and J. J. LAARMAN, 1973: A case of Lobo's Disease in the dolphin Sotalia guianensis. Aq. Mam. Vol. 1, no. 3, p. 26-33.
- WIERSEMA, J. P., 1971: Lobo's Disease (Keloidal Blastomycosis). In BLAKE, R. D., Ed., 1971: Human infections with fungi, actinomycetes and algae. Springer Verlag, New York, Heidelberg, Berlin, pp 577-588.
- WIERSEMA, J P. and P. L. A. NIEMEL, 1965: Lobo's Disease in Surinam Patients. Trop. Geogr. Med., Vol. 17, pp 89-111.
- WOODARD, J. C., 1972: Electron Microscopic Study of Lobomycosis (Loboa loboi). Laboratory Investigation, Int. Acad. Pad., Vol. 27, no. 6, pp 606-612.