

EXPERIMENTS ON THE PREVENTIVE EFFECT OF TOLERIN ON UPPER
RESPIRATORY DISEASES IN RABBITS

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Introduction

In Hungary the major losses in rabbit breeding are due to diseases of the digestive and respiratory systems. The fight against respiratory diseases has already produced results, but these achievements are chiefly due to general preventive methods, like creating isolated populations or improving management hygiene /keeping the animals in an environment which is free of draught, dust and ammonia/. Its reason can be found in the fact that respiratory diseases mostly occur following a decline in the general resistance of the organism. Procedures providing specific immunity /vaccination/ have gained only limited success.

One of the aims of our examination was to obtain an answer to the question, of whether it was possible to increase the general resistance of rabbits with a drug /Tolerin, which is a ⁶⁰Co- γ radiation detoxified E.coli endotoxin/ that improves resistance. Our other purpose was to study how effectively the increased resistance provides the animals protection in an infected environment against upper respiratory diseases.

Material and Methods

We conducted the experiments in 2 phases. In the first phase during laboratory tests first we treated 10 suckling and weaned /between the ages of 4 weeks to 4 months/ angora rabbits with different dosage /0,5-5,0 mg/animal/ of Tolerin i.v. to test its toxicity to the animals. We measured their rectal temperatures throughout 24 hours continuously. In the second

phase of the laboratory examinations we treated with Tolerin ten 3,5 month old New Zealand white rabbits at four-week intervals with a dosage of 1 mg/animal. We took blood samples prior treatment with Tolerin and checked the white blood cell count as well as the qualitative blood picture.

Two months after the second Tolerin-treatment we bled the animals for histological and pathological tests.

For the field trials we used 300 angora rabbits born from artificial insemination at the same time. Half of them we treated with Tolerin at 2-6 and 10 weeks of age/lmg/animal, s.c./. Before each treatment and after the last treatment we looked for chemical signs and divided the animals into four groups according to the symptoms:

0: healthy; +: mild clinical signs; ++: several mild clinical signs; +++: one or more serious clinical symptoms. We performed autopsy on all dead animals.

Results

None of the treated animals developed noticeable symptoms except an increase of rectal temperature following the Tolerin treatment, but 24 hours after the injection it returned back to normal value /figure 1./, to the normal physiological level /Zimmermann, 1927/. In the second phase of the examinations the white blood cell count of the rabbits also agreed with literature data /Weisbroth, 1974/ before treatment. On the 14th day after the first injection this basic level increased up to a 2,7 times higher value, and on the 30th day it was still two times higher than at the beginning /figure 2./. This was the tendency later on as well - though on a lower level - following the subsequent injections /Gábor et al., 1987/.

The examination of the qualitative blood cell count showed a massive lymphocytosis in the animals /figure 3./ that surpassed the level given by the literature /Weisbroth, 1974/. In animals treated with Tolerin at autopsy we found the thymus while it was absent in the controls /in normal cases its atrophy is natural/. Its weight was around 2,2 grams that is the double value of a normal thymus.

During histological examination we learned that in the thymus of treated animals there was a diffuse lymphocyte-increase, while in the controls there was just the usual quantity of fat tissue /Guzsal, 1981/.

The bone-marrow of the tubular bones in treated rabbits was purple-red while it was pink in the controls. Histologically in the treated animals we observed bone-marrow hyperplasy as well as myelo - and erythropoesis. In the controls there was a slight haemopoesis.

The field trials have proved that in the group of animals that had been treated with Tolerin in a dose of 1 mg/rabbit, the mortality was 6,5% less than in the control group /figure 4./ and on P=10% it is significant. There was an important difference between the clinical signs of upper respiratory diseases between the two groups /figure 5./. 4,4% of the animals had such signs in the treated group, while it was 13,6% in the other. This difference is significant on P=1%.

Discussion

We concluded that Tolerin can readily be used for the promotion of the general resistance of domesticated rabbits with no serious side-effects. It works through increasing the number of white blood cells in the bloodstream /mostly that of the lymphocytes/ and aids the production of white blood cells via causing functional hyperplasy of the bone-marrow. It also stimulates the ripening of lymphocytes because it inhibits the physiological atrophy of the thymus /Belák et al., 1983/, it even leads to functional hyperplasy within this organ as well. Thus the Tolerin increases the general resistance through promoting cellular immunoreactivity. Since it has a beneficial effect upon myelo-and erythropoesis, it is possible that it can be used for increasing humoral immunoreactivity as well. A decision in this question requires further investigations. Because it increases the general resistance, thus it decreases the incidence of respiratory diseases that are mainly due to the weakening of the general resistance of the body. As a consequence, if it was cheap and available in large quantities, it could be used in commercial rabbitries for the decrease

of the losses due to respiratory diseases caused by facultative pathogenic agents.

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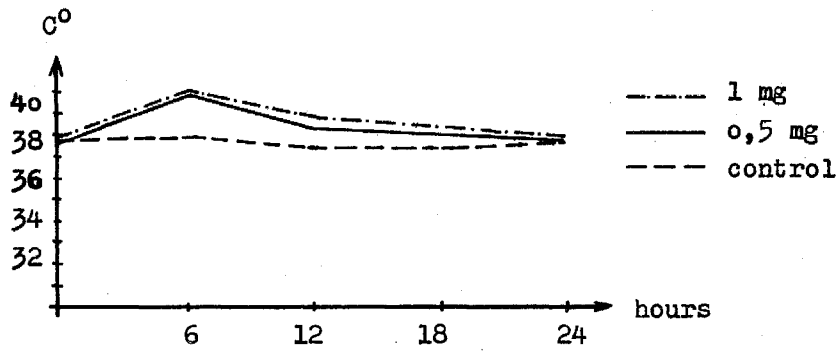


Fig.1.: Examination of the pyrogenic effect of Tolerin

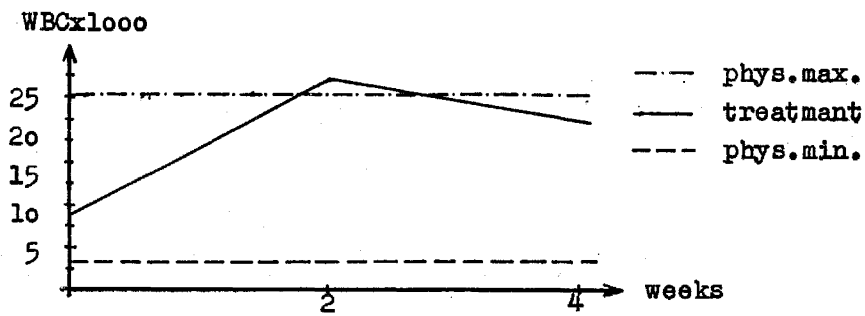


Fig.2.: Changes of white blood cell count after one Tolerin treatment

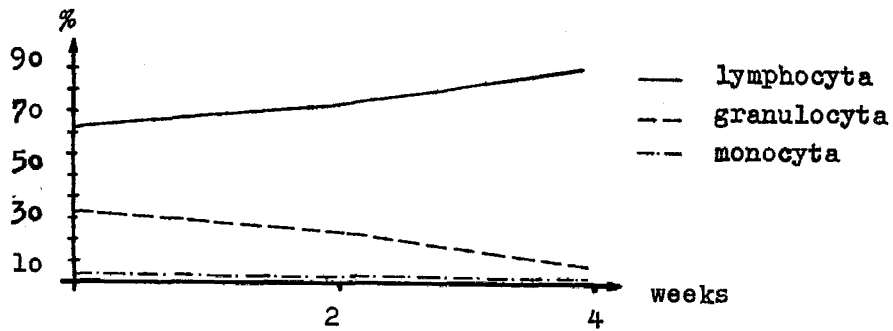


Fig.3.:Changes of qualitative blood picture after one Tolerin treatment

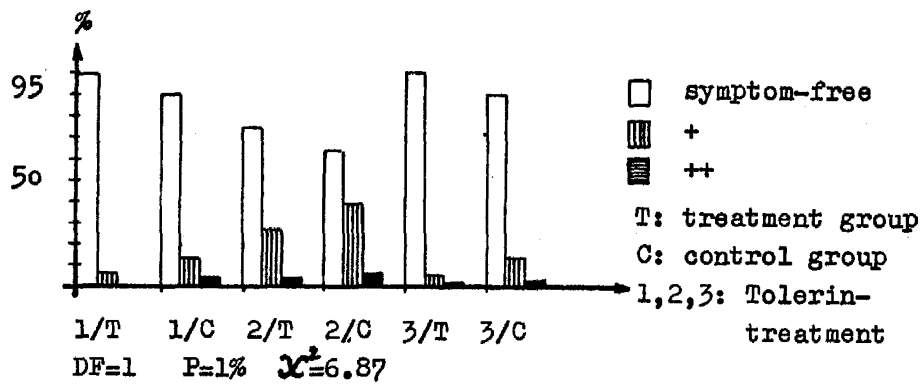


Fig.4:Changes of clinical signs after the Tolerin treatments during the field trials

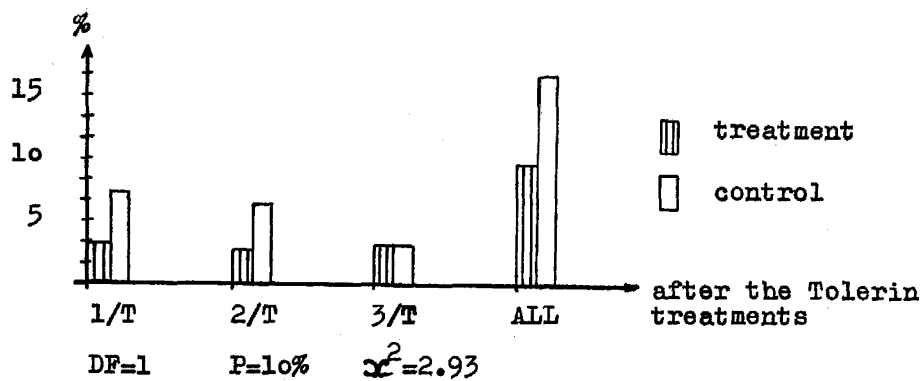


Fig.5.:Changes of mortality losses during the field test of Tolerin

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We examined the effect of Tolerin /E. Coli endotoxin detoxi-
fied by radiation /on domesticated rabbits in laboratory
and field trials. Our conclusion is that it increases the
general resistance of the organism via raising the number
of leucocytes in the bloodstream.

The Tolerin also promotes the production and maturation of
white blood cells via causing functional hyperplasy in the
bone-marrow and thymus /in young rabbits it inhibits the
physiological degeneration of the thymus/.

During the field trials we ascertained that the Tolerin
decreases the losses due to respiratory diseases as well as
their clinical signs given in a dose of one mg/animal sc.
from two weeks of age at four weeks intervals.

VERSUCHE MIT TOLERIN ZUR VORBEUGUNG VON ERKRANKUNGEN DER
OBEREN LUFTWEGE DER KANINCHEN

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Während unserer Untersuchungen unter labormässigen und
betrieblichen Umständen untersuchten wir die Wirkung des
Tolerins /Bestrahlungen mit E.Coli Endotoxin/. Wir stellten
fest, dass Tolerin die allgemeine Widerstandsfähigkeit des
Hauskaninchens verstärkt, und zwar auf solcher Weise, dass
die Anzahl der weissen Blutkörperchen, die in den Blut-
kreislauf gelangen, wächst. Ausserdem belebte die Produktion
und auch die Reife der weissen Blutkörperchen, dass die
funktionale Hyperplasy im Knochenmark und Thymus hervor-
gerufen wird /bei jungen Kaninchen wird die physiologische
Zurückbildung gebremst/.

Während der betrieblichen Untersuchungen stellten wir fest,
dass bei einer Dosis unter 1 mg, sc., das in einem Alter
ab zwei Wochen vierwöchentlich einmal gegeben die Erkrän-
kungen der oberen Luftwege und die klinischen Erscheinungen
gesenkt werden.



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