

OCCUPATIONAL DERMATITIS AMONG VETERINARY SURGEONS CAUSED BY SPIRAMYCIN, TYLOSIN, AND PENETHAMATE

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Abstract. Among nine veterinary surgeons seen within one year because of occupational dermatitis, six had dermatitis from spiramycin (Rovamycin®, Spiramycin®). Six were sensitive to tylosin (Tylan®), and five of these to spiramycin as well. Six were sensitive to penicillin or its derivatives, e.g. penethamate hydroiodide B.P. Apparently sensitization to spiramycin and tylosin was caused by a heavy exposure during preparation of solutions for injection. Sensitization to penethamate derived from local treatment of mastitis in cows.

Brucella infections in cattle and consequently brucella eruptions in veterinary surgeons have been rare in Denmark since 1952, and were eradicated in 1959. Obstetric work, however, traditionally performed without rubber gloves remains the major cause of occupational eczema among veterinary surgeons (4). This condition tends to become most troublesome in late winter when 40% of the calves are born, but it is rarely incapacitating unless an allergic contact sensitivity to some medicament supervenes (4). In 1967 we reported this course of events to occur after use of a strongly sensitizing penicillin derivative, penethamate hydroiodide B.P. (Leocillin®, AB Leo, Helsingborg, Sweden) for local treatment of mastitis in cows (3).

New sensitizers have lately gained entry into the medicine chests of the veterinary surgeons, notably spiramycin adipate (Rovamycin®, Pharma Rhodia, Birkerød, Denmark, Spiramycin®, H. Lundbeck & Co. A/S, Copenhagen-Valby, Denmark) and tylosin tartrate (Tylan®, Elanco Products Ltd., London, UK).

MATERIAL AND METHODS

Between March 1, 1971, and March 31, 1972, 1 female and 8 male veterinary surgeons came for examination

because of a recent aggravation of hand eczema or because of a dissemination of a hand eczema to other body regions.

All were examined by a series of standard patch tests selected, applied and read according to the recommendations of the International Contact Dermatitis Research Group (1, 6). Supplementary tests included all medicaments employed in veterinary practice.

Eight of the nine patients were also examined by scratch tests with 40 protein allergens, including animal hairs, pollens and a number of foods.

RESULTS

Seven of the 9 veterinary surgeons had positive patch tests to one or several medicaments used in their practices, and in 6 the present aggravation of dermatitis found an adequate explanation in the epidermal sensitivities demonstrated (Table I).

Six were sensitive to spiramycin, and 6 to tylosin (Table II). Six had positive reactions to penethamate, benzylpenicillin and/or procain-penicillin (Table III).

Table I

Case no.	Sex	Age (y.)	Actual causes of dermatitis
1	♂	34	Spiramycin, tylosin, penethamate, Streptomycin
2	♂	47	Spiramycin, tylosin, erythromycin, penethamate, penicillin, dihydro-streptomycin
3	♂	43	Spiramycin, tylosin
4	♂	45	Spiramycin, tylosin, procain-penicillin
5	♂	33	Spiramycin, tylosin, procain-penicillin
6	♂	44	Spiramycin, penethamate
7	♂	33	Watch strap (from previous contact sensitive to penethamate and tylosin)
8	♀	27	Obstetrics in cows
9	♂	31	Obstetrics in cows

Table II. Results of patch tests with macrolide antibiotics

NT = not tested

Case no.	Spiramycin			Tylosin			Erythromycin 1 % pet.	Carbomycin	
	1 % pet.	5 % aq.	10 % pet.	1 % pet.	5 % aq.	10 % pet.		1 % pet.	10 % pet.
1	NT	+++	NT	NT	+++	NT	—	NT	NT
2	+	NT	++	+	NT	+	+	NT	NT
3	NT	NT	+++	NT	+	NT	—	—	—
4	+	NT	++	+	NT	+	—	—	—
5	—	++	NT	NT	++	NT	—	—	—
6	+++	NT	+++	—	NT	—	—	—	—
7	—	NT	—	—	NT	++	—	—	—

Three of 8 patients tested gave positive reactions to scratch tests with cow's hair, and in one of these, obstetric work with cows was the dominant cause of his eczema.

Controls

45 consecutive patients with eczema had negative reactions to patch tests with spiramycin adipate 1 % and 10 % pet., and to tylosin tartrate 1 % and 10 % pet.

Spiramycin and tylosin

Spiramycin, erythromycin, carbomycin, oleandomycin and tylosin are, because of their similar ring structure, classified as macrolide antibiotics (Fig. 1). Spiramycin® and Rovamycin® consists of a mixture of spiramycin base I, II and III 86.2 % and adipic acid 13.8 %. The chemical structure of tylosin is not known in detail, but it is assumed to be very similar to that of spiramycin (2, 5).

Macrolide antibiotics are effective against gram-positive and some gram-negative bacteria, rickett-

siae, mycoplasma, mycobacteria, large viruses and spirochaetes.

Spiramycin adipate and tylosin tartrate are given mainly as injections or as additives to drinking water. For these purposes the substances are marketed in vials with sterile solutions for injection, or in plastic bottles containing soluble powders. Spiramycin is also marketed in tablet form, and tylosin as a water-insoluble powder.

In some cases veterinary surgeons make up injectable preparations from the powders (Rovamycin®, and Tylan®) intended as additives to drinking water. The procedure may be as follows: Rovamycin® 100 g supplied in 500 ml plastic bottles is dissolved by adding enough water to fill the bottle. As the powder is very light some dust exposure is unavoidable at this stage. After closure of the bottle the powder is dissolved by shaking. This generates some heat, so that when the bottle is opened, vapour and drops emerge, once again causing some contamination. The solution is next poured into a larger bottle containing 200 ml of propylene glycol, and water is added to make up 1 000 ml. Finally the solution is filled into 200 ml vials which are closed with rubber stoppers.

Table III. Results of patch tests with penicillin and its derivatives

Case no.	Penethamate 25 % olive oil	Benzyl- penicillin 30 % aq.	Procaine- penicillin 30 % aq.	Procaine 2 % pet.
1	+++	—	—	—
2	++	+++	—	—
4	—	—	+++	+++
5	—	—	+	+
6	++	—	—	—
7	++	—	—	—

COMMENTS

A review of the histories and the test results indicated that spiramycin, tylosin and penethamate were the dominant allergens and causes of disability, although in 6 cases the eczema started after irritation from obstetric work with cows, sows and mares. Danish animal stock is not covered by any insurance schemes, and the fee for veterinary treatment must be limited by

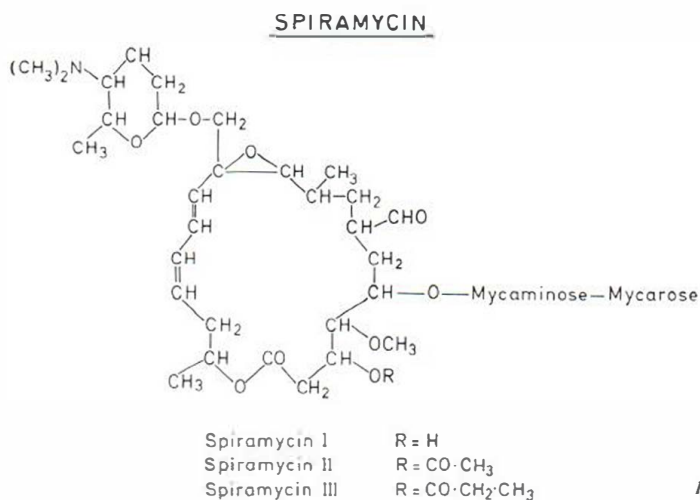


Fig. 1

the value of the animal. As a consequence veterinary surgeons try to reduce the cost of drugs, i.e. by making solutions for injection as described above. These procedures involve a heavy exposure to both spiramycin and tylosin, and apparently the mode of contact causes the high incidence of sensitization to these medicaments.

The purity of the spiramycin adipate and the Tylosin tartrate used for testing is not known. The coincidence of reactions to the two substances is therefore unexplained. The concomitant reactions may be due to cross-sensitization, to identical impurities, or simply to the same type of a severe exposure. If the coincidence of sensitivities were due to cross-sensitization carbomycin, which is closely related to both, might have been expected to give positive patch tests reactions. But reactions to carbomycin, which is not yet marketed in Denmark, were negative.

The present series confirms that penethamate is a common sensitizer and that sensitization does not of necessity induce secondary sensitivity to penicillin G (Table III). The diagnosis penethamate sensitivity thus requires testing with the chemical as such. It is of some interest that sensitization to penethamate, like sensitization to spiramycin, is preventable since it is caused by considerations of economy. Mastitis in cows can be treated by local injection of an oily suspension of penethamate into the udder canal through the teat (3) which leads unavoidably to the contamination of the hands. Systemic treatment by intramuscular injection is faster and more cleanly, but

also more expensive, requiring larger amounts of the antibiotic.

One of the 3 patients with positive scratch tests to cow hair had a flare-up of his dermatitis upon contact with cows. Many veterinary surgeons record similar experiences (4). Patch test with cow hair are usually negative, and the relevance of the scratch test reactions is unknown. So far, this peculiar dermatitis from contact with proteins has not been immunologically investigated.

Veterinary surgeons in practice are constantly exposed to irritants, and any dermatitis consequently tends to take a chronic course. The 6 veterinary surgeons with dermatitis from antibiotics improved once their sensitivities had been revealed and they could avoid direct contact with the allergens. Although none cleared completely, only one changed his job. Most members of this profession are strongly motivated for their work and prefer to continue their practice in spite of the eczema, rather than to change to more monotonous duties, such as meat inspection or dairy control.

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Received September 5, 1972

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