

## DRY GANGRENE OF THE EAR IN WHITE MICE

by

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### SUMMARY

Sporadic dry gangrene of the ears of white mice, and conditions conducive to its occurrence, are described. The incidence of ear necrosis increased markedly when the mice were subjected to cold and when their ears were traumatized by grooming to rid themselves of lice. Louse infestation alone is not a causative factor in the production of ear lesions. Age and breed of mice were other factors which affected incidence. The lesion is usually not important in the maintenance of colonies but might occur in situations where mice are subjected to stress.

### TROCKENER BRAND IM OHR VON WEISSEN MÄUSEN

Sporadischer trockener Brand in den Ohren von weissen Mäusen, und geeignete Bedingungen für dieses Vorkommen, werden beschrieben. Fälle von Ohr Nekrose vermehrten sich auffallend, als die Mäuse der Kälte ausgesetzt wurden, und als ihre Ohren durch Putzen traumatisiert wurden, wenn sie sich von Läusen befreien wollten. Verlausung allein ist nicht die Ursache der Erzeugung von Ohrläsionen. Alter und Maus-Stamm waren andere Faktoren, die dieses Vorkommen beeinflussten. Die Läsion ist gewöhnlich nicht von Bedeutung in Bezug auf die Haltung von Kolonien, aber sie kann in Situationen vorkommen, wo die Mäuse einem Stress ausgesetzt sind.

## LA GANGRENE SECHE DANS L'OREILLE DES SOURIS BLANCHES

La gangrène sèche sporadique dans les oreilles de souris blanches est décrite, ainsi que les conditions facilitant ce phénomène. L'incidence de la nécrose des oreilles augmenta notablement lorsque les souris furent sujets au froid, et lorsque leurs oreilles furent blessées quand elles se paraient pour se libérer des poux. L'infestation de poux seule n'est pas un facteur causatif pour la production des lésions d'oreilles. L'âge et la souche de souris sont d'autres facteurs portant sur l'incidence. La lésion n'est pas généralement importante dans l'entretien des colonies, mais elle pourrait arriver dans des situations où les souris doivent subir quelque tension.

In a series of experiments on the ectoparasite-host relationship between *Polyplax serrata* (Burmeister) and the laboratory mouse (Bell, Clifford, Moore & Raymond, 1966; Bell, Jellison & Owen, 1962; Clifford, Bell, Moore & Raymond, 1967), sporadic occurrence of dry gangrene of one or both ears of some mice was noted. This condition had not been observed previously in the Rocky Mountain Laboratory (RML) colony and, to our knowledge, had not been reported in the literature. Since mice with gangrenous ears also had heavy louse burdens, and the condition took a long time to develop, it was assumed that the phenomenon might be related to level of parasitism or to development of acquired resistance to lice by the mice. This paper reports results of attempts to elucidate the causes of the condition.

## MATERIALS AND METHODS

The majority of mice used in these experiments were the RML strain of white mice. However, in 1 experiment mice of the following strains were used: CFW/N, CDF-1, BALB/c, C57BL and GP. These mice are infested with 2 species of mites (*Myobia musculi* and *Mycoptes musculus*).

The mouse louse *Polyplax serrata* had been eliminated from stock animals, but was reintroduced as desired in various experiments. Infestation (seeding) with lice has been described by Bell *et al.* (1962).

Prior to test, mice were kept singly in glass battery jars or communally in metal boxes with beet pulp as bedding, and with free access to commercial food pellets and water. Room temperature was about 23°C and relative humidity (RH) ranged from 35 to 45%.

*Exposure to cold*

In early experiments mice kept in glass battery jars survived exposure to 5°C for extended periods. However, when mice were exposed to circulating air at 50% RH in wire-mesh cages, 15°C was the lowest temperature that permitted 100% survival for several months. Therefore, this temperature

was selected to test the effects of cold on the development of gangrenous ears. The 50% RH level was chosen arbitrarily. Variations of 1°C and up to 5% RH were noted throughout the test periods.

When mice were tested at controlled temperatures in cabinets (model 706-A; Lab-Line Instruments Inc., 15th and Bloomingdale Streets, Melrose Park, Illinois 60161, USA) with circulated air, they were placed in cylindrical cages of 0.25 inch (6 mm) mesh hardware cloth. A single mouse was placed in each cage, or 2 mice were kept in compartments of a single cage divided by sheet metal. No bedding was used; pellets and water were available as before.

#### *Amputations*

Unilateral (A-1) or bilateral (A-2) amputations of hind legs at the distal end of the tibia were performed, on 1-day-old mice, with sharp scissors. For some experiments only the 2nd and 4th toes (A-T) of one hind foot were amputated at the time of weaning. Mice without amputations were designated as normal (N). All amputations were nearly bloodless and apparently caused little discomfort; nursing was usually resumed within several minutes after amputation.

#### *Louse scoring system*

Louse populations were estimated and scored as described previously (Bell *et al.*, 1966). In this system a score of 40 represents hundreds or thousands of lice. Coordinates on all graphs are based on average scores.

### RESULTS

#### *Description of lesion*

In most cases the lesion progressed rapidly, and most ears were seen at the necrotic stage. Occasionally early lesions were noted, and in this inchoate stage an area of hyperaemia was present in approximately the distal third of the ear. The line of demarcation and future separation was distinct and usually regular (Fig. 1). Serial observations of prodromal lesions revealed that progression to necrosis was not inevitable, and at least temporary regression to an apparently normal state occurred occasionally. However, when the red of hypaeremia was succeeded by grey, reversal was no longer possible. Sloughing occurred within a few days leaving a fairly regular, but thickened tissue edge (Fig. 2). Rarely necrosis and sloughing of the terminal third of the tail were seen, but the relationships (if any) to ear gangrene were not clear.

When only 1 hind limb or alternate toes of 1 hind limb were amputated, the irritation caused by louse populations in the nuchal and occipital areas stimulated assiduous but relatively ineffective scratching. This reaction some-



Fig. 1. Necrosis of left ear and sloughing of right ear.

times caused laceration of the ear which was distinguishable from the gangrenous process because of breach of the integument, ragged border and presence of extravasated blood. Occasionally both conditions were present simultaneously.

*Experiments to elucidate the aetiology of gangrenous ears*

*Louse infestation*

To determine if infestation with lice could be responsible for the occurrence of ear necrosis, 23-day-old mice that had been subjected to varying degrees of leg debility (A-1, A-2, A-T and N) were seeded with lice and kept at room temperature. Their louse burdens were estimated and they were checked for necrosis at weekly intervals (Fig. 3).



Fig. 2. Sloughing nearly complete: smooth healed edge remaining.

Ear necrosis was noted only in mice that were toe clipped or normal; not in those with amputations of one or both feet. The incidence was somewhat higher in the A-T group than in the N group in which lice had been eliminated by self-grooming.

In another experiment of similar design similar louse burdens were achieved in all groups. However, no necrotic ears developed in any of the mice kept for 139 days. The only difference between the 2 experiments was that they were done at different times of the year, which suggested that temperature or humidity might be a causal factor in producing ear necrosis.

#### *Cold*

Cold is recognized as a cause of peripheral vasoconstriction and presumably could affect the process leading to gangrenous ears. To test this possibility groups of 15 mice each of 3 different ages, which had various degrees of leg

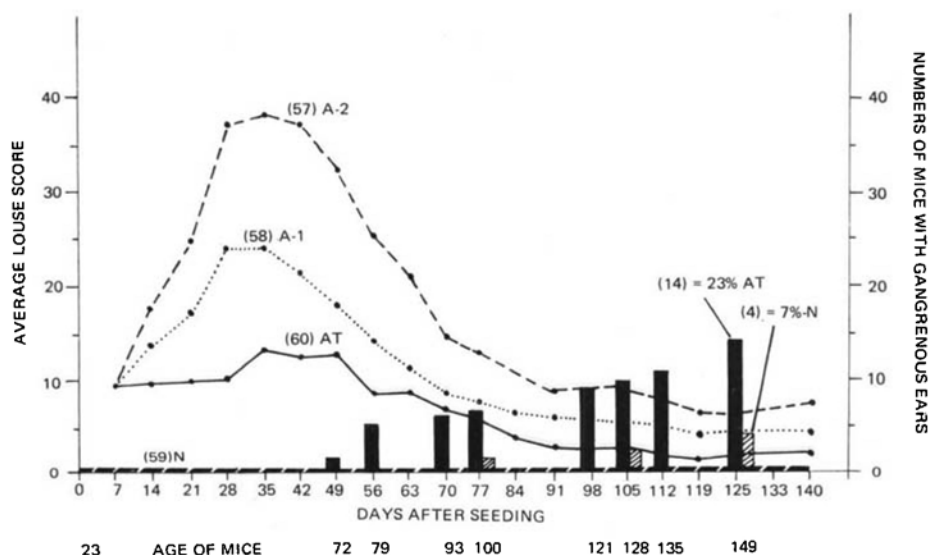


Fig. 3. Occurrence of gangrenous ears in louse-infested mice kept at room temperature. Lines show average louse scores. Columns show cumulative incidence of ear necrosis. Numbers of mice per group in parenthesis.

debility (A-1, A-2, A-T and N), were exposed to cold ( $15^{\circ}\text{C}$ , 50% RH). These mice were kept in glass battery jars with beet pulp for bedding. Ear lesions occurred in all groups of mice, but the condition appeared sooner in the younger mice, i.e. mice 6 weeks old when exposed to cold developed lesions after 4 weeks; those 10 weeks old required 5 weeks; and those 14 weeks old,

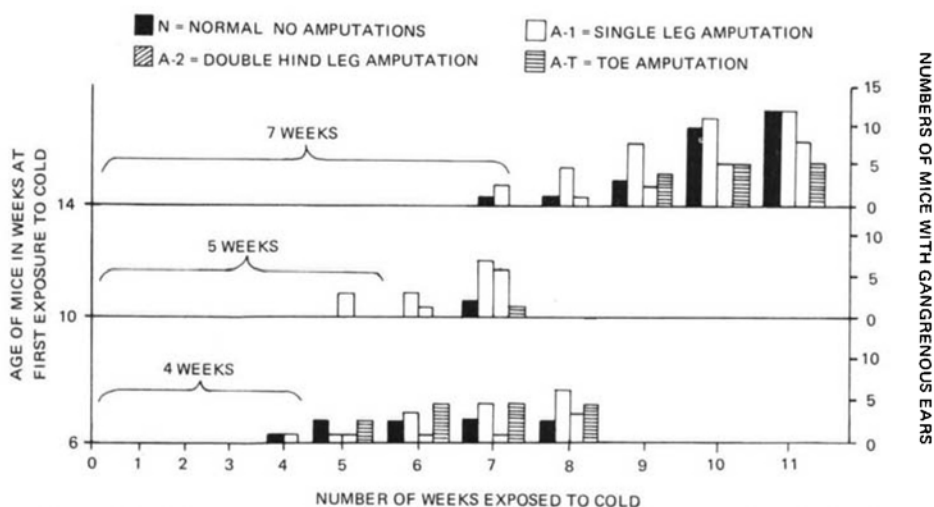


Fig. 4. Effect of age on occurrence of gangrenous ears in normal and amputee mice kept at reduced temperature ( $15^{\circ}\text{C}$ ).

7 weeks (Fig. 4). Controls not exposed to cold did not develop gangrenous ears during the 17 weeks they were observed. No correlation was noted between level of amputation and the percentage of mice that developed necrotic ears. However, the 14-week-old group eventually had a higher percentage of mice with gangrenous ears than the younger groups.

#### *Louse infestation and cold*

At the same time as the 'cold-only' experiment was conducted, groups of 12 mice, with the same levels of amputation, were seeded with lice, held for 63 days until the louse populations were reduced, and then placed in the cold room (15°C, 50% RH) and observed for several weeks. All mice in this phase of the experiment were 14 weeks old. The mice were also housed in glass battery jars and provided with bedding.

The results of this experiment are given in Fig. 5. Gangrenous ears appeared first in mice that were toe-clipped, and this group was the only one in which 100% of the mice evidenced this syndrome. By day 139 all groups of mice had a high proportion of gangrenous ears, those still infested with lice somewhat higher than the N group in which lice had been eliminated by self-grooming.

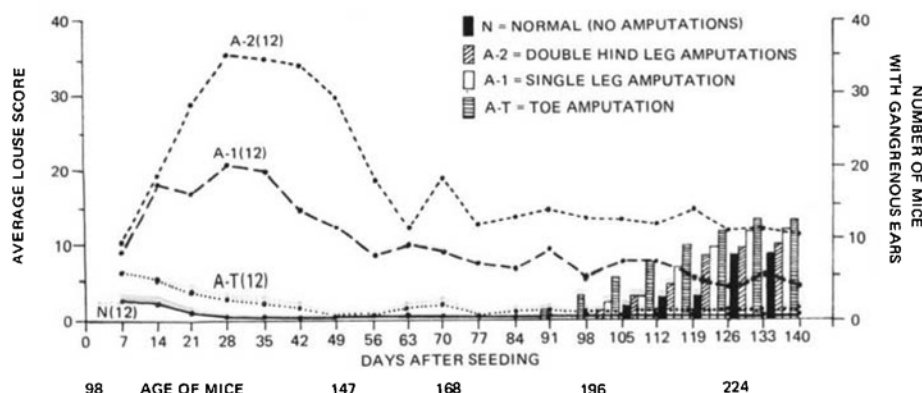


Fig. 5. Influence of reduced temperature (15°C) development of gangrenous ears in louse-infested mice. Lines show average louse scores. Columns show cumulative incidence of ear necrosis.

#### *Grooming trauma, cold and strain difference*

Previous experiments indicated that when mice with alternate toes amputated (A-T) were infested with lice, gangrenous ears often appeared earlier and occurred in a higher percentage of the mice. This suggested that grooming attempts in response to the lice could be a predisposing factor in the production of this condition. If true, the appearance of gangrenous ears should correlate with the side of amputation. An experiment to test this hypothesis was com-

bined with one to determine if this condition is peculiar to the RML mouse or if it could be induced in various other strains of mice.

In this experiment 21-day-old mice of 6 strains were subjected to toe amputation (A-T) on the right hind leg. They were seeded with lice, placed in the cold room (15°C, 50% RH) 21 days later and checked weekly for lice and for ear lesions. The mice were housed in hardware wire cages without bedding, thus insuring more direct exposure to the cold. The results are presented in Fig. 6.

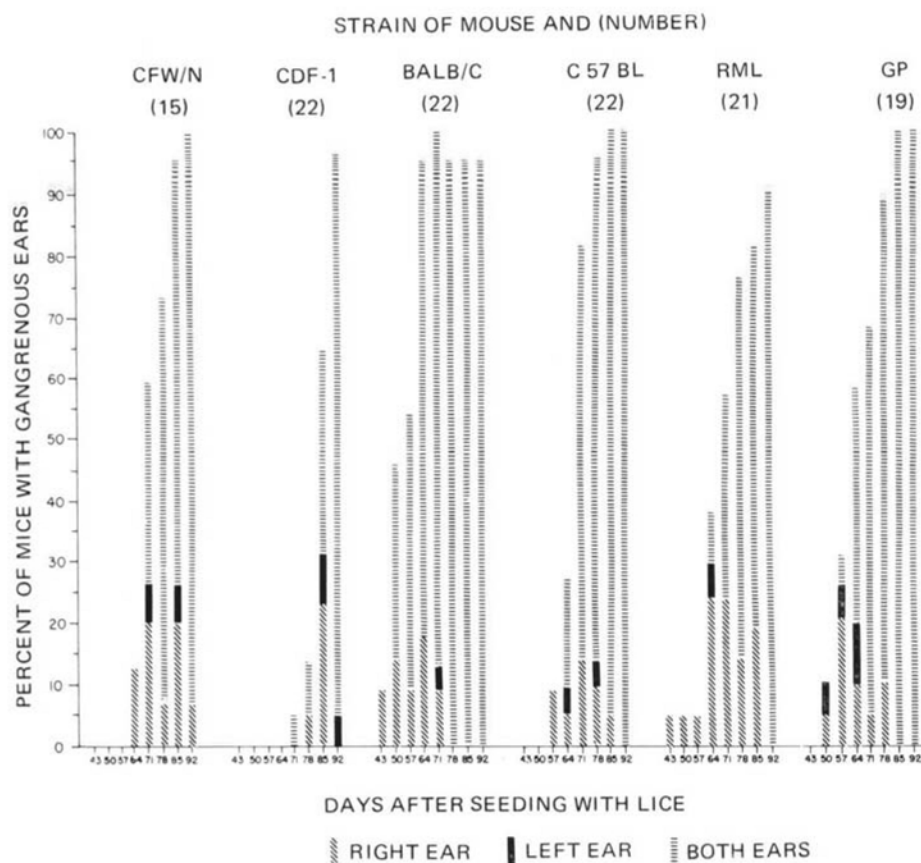


Fig. 6. Comparative susceptibilities of several strains of mice to ear gangrene after toe amputation, and correlation of side of first onset with side of amputation.

In almost all groups the lesion appeared first on the side of toe amputation, i.e. the right ear, but later occurred on the other side, and eventually the lesions were bilateral. Nearly 100% of the mice in the test developed necrotic ears within 71 days of exposure to cold. BALB/c mice were appreciably more susceptible than the other strains, whereas CDF-1 and CFW/N were more



resistant. In addition, except for RML mice, both the louse population (not shown in the graph) and the incidence of early lesions were higher in males of all strains; 16 of 23 early lesions occurred first in males.

#### DISCUSSION

This previously unreported, but well-defined and obvious lesion of the ears of mice, attracted our attention when it occurred sporadically in experiments concerned with various aspects of the host-parasite relationship between laboratory mice and the louse *Polyplax serrata*. Systematic recording of this lesion revealed that it occurred without apparent relationship to the various experimental procedures. Experiments designed to determine the cause of gangrenous ears in mice indicated the following complex aetiology.

Cold is an effective agent, probably specific, that augments the incidence and accelerates development of ear lesions. These experiments also demonstrated that younger mice are more susceptible to the necrotizing effect of cold. Whether other factors such as stress of isolation (Fox, 1968; Ratcliffe & Snyder, 1967; Schmidt & Rehkemper, 1967) are also involved is not known; however, Selye (1967) observed that stress inhibited ischemic necrosis.

Trauma which results from more assiduous grooming in the presence of lice can be an ancillary causative factor. This is indicated by the fact that in all 3 experiments where mice were toe clipped (A-T) and seeded with lice, gangrenous ears appeared earlier and occurred in a higher percentage of the mice than in any other group. Louse infestation alone does not appear to be a specific augmenting factor. This was demonstrated in the experiments where heavily infested mice had fewer ear lesions than those with lower infestations and normal mice.

There are significant differences in the susceptibility of the various strains of mice to gangrenous ears. BALB/c mice were the most susceptible and lesions developed in them 3 to 4 weeks before the more resistant groups (e.g. CDF-1 and CFW/N). Individual differences between mice seem to determine that occasional individuals will be particularly susceptible to development of the lesion. Individual predisposition is difficult to document, except from observations of its occasional occurrence in large groups of animals under apparently similar circumstances.

Under ordinary conditions of mouse colony maintenance ear gangrene is not a common or serious problem, but the lesion becomes prominent and could be important when mice are subjected to specific conducive conditions.

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