with *Streptococcus fecalis* R (ATCC 8043) were made according to the procedure of Stokes *et al.*(8) and with *Leuconostoc mesenteroides* (ATCC 8042) according to the procedure of Dunn *et al.*(9). The inability of diaminopimelic acid from *Escherichia coli* to satisfy the lysine requirement of *Neurospora crassa*—lysineless (33933) was determined according to the procedures of Mitchell and Houlahan(10).

*Summary.* A convenient procedure by which diaminopimelic acid may be readily isolated from the culture filtrate of an *Escherichia coli* mutant is described. The purified diaminopimelic acid resembles that isolated by Work(1) from bacterial hydrolysates with respect to water solubility and absence of significant optical activity. The diaminopimelic acid isolated may be presumed to be the internally compensated *meso* isomer. The possibility that a more water soluble L(+)-diaminopimelic acid may exist in once-crystallized preparations that show only one ninhydrin reactive component was not excluded.

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## Effect of Isoniazid on Early Acute Inflammatory Response in Mice. (20116)

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Recent observations on surgical and postmortem lung specimens from patients treated with Isoniazid for tuberculosis revealed extensive healing(1). The granulation tissue in these healing lesions was very vascular and remarkably free from necrosis and inflammation. For this reason it was decided to determine whether Isoniazid had any effect on the host responses apart from its anti-bacterial activity. The local response to inflammation produced by oil of turpentine in mice was investigated.

*Experimental procedure.* Seventy mice (Swiss Albino) weighing 25-30 g were divided into 2 equivalent groups. One group received 0.25 mg each of Isoniazid (Rimifon) 12 hours prior to subcutaneous injection over the sternal region of 0.025 ml of oil of turpentine. At the time of the oil of turpentine injection, another dose of Isoniazid was administered and thence twice daily until sacrifice. The other group of animals received the oil of turpentine in the same dose and at the same time as the preceding group. Injections of saline were given to this group at the same time that the preceding group received Isoniazid. Fifteen animals in both groups were sacrificed 7 hours and 5 in each group 16, 24, 48 hours and 5 days after oil of turpentine injection. They were autopsied and the area of oil of turpentine injection was excised and prepared for

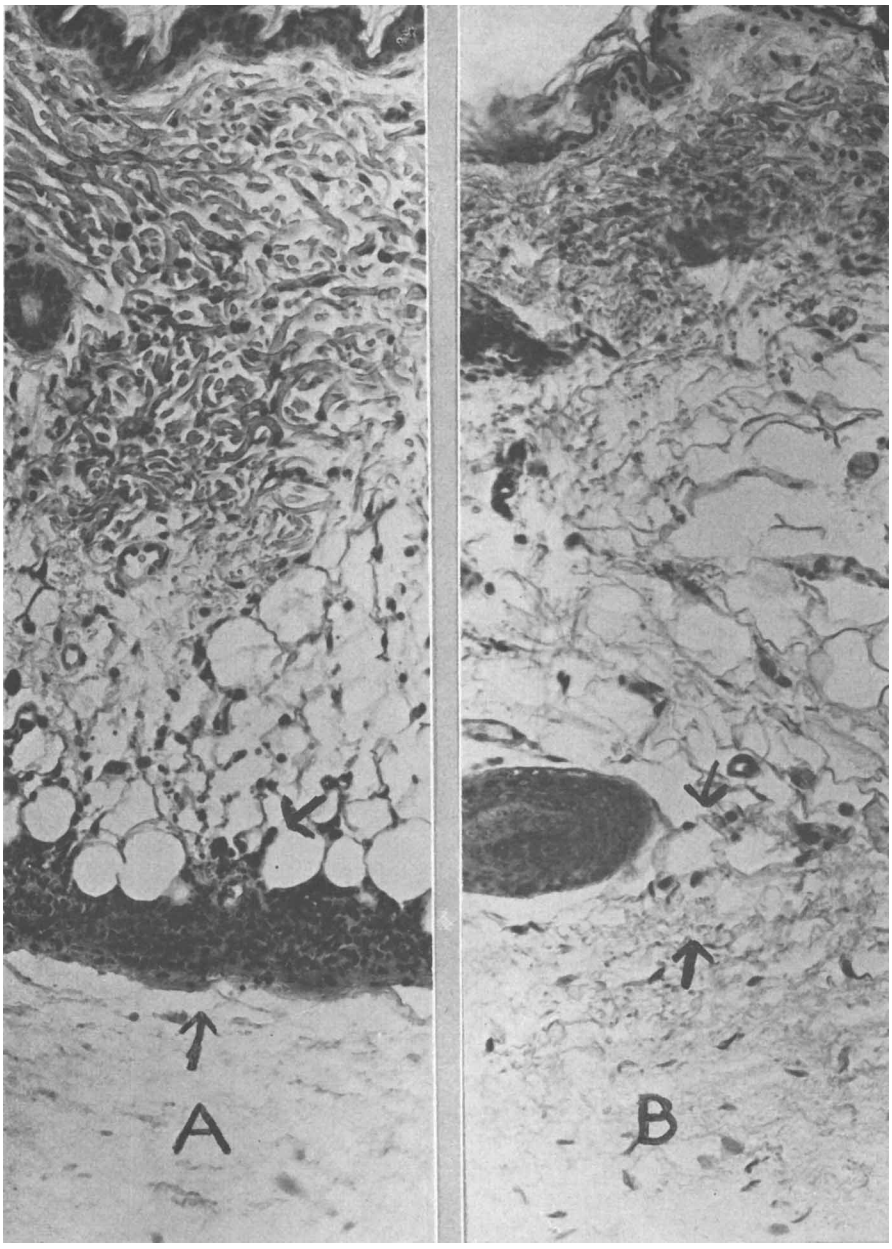


FIG. 1. (A) Photomicrograph (H & E × 350) showing leucocytic zone in control mouse. (B) Photomicrograph (H & E × 350) showing sparse infiltration of leucocytes in Isoniazid treated mouse.

histological examination. The spleens of all animals were weighed and prepared for histological examination. *Another group* of 20 animals were adrenalectomized and divided into 2 groups. One group received 0.25 mg each of Isoniazid 12 hours prior to subcutaneous injection over the sternal region of 0.25 ml of oil of turpentine. At the time of the oil of turpentine injection, another dose of Isoniazid was administered. The other 10 animals received oil of turpentine in the same dose and at the same time, but injections of saline were substituted for Isoniazid. These animals were all killed 7 hours after oil of turpentine

injection and inflammation sites were excised and prepared for histological examinations. The *third group* of 20 mice were wounded on their backs by a special circular punch. These animals were divided into 2 groups and one group received Isoniazid for 5 days in the same dose as the above groups while the other received saline injections. At the end of 5 days the animals were sacrificed. The wounds were excised and prepared for histological examination.

*Findings.* In the 7-hour post oil of turpentine injection control group of animals (those receiving saline injections) surrounding the site of edema produced by the oil of turpentine was a definite zone of inflammatory cells consisting mainly of polymorphonuclear leucocytes. In this zone there were numerous engorged vessels. The zone of leucocytes was compact and measured anywheres from 5-15 cells in thickness (Fig. 1-A).

In the 7-hour Isoniazid treated group of animals, an area of edema corresponding to the area of oil of turpentine injection was present. However, in this group, the leucocytic zone was distinctly less definite and less cellular (Fig. 1-B) at the margin of the edema. There were in some animals occasional scattered leucocytes, monocytes, and lymphocytes. Engorgement of the vessels was not as pronounced as in the former group. Most animals in this group failed to show a distinct leucocytic zone.

In the 16-hour post turpentine injection animals, the differences between the Isoniazid treated and the control animals was less distinct. No differences were noted in the degree and character of inflammation between the 2 groups at 24, 48 hours, and 5 days. In the adrenalectomized animals, the appearance at the end of 7 hours post turpentine injection was identical to that of the non-adrenalectomized animals.

There was no difference in the spleen size in both groups and no evidence of disintegration of lymphocytes or change in size of the Malpighian bodies.

Examination of the degree of granulation tissue formation in the third group of animals that were wounded and sacrificed at the end of 5 days revealed no differences in the degree of wound healing between the Isoniazid treated animals and the control group.

*Discussion.* A recent report(2) indicated that irritation of the hind extremities of rats that were treated with Isoniazid showed diminished amount of edema and temperature rise as compared with control animals. The observations reported here support this finding. It seems, therefore, that Isoniazid apart from its specific anti-bacterial activity exerts a non-specific delaying action on the hosts acute inflammatory response. This effect on the inflammatory response occurs only during the early phases and is temporary. This effect apparently is not mediated through the adrenal gland for the findings were essentially the same in the intact animals and in the adrenalectomized animals. There is also apparently no direct effect on the formation of granulation tissue as manifested by the rate of wound healing and its histological appearance. This non-specific inhibition of the acute inflammatory response may be one of the factors responsible for the rather sudden drop in temperature, marked diminution in sputum, and increase in the feeling of well-being in Isoniazid treated patients with tuberculosis.

*Summary.* 1. Isoniazid temporarily delays the early acute inflammatory response to oil of turpentine in mice. 2. Adrenalectomy does not influence the effect of Isoniazid on early inflammation. 3. Isoniazid has no effect on the rate of wound healing in mice.

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