as a major, or perhaps as the sole, source of potential immunologically competent cells. Furthermore, these results imply that the thymus is not the source of lymphoid precursor cells, but rather that it provides a critical site for the maturation of these cells.

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Immunogenic Activity of Lipids of *M. tuberculosis*

Lipids of mycobacteria are known to be immunogenically active components of tubercle bacilli[1]. First of all, it was surprising that mycobacteria contain lipids up to 35 per cent of their dry weight[2]. This fact did not escape the notice of immunologists. It seemed highly improbable that this fraction of the mycobacteriae should not contain antigens or—more likely—haptens. Since alcohol-soluble lipids form stable aqueous suspensions, they can be examined relatively easily. However, the majority of mycobacterial lipids consists of waxes which form no stable aqueous suspensions and usually exhibit an anti-complementary action. By means of a newly developed microprecipitin technique[3] it became possible to investigate all kinds of lipids, independently from their solubility in organic solvents.

The extracts were prepared according to the method described by Aebi *et al.*[4]. Seven fractions were obtained: fats, phosphatides, waxes *A*, *B*, *C* (cord-factor) and *D*, and firmly bound lipids. It has been shown that only three of these fractions contained compounds capable of combining with antibody[5]. These fractions were the phosphatides and the waxes *B* and *D*. All other lipids were serologically inactive. The phosphatides and the waxes *B* showed no strain-specificity. However, the wax *D* might have strain-specificity[6]. It is interesting to note that *C* (cord-factor), the toxic substance of mycobacteriae, did not combine with antibody. Consequently, antitoxic immunity might be impossible.

The waxes *B* did not always contain serologically active substances. This might be due to minor variations of the fractionating procedures. The active substance of the phosphatide fraction consisted of phospholipids, which contained inositol and 2–5 mannoses[7]. After saponification, phospholipids gave no precipitation, while with the water-soluble part of the wax *D* a weak precipitation could be observed. (Pure phospholipids and many other fractions were kindly supplied by Prof. E. Lederer and Mme. E. Vilkas, Gif-sur-Yvette, France.) The hydrophobic part of the molecules (for example, mycolic acid) had no antibody-combining capacity. Evidence available at present indicates that the determinant groups of lipid haptens are hydrophilic.

The immunogenic activity of mycobacterial lipids was experimentally tested in guinea-pigs. Groups of 10 guinea-pigs each of mixed colour and sex, approximately 500 grams in weight, were used. Groups of guinea-pigs were inoculated subcutaneously with phosphatides (0·5 mg phosphatide per ml.), wax *B* (0·25 mg wax *B* per ml.), wax *D* (0·5 mg wax *D* per ml.) with and without bovine serum albumin (0·5 mg/ml.) in 1 ml. of Freund's adjuvant. Control animals received Freund's adjuvant alone (1 ml., 'Arlacel *A*', Paraffinöl, Merck, saline), heat inactivated bacteria (1 mg/ml.) of the strain *H* 37 *Rv*, and living bacteria of the *BCG* strain (1 mg/ml.).

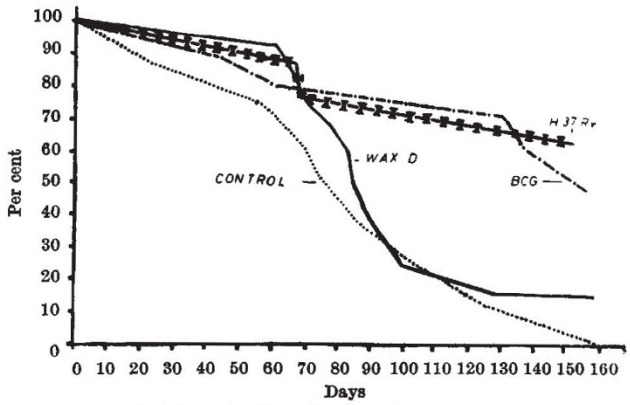

Fig. 1. Survival-time of guinea-pigs (wax *D*). Day 0 represents the day of challenge (4 months after immunization)

In order to avoid non-specific reactions, the animals were infected with 1 mg of virulent bacteria of the strain *H* 37 *Rv* 4 months after immunization. They were observed for 160 days. After that period all control animals inoculated with Freund's adjuvant alone died. The tuberculosis was diagnosed macroscopically.

Fig. 1 shows the results of a typical experiment. The survival time of the control group and of the test group (wax *D*) did not differ significantly. The results of the other control experiments (heat-killed *H* 37 *Rv* and *BCG*) indicated a partial protection against tuberculosis; the difference between the survival time of these groups is significant. The phosphatides, waxes *B* and waxes *D* failed to provide measurable immunity, even when administered together with bovine serum albumin.

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PATHOLOGY

Cutaneous Elastin in Ehlers–Danlos Syndrome

Ehlers–Danlos syndrome (cutis hyperelastica, india-rubber skin), a rare heritable generalized disorder of the connective tissues, is characterized by hyperextensibility of the skin, hyperlaxity of the joints, fragility of the skin, and, not infrequently, by one or a combination of such internal manifestations as cardiac anomalies, dissecting aneurysm of the aorta and diaphragmatic hernia[1]. Previous investigations directed towards identifying the fundamental defect in the connective tissues, using the methods of light and electron microscopy, have led to contradictory results. Many investigators have described an increase in the amount of elastin in the corium while others have observed a normal or even a decreased amount of elastin[1]. Similar controversy exists over the possibility that the collagen is either quantitatively or qualitatively abnormal in this disease[1,2]. The purpose of the work reported here was to isolate elastin quantitatively from the skin of patients with this disease and from the skin of normal, control subjects, and to examine chemically the purified elastin isolated from these two sources.

Normal human skin was obtained as necropsy specimens from the thighs of Caucasian females. The skin from four female patients with Ehlers–Danlos syndrome (E-D) was obtained as biopsy material from the same site as in