collected on Millipore filters. 2) Following a single intravenous injection of $S^{35}O_4$ rat peritoneal mast cells take up the radioactivity; the maximum is reached by 48 hours. No loss of radioactivity is evident in the following 5 days. Radioactivity in other free cells of peritoneal fluid attains a maximum at 4 hours and then falls rapidly to low levels.

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Local Shwartzman Reaction in Rabbit Oral Mucosa with Endotoxin from Oral Bacteria.* (25914)

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Although endotoxins from many bacteria have been isolated and tested for toxicity, little work has been devoted to endotoxins from oral microorganisms. Recently, endotoxins from oral bacteria, isolated by tryptic digestion of cells and also by the phenol-water extraction method, were shown to possess many chemical properties and biological activities characteristic of classical lipopolysaccharide endotoxins(1,2). Primary toxicity to rabbit skin was demonstrated, and the localized Shwartzman reaction of hemorrhagic necrosis was produced by administering these endotoxic preparations first locally into skin, and then intravenously. The local Shwartzman effect has been achieved with many endotoxins in different tissues(3,4) yet no successful attempts seem to have been made to produce this reaction in tissues of the oral cavity. Because of the possibility that bacterial endotoxins may have etiologic significance in oral soft tissue diseases either through primary local toxicity or through Shwartzman-like effects, one of the recently isolated endotoxins was tested in rabbit oral mucous membrane.

Materials and methods. New Zealand white rabbits weighing 1.7 to 2.5 kg were anesthetized by intravenous injection of 40 mg per kg of pentobarbital and access to the posterior oral region was obtained by means of a rodent mouth prop previously described (5). With a modified 30 gauge needle, 50-100 μg (0.2 ml) of an endotoxin prepared by the phenol-water method from *Veillonella* organisms(1) was injected into an area which included the gingiva and palatal mucosa adjacent to the last 2 upper molar teeth. The corresponding site of the contralateral side was given a control injection either of 100 μg (0.2 ml) of soluble products from a human oral strain of viridans streptococcus or of 0.2 ml of 0.85% sodium chloride (saline). The streptococcal products contained proteins(6), carbohydrates (Molisch), and chloroform-soluble lipids, derived also by the phenol-water extraction procedure. Comparable dos-

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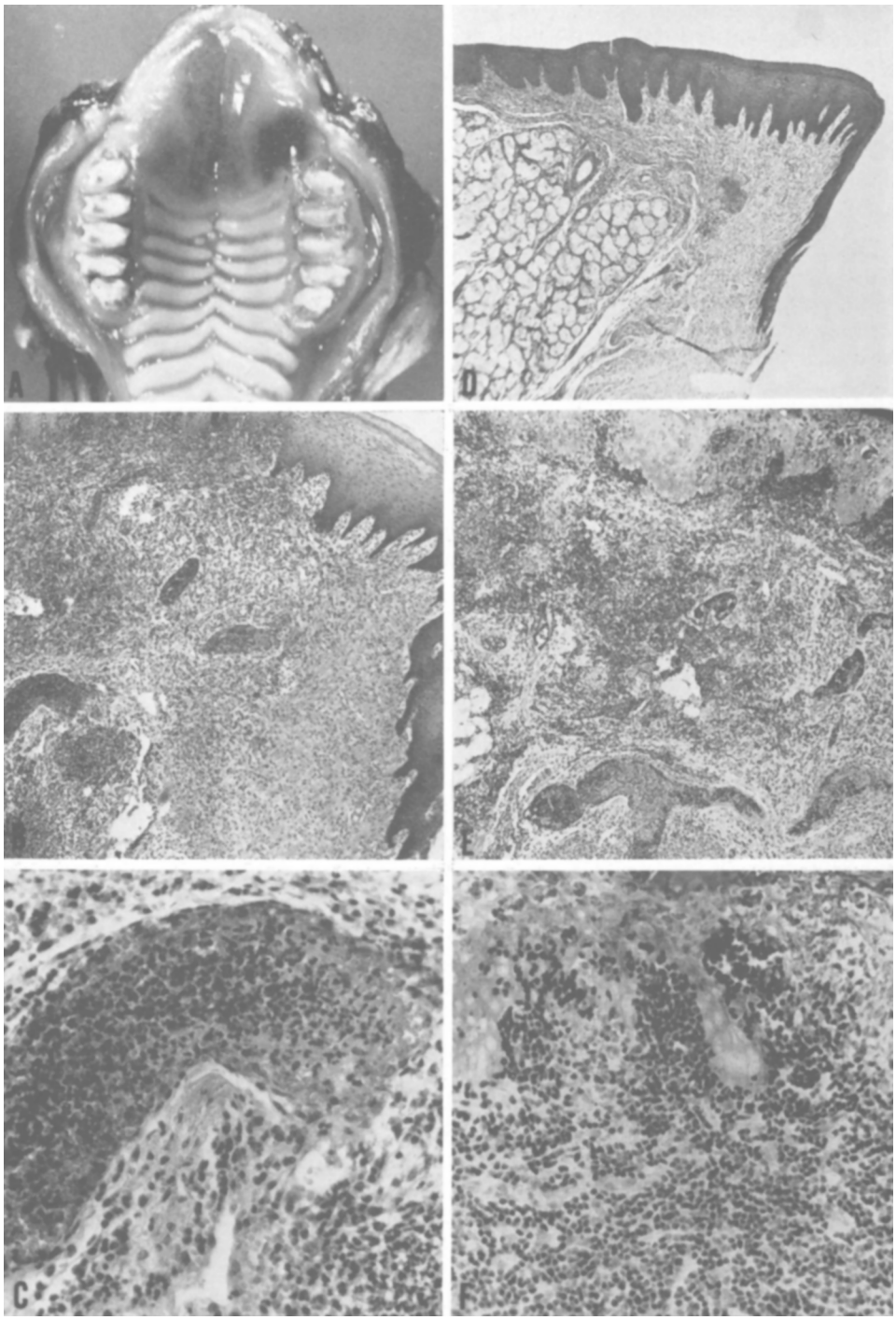

FIG. 1. Rabbit oral tissue reactions following intrav. endotoxin 14 hr after local inj. of *Veillonella* endotoxin and of streptococcal products.

A. Shwartzman reaction in gingivo-palatal mucosa of upper right jaw. Left side of jaw shows negligible reaction to streptococcal products.

B. Shwartzman reactive tissue stained to show diffuse and focal leucocyte infiltration and

ages of these substances were also injected into the shaved skin of the animals. To test for the Shwartzman reaction, rabbits were given 125 μg of *Veillonella* endotoxin in the marginal ear vein 12-24 hours after local injection. Approximately 6 hours following the intravenous dose, animals were sacrificed, and tissue surrounding and including the molar teeth was fixed in formalin. Subsequently, the specimens were decalcified in 5% formic acid, imbedded in paraffin, and sectioned at 7 μ. In some instances, the soft tissue which included the lesion was dissected from bone and tooth and processed for histological examination without decalcification. Sections stained with hematoxylin and eosin, with Lillie's azure-eosin, and by the periodic acid-Schiff method were examined microscopically.

Results. In rabbits given preparatory and provoking injections of endotoxin, gross signs of the local Shwartzman reaction were evident. Dark red hemorrhagic areas became visible in the prepared sites within several hours following the intravenous dose, whereas control sites injected with streptococcal products showed barely perceptible discoloration (Fig. 1A). Histologically, the Shwartzman lesions showed the classical features previously described in skin(2,7,8,9) including extensive leucocyte infiltration (Fig. 1B), leucocytic thrombi (Fig. 1C), and hemorrhage (Fig. 1E,F). Control sites given streptococcal products and provoked with intravenous *Veillonella* endotoxin contained an occasional focus of necrosis with minimal leucocytic response and hemorrhage (Fig. 1D). In sites prepared with endotoxin but not provoked, the leucocytic response was considerably less severe than in the Shwartzman lesions and hemorrhage was absent. These unprovoked endotoxin lesions, however, contained much heavier leucocytic infiltration than either the provoked or the unprovoked lesions obtained with comparable amounts of streptococcal products. This difference in polymorphonuclear response was equally evident in both oral mucosa and skin. Comparison of response of oral mucosa and of skin to similar local injections or to similar combinations of local and intravenous injections revealed that gross and histologic manifestations following a specific type of insult were basically similar in both tissues.

Discussion. It has yet to be established that the laboratory demonstration of a local Shwartzman reaction in oral tissues by injection of endotoxin from organisms of the gingival crevice has a direct counterpart in human disease. However, the finding that a relatively temporary alteration in the blood can provoke a violent reaction in local sites within the oral cavity reflects the close relationship existing between oral tissue reactivity and systemic changes, and at least suggests that a similar mechanism may operate in oral disease. Periodontal conditions which should be considered in the light of the Shwartzman phenomenon include acute Vincent's necrotizing gingivitis and the acute exacerbations of chronic gingivitis frequently associated with an episode of generalized illness. In both of these acute conditions there is evidence of interplay between local tissue reactivity and somewhat temporary systemic alterations.

It is significant that the reaction of oral mucosa to injection of different substances resembles rather closely the skin reactions to these same substances. This finding gives support to use of skin as a convenient tissue for testing substances thought to be toxic to mucous membranes, and thus validates investigations of experimental infections in skin with oral bacteria(10,11).

Summary. The local Shwartzman reaction was elicited in the rabbit oral cavity and skin with endotoxin prepared by phenol-water ex-

several venous thrombi. Crevicular epithelium of upper right molar at right. H & E 50×.

C. High power view from B, showing numerous leucocytes in typical thrombus. H & E 209×.

D. Tissue adjacent to upper left molar showing small area of necrosis and minimal leucocytic response to local inj. of streptococcal products and intrav. endotoxin. H & E 51×.

E. Section from same block as B and C stained to show extravascular and intravascular distribution of red blood cells; white cells unstained. Alcian Blue-eosin B. 61×.

F. High power view of sub-epithelial area from E showing hemorrhage. Alcian Blue-eosin B. 238×.

traction procedure from a strain of oral *Veillonella*. Lipid-carbohydrate-protein products prepared by same procedure from viridans streptococci, or a solution of physiologic saline did not produce this reaction in either tissue. Lesions obtained in oral mucosa with each substance were grossly and histologically similar to lesions obtained with the same material in skin.

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Effect of Adrenalectomy and Cortisone on Eruption Rate of Incisors in Young Female Albino Rats.* (25915)

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Schour and Van Dyke(1) reported that rate of eruption of the continuously erupting rat incisor became progressively slower and finally ceased in hypophysectomized rats. Administration of growth hormone produced only a slight increase in rate of eruption of such animals but had no effect in intact rats. Baume *et al.*(2) observed that thyroidectomy in young rats produced a reduction in rate of eruption although not so severe as that produced by hypophysectomy. These authors (3) also reported that simultaneous administration of thyroxin and growth hormone in hypophysectomized rats brought about a restoration of the tissues of the incisor and an increase in rate of eruption. Schour and Rogoff(4) observed a disturbance in calcification of dentin in the rat incisor following adrenalectomy; however, due to the short survival period, rate of eruption was not measured. Leroy and Domm(5) reported that cortisone produced precocious eruption of incisors in young rats when administered to pregnant mothers, to the fetus *in utero*, or in newborn shortly after birth. Domm and Marzano(6) found that cortisone also accelerated rate of eruption of incisors when administered in sexually mature rats. Since adrenal function is depressed following hypophysectomy and since the rate of eruption of the rat incisor has been shown to be stimulated by adrenal cortical hormones we were interested in determining the effects of adrenalectomy and of cortisone and salt therapy on this rate in young female adrenalectomized rats.

Procedures. Twenty-four female rats, of the Sprague-Dawley strain, bilaterally adrenalectomized at 39 days of age, and 12 unoperated controls of the same age were studied. Twelve operated and 6 normals received daily subcutaneous injections of 1.5 mg of cortisone,‡ 6 days per week for 6 weeks. The remaining animals served as operated and intact controls. All controls received injections of physiological saline while adrenalectomized controls in addition received 1% NaCl in drinking water. At the end of the sixth week all treatment, daily injections and NaCl in drinking water was discontinued and observations continued for a second 6-week period.

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‡ Cortisone (Cortone Acetate) generously supplied by Merck, Sharp & Dohme, Division of Merck & Co., Philadelphia, Pa.