difficulties, and, in addition, the hormone could be self-administered.

The administration of drugs by the aerosol route has long been an accepted mode of therapy. Many bronchodilators, antibiotics and the steroid hormone, cortisone, have been satisfactorily given by this method. The bronchopulmonary epithelium is highly vascular and offers an extensive area for absorption. When penicillin and other of the antibiotics are employed in this manner, blood levels comparable to those obtained when these agents are introduced either intramuscularly or intravenously are reached. There are some substances, however, which cannot penetrate this capillary barrier and are not absorbed by this means.

Rud(9), and Bonner and Homburger(7) demonstrated that simple fasting can produce a significant drop in the eosinophil levels in normal people. Hence, in order to overcome this physiological alteration, control counts were made shortly after breakfast.

The absence of adrenal insufficiency and the potency of the preparation used were indicated by previous response of the same subjects to intramuscular administration of the same lot of ACTH. Thus, it is apparent that ACTH, given by the aerosol route, is not absorbed.

Summary. Observations on 6 normal subjects showed that eosinopenia did not occur following aerosol administration of ACTH, indicating that ACTH is not absorbed from the bronchopulmonary tree.

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Received April 14, 1952. P.S.E.B.M., 1952, v80.

Crystalline Material in Gastric Secretion. (19547)

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Following the report by Hollander(1) which described from light microscopy unidentified crystalline structures in dried smears of gastric juice, the attempt was made here to identify definitely the crystal molecule by means of electron and x-ray diffraction and to reproduce the dried, crystalline forms on electron microscope specimen screens. Human gastric secretion, obtained by Rehfuss tube from the stomachs of routine hospital patients was used in some experiments; specimens were also studied of mucus from Heidenhain pouch dogs obtained by topical stimulation with acetylcholine.*

Both the human and animal material were analyzed by electron and x-ray diffraction and found to be at least 90% NaCl. Table I shows the x-ray data. With the exception of a few low intensity lines the NaCl values were reproduced exactly by the mucus. The few extra lines were not identifiable. The only identified compound in both x-ray and electron diffraction was NaCl.

Small drops of the mucus were placed upon prepared electron microscope screens and dried slowly in air, and in the resultant electron micrographs all of the forms observed in the light microscope were discovered. Fig. 1, 2, 3, and 4 illustrate the appearances. Rela-

* Samples of dog secretion were obtained from Dr. Franklin Hollander, Mount Sinai Hospital, N. Y. City.

TABLE I. "d-values" and Intensities of Diffraction Patterns of Gastric Secretions.

Gastric secretion				NaCl reference	
X-ray		Electron		X-ray	
d	I	d	I	d	I
3.47 Å	.1				
3.27	.4	3.27 Å	.5	3.27 Å	.5
3.15	.7	3.15	.4	3.14	.4
2.82	1	2.82	1	2.82	1
2.22	.6	2.23	.3	2.21	.3
2	.9	2.01	.9	1.99	.9
1.82	.3	1.82	.9	1.81	.1
1.71	.2	1.72	.4	1.70	.4
1.63	.6	1.64	.6	1.63	.6
1.58	.2				
1.41	.5	1.41	.5	1.41	.5
				1.30	.2
		1.34	.7		
1.29	.2			1.28	.1
1.26	.6			1.26	.7
1.16	.6	1.15	.6	1.15	.6
1.11	.1				
1.09	.1			1.09	.3
1.05	.2				
.999	.5			.998	.5
.958	.1				
				.954	.2
.943	.5			.941	.5
.894	.5			.892	.5
.852	.4			.851	.5
.842	.1				
.817	.1			.815	.2
				.790	.2
.783	.2			.783	.4

tively large droplets produce the ferns and fronds of Fig. 1, 2, and 3. Small dilute droplets produced the single crystals of Fig. 4. Fig. 1 and 2 are reminiscent of parts of Fig. 4 and 5 in reference 1, and Fig. 3 is similar to parts of Fig. 2 in the same reference except for the larger magnification and superior resolving power of the electron microscope.

In Fig. 4 and others the single crystals appear to be cubic as would be expected of NaCl. Further evidence that the crystals are NaCl comes from electron bombardment experiments. When NaCl and some other crystals are bombarded by intense electron beams they evaporate in a characteristic manner, leaving a 3-dimensional residual envelope behind. Such envelopes of a large crystal and of some tiny crystals are seen in Fig. 4.

The evaporation of these crystals from gastric mucus progresses in a manner identical with that reported by Watson and Preuss(2) for NaCl. Fig. 5 shows before bombardment a particularly dense field in which no crystals are visible except in cracks and fissures in the deposited material (see arrows). Fig. 6 shows the same field after bombardment, and the crystals are now visible as residual envelopes. Even over the opaque part of the field the heat of the beam has driven off the crystal content and the locations of many large crystalline areas, previously invisible are demonstrated.

In addition to the crystalline component of the mucus there is also the non-crystalline, opaque substance which is nicely visible as background material in Fig. 7.

These observations authenticate the earlier beliefs of Henning and Norpoth(3) that the single crystals and fern-like aggregates were NaCl. The physical appearances which the crystalline material takes are not particularly significant and may be affected by such things as rate of drying, concentration of solution and presence of foreign organic matter: the chemical nature is not. The fern-like fronds are not specific for any particular crystalline substance but are often observed in biological specimens where foreign matter is present to affect the laying-down of the solid crystals. If the resolution and magnification are sufficiently increased, as in high resolution electron microscopy the ultimate single-crystal, cubic nature of such dried deposits of NaCl can always be demonstrated (Fig. 8). Certainly the effects cannot be attributed to stains used in the light microscope procedures because no stains are used in the electron microscopy although the same effects are produced.

The relatively high percentage of NaCl does not rule out the possibility of the presence of minute amounts of other crystalline material. The few additional x-ray lines demonstrated in the present work indicate that other crystals are indeed present. They might be gastric mucins. To identify them by x-ray diffraction would require concentration of the unknown with elimination of the NaCl.

Summary. Human and canine gastric secretion mounted upon electron microscope specimen screens is found to dry in fern-like patterns of tiny single crystals. These crystals evaporate under electron bombardment in a manner similar to NaCl. X-ray diffraction analysis of the dried secretions gives a strong

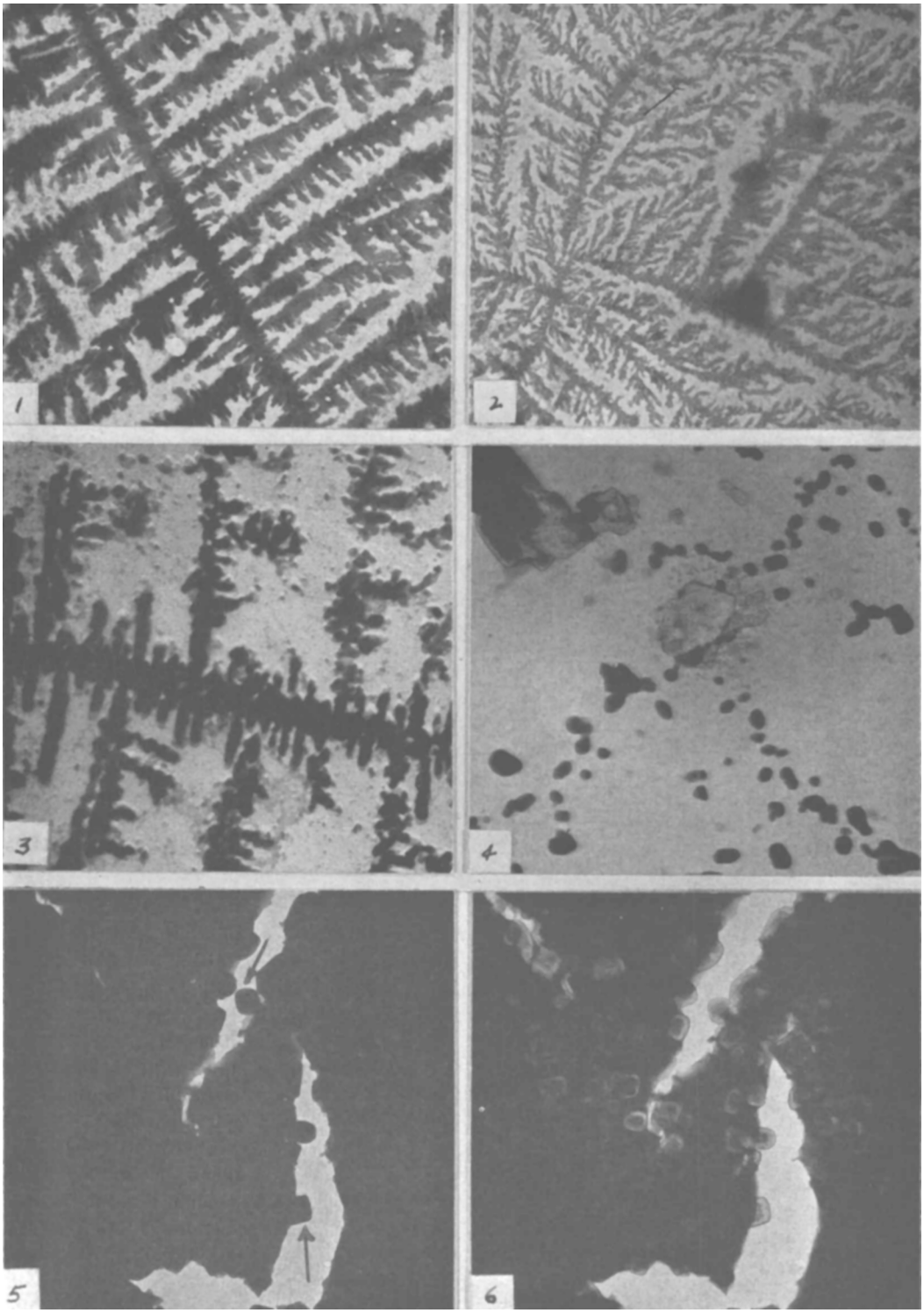

FIG. 1. Fern-like deposits of crystalline material in dried gastric secretions (human), ×7000.
FIG. 2. Same as Fig. 1, ×7000.

FIG. 3. " " " 2, ×5000.
FIG. 4. Single crystals in dried smears of gastric secretion (human), ×5000.
FIG. 5. A very thick deposit of dried gastric secretion (human) before electron bombardment, ×3000.
FIG. 6. The same field as Fig. 5 after electron bombardment, ×3000.

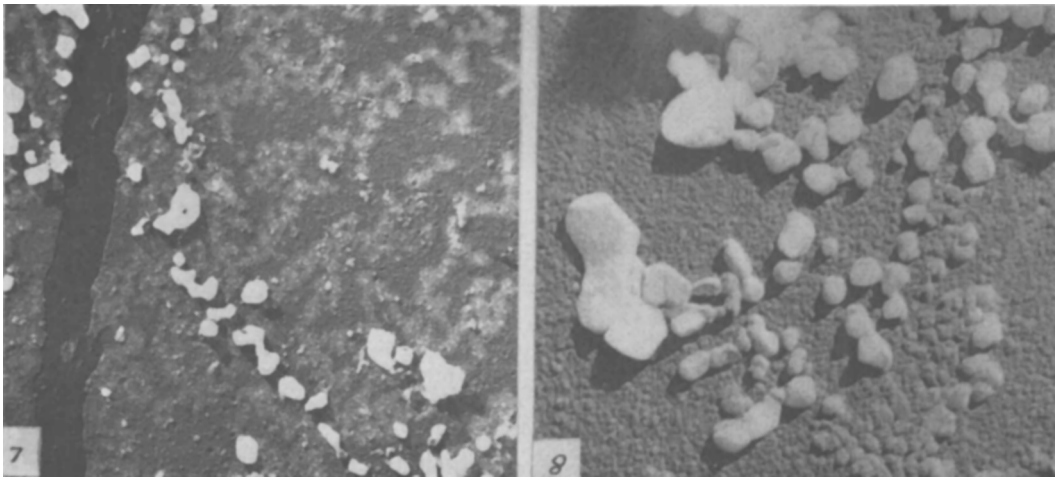

FIG. 7. A shadow cast preparation of gastric secretion (human) showing large NaCl crystals and amorphous background material, ×4200.
FIG. 8. A shadow cast preparation of NaCl itself. The field is part of a frond at high magnification to show the manner in which the fronds are formed of countless tiny crystals, ×25000.

NaCl identification with some weak unidentified lines also present.

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Received April 15, 1952. P.S.E.B.M., 1952, v80.

Diphenylacetyl-1,3-Indandione as a Potent Hypoprothrombinemic Agent. (19548)

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As a result of the therapeutic importance of anticoagulant drugs, the literature reveals a continuing search for compounds which will inhibit blood coagulation. A recent review by Seegers(1) includes a summary of the published information on prothrombinopenic substances, citing studies on indandione derivatives as hypoprothrombinemic drugs. A number of 1,3-indandiones, including two previously studied by Kabat, Stohlman and Smith (2), were prepared in these laboratories and submitted to us for evaluation as to their potential prothrombinopenic properties. Out of the group studied, 2-diphenylacetyl-1,3-indandione (U-1363; Dipaxin*) was a particularly potent hypoprothrombinemic substance.

The data establishing the above observation,

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