

Table II.—Summary of development of biotin deficiency symptoms through 6 weeks on test diet

Weeks	Symptoms
2	Dull rough coat
3	Slight achromotrichia
4	Slight alopecia on ventrum Coat light colored Incrustations about eyes
5	Ventrum bare Coat very light colored Bare patches on hind dorsum Nose and mouth swollen Eyes sealed shut Jittery, jerky movements Kangaroo stance
6	Complete alopecia

approximately 1 mm per day and finally disappearing at about the time full length is attained. The hairs are consistently lighter in color than the normal coat.

Injections of 4 micrograms of biotin per day quickly alleviate the symptoms. During the first week the dermatitis, the swelling of nose and mouth and the incrustations about the eyes disappear; this is accompanied by a sharp increase in weight. By 2 weeks there is great improvement in disposition and behavior. In some denuded areas, hairs appear shortly after the first injection; progressively hairs appear in other areas. The earlier hairs are lighter than normal while those emerging later are light at the tips and dark at the bases. Finally hairs appear which possess full pigmentation. Hairs attaining full length as early as 11 days after the initial injection are retained. By 4–6 weeks all animals appear normal.

Biopsies of skin show the epidermis of deficient animals to be noticeably thicker than that of controls. This thickening is primarily in terms of the stratum corneum although thickening in the stratum germinativum is also apparent. Mitotic figures in the basal layers are plentiful being slightly more numerous than in normal skin. The epidermis is moderately keratotic and contains abundant keratohyalin granules. The orifices of the pilosebaceous units are markedly dilated and are commonly plugged with keratinized debris. The sebaceous glands are for the most part normal although occasionally a gland appears disrupted. The hair follicles appear normal and often exhibit hairs in various stages of development. Also present are resting hairs the clubs of which are normal but frequently the shafts are broken below the surface of the skin.

Discussion. Incorporation of egg white in the diet of the hamster produces symptoms similar to those attributed to biotin deficiency in the mouse. In mice the rate and cycles of hair growth are unaffected by deficiency. The alopecia is the result of faulty hair retention which appears to be due to imperfect keratinization of the hair shaft adjacent to the club (RAUCH⁶). The same is true of the hamster where hairs are observed to elongate at the normal rate but break off as full length is attained. Deficiency produces progressive achromotrichia in the hamster as well as in the mouse. Even during deficiency pigment is elaborated and incorporated into the growing hair. As the biotin level falls, however, so does the intensity of the pigment. In this way, the hair is progressively lighter from tip to base and from one hair generation to the next. The fact that this sequence is easily and quickly

reversed upon administration of biotin is further indication that the process of pigment synthesis is particularly sensitive to biotin level.

Skin taken from deficient animals reveals changes resembling more those described by MONTAGNA⁷ for the mouse than those of the rat. In the hamster the skin is dry rather than covered with brownish incrustations as in the rat. There is only moderate keratosis in the hamster and the mouse as compared to the extensive hyperkeratosis developed in the rat. The sebaceous glands in the hamster seem to be less disturbed structurally than either in the mouse or rat, although the dryness of the skin is suggestive of impairment of sebaceous secretion.

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Zusammenfassung

Durch einen Eiweissgehalt von 40% in einer Diät wurde ein extremer Biotinmangel erzeugt. Folgende Symptome waren das Resultat: Wachstumshemmung, Hautentzündung (Dermatitis), Haarausfall und Verlust der Haarfarbe. Durch tägliche Dosen von 4 µg Biotin konnte dieser Zustand rasch gebessert werden.

⁷ W. MONTAGNA, Proc. Soc. exp. Biol. N. Y. 73, 127 (1950).

Zur Frage der entzündungshemmenden Wirkung des Phenylbutazon bei hypothyreotischen Ratten

Am Formalin-Pfotenödem normaler Ratten zeigt Phenylbutazon (Butazolidin Geigy) eine ausgeprägte anti-inflammatorische Wirkung (DOMENJOZ, THEOBALD, WILHELMI, WILHELMI *et al.*¹). In der vorliegenden Arbeit berichten wir über den entzündungshemmenden Wirkungsgrad des Phenylbutazon an der Formalinarthrit hypothyreotischer Ratten.

Methodik. Den Versuchstieren verabreichten wir in 24stündigem Abstand 4-Methyl-2-Thiouracil (MTU) während einer Zeitspanne von 18 und 31 Tagen in einer Dosierung von 100 mg/kg/Tag per os (Emulsion mit Gummi arabicum). Der Entzündungsversuch (Methodik nach DOMENJOZ *et al.*²) erfolgte 24 Stunden nach der letzten MTU-Verabreichung. Phenylbutazon wurde in einer Dosierung von 200 mg/kg s. c. 30 min vor der subplantaren Injektion von 0,1 cm³ Formalin 3prozentig appliziert. Die Pfotenschwellung wurde 135 min nach Injektion des Phlogistikums gemessen.

Ergebnisse. Aus den Daten der Tabelle ist zu ersehen, dass Phenylbutazon 200 mg/kg s. c. an der normalen Ratte eine intensive Hemmung der Formalinentzündung

¹ R. DOMENJOZ, Arch. exp. Path. Pharmac. 225, 14 (1955). – W. THEOBALD, Arch. int. Pharmacodyn. 103, 17 (1955). – G. WILHELMI, Medizinische 1591 (1952). – G. WILHELMI und J. R. CURRIE, Schweiz. med. Wschr. 84, 1315 (1954).

² R. DOMENJOZ, K. MÖRS DORF, E. G. STENGER und W. THEOBALD, Arch. exp. Path. Pharmac. 230, 325 (1957).

⁶ H. RAUCH, Physiol. Zool. 25, 145 (1952).

Tabelle. Antiphlogistische Wirkung von Phenylbutazon 200 mg/kg s.c.am Formalinpfotenoedem normaler und hypothyreotischer Ratten.
K Kontrollen; Ph Phenylbutazon

Behandlung	Tierzahl n	Tiergewicht g	Schwellung in mm ³ nach 135 min	ε ±	Oedem- hemmung in %	Sign. Diff. D
1. Normale Ratten						
K	33	145	214	11,4	—	—
Ph	20	147	85	15,8	60	6,7
2. 18 Tage 100 mg/kg/Tag p. o. MTU						
K	54	154	234	13,7	—	—
Ph	55	155	166	13,0	29	3,6
3. 31 Tage 100 mg/kg/Tag p. o. MTU						
K	57	150	189	13,7	—	—
Ph	60	164	138	13,1	27	2,7

von 60% bewirkt, während bei hypothyreotischen Ratten die Schwellung lediglich um 29 beziehungsweise 27% gehemmt wird. Hingegen wird durch die MTU-Vorbehandlung bei den jeweiligen Kontrollratten (234 beziehungsweise 189 mm³) keine nennenswerte Änderung der Schwellungsintensität gegenüber unbehandelten Tieren (214 mm³) ausgelöst.

Längerdauernde MTU-Behandlung der Ratten beeinflusst somit nicht die Fähigkeit des Pfortengewebes, auf eine Irritation im Sinne einer Entzündung zu reagieren. Ob die thyreostatische Wirkung des Phenylbutazon in Zusammenhang mit den beschriebenen Versuchsergebnissen steht, kann zur Zeit nicht beurteilt werden. Weitere Versuche sind zur Interpretation dieser Befunde erforderlich.

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Summary

Following pretreatment of rats by 4-methyl-2-thiouracil the anti-inflammatory action of phenylbutazone on formalin edema is strongly diminished.

PRO EXPERIMENTIS

Description of a Corona-Type Loudspeaker Used in Bioacoustic Research¹

Rapid developments in jet-propulsion devices have focused interest in recent years on the problem of the effects of noise on man. It is now well established that intense acoustic noise can constitute a health hazard in several ways: (1) through causing ear damage; (2) through creating unsafe working conditions because of interference with speech communication, and (3) through causing general disabling effects not directly involved with hearing, such as excessive fatigue, extreme irritability, and loss of neuro-muscular coordination².

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² H. DAVIS, *Ann. Otology, Rhinology and Laryngology* 58 [3], 732 (1949). – H. O. PARRACK, *Noise-Causes, Effects, Measurement*,

For several years we have used laboratory animals in studies of the harmful effects of intense noise on bodily functions other than hearing. These studies have shown that intense noise at low frequencies (140 decibels, 150-4800 cycles/s) does not seem to overtax the animal's adaptive defense mechanisms³. Some laboratory animals, however, can hear up to 40 kilocycles⁴. Presumably they also have maximal sensitivity at much higher frequencies than humans whose upper hearing limit is about 12-15 kilocycles. In view of this, it was felt necessary to extend our noise studies to much higher frequencies than were previously used.

Unfortunately, most of the available high frequency sound sources such as the Galton whistle or various air sirens can generate only one frequency at a time. In contrast, turbo-jet engines, besides producing low frequency sound, generate a wide-band high frequency spectrum. The present report deals with the design and construction of a high frequency sound source capable of producing intense noise over a wide-band frequency spectrum. The type of noise generator designed is basically a thermal sound source.

It has long been recognized that an electric arc discharge in air can serve as a thermal sound source. When such a discharge is interrupted or modulated at an audio rate, it is referred to as a 'singing arc'. Another type of electric discharge, the radio frequency corona, can also serve as a sound source when it is modulated. Due to its low efficiency, a speaker of this type was not considered practical for many years. However, by 1953 SIEGFRIED KLEIN had developed a new corona type speaker which he called the 'Ionophone'⁵. In the Ionophone the sound is radiated directly from an audio modulated radio frequency corona at the apex of an air filled horn. Since there are no moving mechanical parts, only air molecules and ions, it was felt that the Ionophone might prove useful for bioacoustic studies of the effects of high intensity noise at higher frequencies than one can attain with conventional diaphragm type speakers.

Costs, Control. Univ. of Mich. Press, Ann. Arbor, Mich. (1952) 45-53.

– P. BUGARD, *Rapports du II^e Congrès Technique Nationale de Sécurité et d'Hygiène du Travail*, La Baule, Sept. 27-30, 1-14 (1953).

³ A. ANTHONY and E. ACKERMAN, *J. Acoust. Soc. Amer.* 28 [2], 270-274 (1955). – A. ANTHONY and S. BABCOCK, *Exper.* 14 [3], 104 (1958).

⁴ G. PESTALOZZA and H. DAVIS, *Amer. J. Physiol.* [3] 185, 595-600 (1956).

⁵ S. KLEIN, *Acoustica* 4, 77 (1954).