

data indicate, as do the data in Table 1, that liver contains some substance which reduces the incidence of the short-boned condition. The authors are not ready to advance an explanation for the difference between the sets of data from confined birds which received cod-liver oil and from those which received viosterol.

*Summary and Conclusions.* Abnormal embryos and chicks, with relatively short bones, were frequently produced in eggs laid by birds which received diets lacking in some factor or factors present in wheat germ, liver, and whey. The activity, amount or utilization of this factor or these factors was augmented by permitting the birds access to direct sunlight and green range.

8170 P

### Reaction at Site of Injection of Mercurial Diuretics as Influenced by Theophylline.

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The comparative toxicity of mercurial preparations has usually been studied from the point of view of "minimal toxic dose" in the sense of causing death in a fixed period of time. The literature on this subject has been fully reviewed by Fourneau and Melville.<sup>1</sup> However, very little attention has been paid to the local reaction at the site of injection. The frequent occurrence of venous thrombosis and necrosis from the use of mercurial diuretics is of considerable importance. v. Issekutz and v. Vegh<sup>2</sup> combined a mercurial diuretic with theophylline and suggested that the latter, having weak acidic properties, neutralized the alkaline reaction (responsible for the pain) that is produced upon hydrolysis of the mercurial salt. This combination was introduced as novurit, but is known in this country as mercupurin.\* Recently Fulton and Bryan<sup>3</sup> found that

<sup>1</sup> Fourneau, E., and Melville, K. I., *J. Pharm. and Exp. Therap.*, 1931, **41**, 21.

<sup>2</sup> v. Issekutz, B., and v. Vegh, F., *Arch. f. exp. Path. u. Pharm.*, 1928, **138**, 245.

\* Mercupurin is a complex mercurial salt differing from that of salyrgan in possessing a cyclopentane instead of a benzol ring. In addition, it has 5% theophylline, 3.5% of which is claimed to be chemically bound to it. Aminophylline is the double salt or mixture of theophylline and ethylene diamine. It has the advantage over theophylline of greater solubility.

<sup>3</sup> Fulton, N. M., and Bryan, A. H., personal communication.

in animals both salyrgan and mercupurin produced definite necrotic lesions, but the former was more severe in extent and degree of reaction. They noted that there was a striking absence of slough formation when a mercurial salt, to which 5% theophylline was added, was injected subcutaneously.

We have compared the local action of mercurial diuretics with and without theophylline and have attempted to establish a quantitative relationship. The preparations used were mercupurin, the theophylline-free mercurial salt contained in mercupurin, salyrgan, salyrgan plus aminophylline (so that the theophylline content was equivalent to that of mercupurin) and as a control—aminophylline, physiological saline and distilled water.\* Equivalent amounts of the drugs as regards mercurial content were used. The following series of experiments were performed:

(1) Doses of 0.05 cc. of various dilutions (undiluted to 1:100) of the drugs were injected intracutaneously into the abdominal wall of 12 rabbits. Each rabbit was given at the same experiment the various dilutions of at least 3 diuretics and the control drugs. It was noted that salyrgan and the mercurial salt of mercupurin free of theophylline produced in all dilutions an immediate well-circumscribed necrotic lesion, with absence of wheal formation and erythema. Mercupurin and the other mercurial salt, to which aminophylline had been added, produced in dilutions up to 1:10 a diffuse erythematous wheal. At the end of 24 hours the mercurial salts free of theophylline differed from the others in that they exhibited larger areas of necrosis and induration even with greater dilutions.

(2) The preparations undiluted were injected into the ears of 6 rabbits. The drugs lacking theophylline produced an immediate necrotic obliteration of all vessels in the vicinity and a striking absence of defense reaction. The lesions progressed, so that within 24 hours, a definite slough was evident. The drugs containing theophylline caused a diffuse wheal and vasodilatation with absence of slough formation.

(3) Histological studies of the areas injected and removed at various intervals from one-half to 48 hours revealed a striking absence of cellular response but extensive necrosis with salyrgan. Mercupurin caused necrosis limited to the needle tract and a cellular response resulting in abscess formation containing large numbers of polymorphonuclear leucocytes. These exhibited various stages of karryorhexis.

(4) Microinjections (6 for each drug) into the mesenteries of 12 mice by means of the Chamber's technique demonstrated the

high degree of toxic action upon mesenchymal tissue and blood vessels with those preparations not containing theophylline.

(5) It was found that intracutaneous injections in man (9 subjects) of 0.02 cc. of the drugs free of theophylline using dilution 1:10 produced a greater local reaction as regards extent, severity and duration than those preparations containing theophylline. In the dilution used the greatest reaction was the production of a small superficial slough.

It has been demonstrated that the presence of theophylline in combination with a mercurial diuretic definitely decreased the local toxic action. This was true not only for the animal experiments but also for man.

### 8171 C

#### Blood Alcohol and Its Relation to Intoxication in Man.\*

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A method was described<sup>1</sup> for the detection of blood alcohol based on the Naville modification of the Nicloux method. It differs from the above modification in that the proteins are precipitated with the ordinary Folin-Wu reagents and the distillation is carried out with a modified ice condenser. When applied to blood distillates the method gives an average per cent error of 5.09 with a range of 0.3 to 15.0. The greater error is encountered in blood samples containing less than 10.5 mg. of alcohol. Schumm and Fleischman<sup>2</sup> showed that during the first hour the blood alcohol rose more rapidly than did the spinal fluid, but that during the decline of the blood alcohol the spinal fluid surpassed it and remained at a higher level. Abramson and Linde<sup>3</sup> showed that the alcohol content of the spinal fluid rose more slowly than that of the blood and reaches its maximum later. This maximum is lower than that

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<sup>1</sup> Turner, R. G., *J. Pharm. and Exp. Therap.*, 1932, **44**, 305.

<sup>2</sup> Schumm, O., and Fleischman, R., *Deutsche Z. f. Neivenheilkunde*, 1913, **46**, 275.

<sup>3</sup> Abramson, L., and Linde, P., *Arch. Internat. de Pharmacodynamic et Ther.*, 1930, **39**, 325.