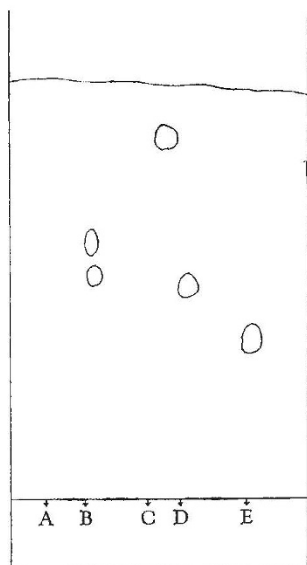

Fig. 1. Chromatogram of urine extracts from rats. *A*, Control urine extract of rat; *B*, total urine extract of rat receiving secobarbital (30 mg/kg); *C*, secobarbital; *D*, 5-(2,3-dihydroxypropyl)-5-(1-methylbutyl) barbituric acid; *E*, 5-hydroxy-5-(1-methylbutyl) barbituric acid. Absorbing spots were marked under ultra-violet light (254 mμ) when chromatogram was exposed to ammonia vapour

of 5-(2,3-dihydroxypropyl)-5-(1-methylbutyl) barbituric acid, a metabolite of secobarbital.

Identification of the other spot is now being examined.

I thank Dr. W. J. Waddell, University of North Carolina, Chapel Hill, North Carolina, for sending metabolites of secobarbital.

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Combined Toxicity of Staphylococcal Enterotoxin and α-Methyl-3,4-dihydroxy-l-phenylalanine (Methyl-dopa)

THE absence of a measurable pharmacological action of *Staphylococcus* enterotoxin in small laboratory animals limits investigation of the mode of action of this toxin. In view of published work in which drug interactions have been used to examine mechanisms of action[1,2] we undertook an investigation of the toxicity of combined treatments of *Staphylococcus* enterotoxin and methyl-dopa in mice.

Crystalline *Staphylococcus* enterotoxin was dissolved in phosphate buffer (0·02 M, *p*H 7·2). α-Methyl-3,4-dihydroxy-l-phenylalanine (methyl-dopa) was dissolved in water acidified by hydrochloric acid in order to effect solutions. LD_{50} values were estimated by the Reed and Muench method[3] from the total deaths recorded 48 h after administration of the drug in female, random-bred, Swiss albino mice (28 ± 2 g).

Table 1 shows the LD_{50} of methyl-dopa alone and methyl-dopa when given 2 h after *Staphylococcus* enterotoxin. It can be seen that the toxicity of methyl-dopa is enhanced by a prior injection of 200 μg/kg of the enterotoxin. This dose of enterotoxin, when given alone, is far below the minimum toxic dose.

Table 1. TOXICITY OF METHYL-DOPA IN MICE PRETREATED WITH STAPHYLOCOCCAL ENTEROTOXIN

Enterotoxin dose (μg/kg, intraperitoneal)	No. of mice used	Methyl-dopa LD_{50} (mg/kg, intraperitoneal)
—	120	745
200	140	390

Table 2. TOXICITY OF STAPHYLOCOCCAL ENTEROTOXIN IN MICE PRETREATED WITH METHYL-DOPA

Methyl-dopa dose (mg/kg, intraperitoneal)	No. of mice used	Enterotoxin LD_{50} (μg/kg, intraperitoneal)
—	78	> 3,000
400	180	54

Table 2 illustrates the LD_{50} of *Staphylococcus* enterotoxin alone and when given 2 h after 400 mg/kg of methyl-dopa. The LD_{50} of *Staphylococcus* enterotoxin is markedly reduced in mice pretreated with methyl-dopa.

Toxicity of methyl-dopa in enterotoxin-treated mice was almost doubled. At the same time the toxicity of the enterotoxin in mice treated with methyl-dopa was increased more than 60 times. Since both agents when given alone in the doses used are non-toxic, the investigation reported here of combined action demonstrated a marked potentiation of the toxicity.

Methyl-dopa depletes the tissues of potent biogenic amines[4], and this phenomenon may be related to the mode of action of the *Staphylococcus* enterotoxin. Further work with other enterotoxin-drug combinations may yield more information on the mechanisms involved.

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PATHOLOGY

An Alteration in Cell Morphology under the Influence of a Tumour RNA

THE roles of nucleic acids have recently become much more firmly established, mainly through work on bacteria and viruses. DNA is almost certainly the genetic material of higher organisms, bacteria and some viruses[1] although other viruses have RNA as their genome[2].

'Messenger' RNA functions to pass information from DNA[3] and probably controls the biosynthesis of proteins through interaction with ribosomes, the RNA of which appears to have a structural function.

However, a biological role has been reported for mammalian RNA: de Carvalho and Rand[4] reported the inhibition of the growth of tumour cells by normal RNA, and Niu[5] has suggested RNA may play a part in cell differentiation. Benitez, Murray and Chargaff[6] have found a morphogenetic role for normal RNA and this communication reports the effect of an RNA preparation on tissue culture cells.

Primary cultures of hamster kidney and of a stilbœstrol-induced hamster kidney tumour as first described by Horning and Whittick[7] were prepared and supplied through the courtesy of Dr. Dudgeon and Mr. Owen of the Glaxo Laboratories. The cultures were grown at 37° C either in a roller tube assembly or as stationary tubes with removable coverslips. These were either examined directly or after neutral formalin fixation and hæmatoxylin–eosin staining.

Fresh RNA preparations were made from normal kidney and implanted kidney tumours from the same animals by Dr. Kirby of this Institute. Both were dis-

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