Table 1. Eight Independent Bioassay Results comparing Synthetic Corticotrophin (Tetraicosapeptide-Ciba) with the Present International Corticotrophin Standard by the Method of Rerup and Hedner

	Assay day	No. of mice	Weight factor of assay = W_1	Log potency ratio = M	Potency ratio = antilog M	$P = 0.05$ confidence limits
(*a*) Subcutaneous injection	18.12.64	12	18·6	1·3370	21·7 (I.U./mg)	
	10.3.65	16	68·0	1·5686	37·0	
	11.3.65	16	99·7	1·5473	35·3	
	12.3.65	16	59·7	1·4721	29·7	
	Total	60	246·0	Weighted mean 1·5190	33·0	24·6–44·3
(*b*) Intravenous injection	12.1.65	16	85·0	2·4105	257	
	9.3.65	16	65·9	2·3943	248	
	16.3.65	16	74·3	2·4055	254	
	19.3.65	16	183·9	2·4146	260	
	Total	64	409·1	Weighted mean 2·4088	256·4	204–322

favourable efficiency when given extravascularly. It is partly for these reasons that the now official International and U.S.P. Corticotrophin Standard preparations are of the corticotrophin *A* type, a fact which has practically eliminated bioassay discrepancies (crude corticotrophin is now rarely used). The reasons for the foregoing bioassay discrepancies are unknown, but it is most likely that they lie in the different rates of inactivation of the different types of ACTH at the site of extravascular administration.

The recent introduction of synthetic corticotrophin (tetraicosapeptide-Ciba), which due to its lower molecular weight should belong to the corticotrophin *B* type, has created a new situation, since formerly this type was not in general use. We tested the hypothesis of a type-difference between the synthetic tetraicosapeptide and the International Standard for corticotrophin (corticotrophin *A*) by a method utilizing the increase in the corticosteroid-level of mouse plasma. This method, devised by Rerup and Hedner[4], has been shown to give valid potency estimates for corticotrophin *A* preparations. Typical results are shown in Table 1.

It will be noted that the synthetic tetraicosapeptide when given subcutaneously showed only about 13 per cent of the activity expected from the assay using intravenous injection. Thus there can be no doubt concerning the strong biological difference between the present (International and U.S.P.) standard and the synthetic peptide. From this it follows that, so long as the international unit is used as a reference for corticotrophic activity, labelling of the synthetic product in weight units (mg) is inappropriate, since there does not appear to exist a fixed constant of equivalency of weight unit to biological unit. The findings indicate the need for (*a*) a clear distinction between preparations for intravenous and subcutaneous use (U.S.P. 1955)[5]; (*b*) a parallel study in man and laboratory animals to assess the equivalent of 1 mg of the tetraicosapeptide in international units after both intravenous and subcutaneous injections.

C. Rerup

Department of Pharmacology,
The Royal University,
Lund, Sweden.

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PATHOLOGY

Carcinoma of the Glandular Stomach in Rats given Diets containing Aflatoxin

Spontaneously occurring carcinoma of the glandular stomach in the rat is exceedingly rare. In a large series Bullock and Curtis[1] reported a single case, while Stewart *et al.*[2] in a review of the literature failed to find a convincing example of adenocarcinoma of the stomach in the rat. Experimentally, Hare *et al.*[3] produced a low incidence of glandular carcinoma on intramural injection of the carcinogenic polycyclic hydrocarbons. The same substances on feeding failed to induce carcinoma of the stomach. Stewart *et al.*[2] have since demonstrated that oral administration of *N*,*N*′ 2,7-fluorenylene*bis*acetamide will induce a low incidence of stomach adenocarcinoma (4 in 47 rats), and Schoental[4] has reported the induction of malignant adenocarcinoma with *N*-nitroso-*N*-methylurethane (NMU). It is the purpose of this communication to describe the incidence of carcinoma of the glandular stomach observed in a series of experiments in which the toxicity of groundnut meal containing aflatoxin was investigated.

In our original experiments to examine the toxicity of groundnut meal we reported two definite adenocarcinomas of the stomach while a third animal had multiple metastases from a histologically similar adenocarcinoma. These experiments were started when the rats were about 5 weeks old and the animals were killed 66–76 weeks after the start of the experiment[5].

In further experiments rats have been given a diet made up with 50 per cent of the same batch of groundnut meal. The level of aflatoxin in the diet was 3–4 p.p.m. In one experiment 6 male rats 1 year old were given the diet to test its effects on old rats. Five of the 6 rats survived for more than 39 weeks, the sixth dying of middle-ear disease after only 9 weeks on the diet. Of these animals 3 showed anaplastic hepatocellular carcinomas. Two of these animals also had a further primary carcinoma, one an adenocarcinoma of the rectum and the other an adenocarcinoma of the stomach. The rat with the stomach carcinoma was 104 weeks old. In other experiments to be reported in detail elsewhere, the effects of short-term administration of aflatoxin were investigated.

Six young rats were given the diet for 3 weeks and then returned to a normal diet; one animal which lived for 106 weeks after return to the normal diet developed a carcino-sarcoma of the stomach. In this group of 6 animals only one developed a hepatic carcinoma.

Thus a total of four confirmed and one probable carcinoma of the glandular stomach have been seen in rats fed aflatoxin. Although the overall incidence is low, the tumours reported here are of considerable interest in view of the difficulty with which this type of carcinoma can be induced.

It has been suggested that aflatoxin may play a major part in the aetiology of human liver carcinoma in some parts of the world[6]. Carcinoma of the glandular stomach also shows an interesting geographical distribution, and it is possible that this type of food contaminant may be a factor in the aetiology of carcinomas in organs other than the liver.

W. H. Butler
J. M. Barnes

Toxicology Research Unit,
Medical Research Council Laboratories,
Woodmansterne Road,
Carshalton, Surrey.

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Experimental Pyelonephritis in the Rhesus Monkey

Experimental work on pyelonephritis has been confined to rabbits, rats and mice[1]. The investigation on rhesus monkeys recorded here was undertaken because this species is phylogenetically close to man and, therefore, has better chances of developing the various characteristics of the human disease rather than any other labora-