in by the reciprocal action of central and peripheral stimuli because of the mutual alterations induced by signals in these two channels. Nonetheless, the present interest in this field[4] is expected soon to clarify our understanding of the descending influences on the ascending activating reticular system.

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Résumé

La stimulation des noyaux non-spécifiques du thalamus chez le chat non anesthésié, provoque des réponses de recrutement dans le mésencéphale. Il est démontré que ces réponses sont analogues à celles qu'on enregistre classiquement sur le cortex et que les neurones réticulés participent à cette activité induite. Ces résultats impliquent l'existence de relations réciproques entre les structures diencéphaliques et mésencéphaliques qui contrôlent le niveau d'activation cérébrale.

[4] W. R. ADEY, J. P. SEGUNDO, and R. B. LIVINGSTON, J. Neurophysiol. *20*, 1 (1957).

Inhibition of Anaphylactic Shock by Oral Lipids

In the course of a comparative study on the mechanism of action of anti-allergic substances undertaken in our laboratories, it was found that dietary lipids can produce an immediate anti-allergic effect inasmuch as guinea-pigs may be protected against lethal anaphylactic shock within 1 h after the ingestion of certain lipids. The following is a preliminary account of these experiments.

Methods.—Male guinea-pigs weighing from 300–350 g were sensitized by a single subcutaneous dose of 0·5 ml of a 20% (v/v) egg-white solution. Three weeks later, anaphylactic shock was elicited by an intravenous injection of 0·2–0·3 ml of a 2% (v/v) egg-white solution. This procedure resulted in the death of 39 out of a total of 47 control animals and never killed less than $^3/_4$ of the actual control group run in the same series. The egg-white used in these experiments was obtained from several fresh eggs; it was homogenized by repeated freezing and thawing and straining through gauze. Identical batches were used for sensitization and challenging. The lipids to be tested were warmed to 38–40° C and fed drop-wise with a pipette. In most cases, the amount administered was 2 ml/animal and the interval between feeding and challenging 60 min. In a few cases the interval between feeding and challenging or the amount of lipid fed were varied. Oils and fats were employed as available from various commercial sources. Cod-liver and sesame oil were of the type specified by the Swiss Pharmacopoea (Ph. H. V.). Linoleic and linolenic acid (Hoffmann-La Roche) were obtained from ampoules sealed under nitrogen and mixed with the specified amounts of arachis oil or propylene glycol *ex tempore* 5 min prior to being fed.

Results (see Table). – A single oral dose of certain lipids exerted a protective effect against lethal anaphylactic shock in the guinea-pig. The list of active lipids comprises three oils of vegetable origin, i.e. cotton-seed, sesame and corn oil, and one animal fat, i.e. bone oil. The effects obtained with arachis oil, linolenic acid and cod-liver oil are probably not significant in view of the restricted number of animals employed. Olive oil, soy bean lecithin mixed with arachis oil, linoleic acid, fresh cream, butter, lard and egg-yolk were ineffective in the amounts studied.

From the experiments performed with corn oil it is evident that a minimum of lipid must be fed in order to obtain protection. With the material employed here, the minimal dose would seem to lie between 1 and 2 ml.

The lacteals of animals dying from anaphylactic shock within 5 to 20 min after challenge, i.e. 65 to 80 min after feeding of the lipid were visible as white turgescent strings; in a few cases, the serum taken from such animals at death was slightly opaque. Likewise, in cases where 2 ml amounts of corn oil etc. were fed to non-sensitized guinea-pigs or to guinea-pigs sensitized but not challenged, the lacteals showed the same whitish content 90 min after receiving the lipid. Of the sensitized guinea-pigs protected against lethal anaphylactic shock by corn oil or by sesame oil, a few were killed in order to examine the lacteals after the animals had recovered, i.e. 20–30 min after challenging. In all these protected animals, the lacteals were entirely transparent. It would thus appear that during anaphylactic shock in the guinea-pig some clearing agent is released—most probably from the intestinal tract.

Lipids	Amount fed* (ml)	Protection**
Vegetable		
Arachis oil	2	3/10
Cotton-seed oil	2	6/10
Sesame oil	2	7/14
Olive oil	2	2/10
Corn oil	2	7/13
	1	2/7
	0·5	1/5
Soy bean lecithin	1	2/10
plus arachis oil	1	
Linoleic acid	0·5	1/8
plus arachis oil	1·5	
Linolenic acid	0·5	2/5
plus propylene glycol	1·5	
Animal		
Fresh cream	2	2/8
Butter	2	1/9
Lard	2	2/8
Egg-yolk	2	2/9
Cod-liver oil	2	3/8
Bone oil	2	4/10
Controls (no feeding)	–	8/47
Controls: Peptone 10%	2	1/9

* Oral administration of lipids etc. 1 h before challenging.
** Number of animals protected/number of animals employed.

From further experiments with corn oil in 2 ml amounts it became evident that the protective activity of this lipid sets in when absorption has reached a certain level, i.e. in this case not until 30–45 min have passed; it then lasts for about 2 to 3 h and is practically finished 5 h after feeding the lipid.

Preliminary but unequivocal experiments in which groups of sensitized guinea-pigs were fed with corn oil and simultaneously injected with anti-anaphylactic doses of *Proteus* polysaccharides[1] or antihistamines, such as tripelennamine or promazine, showed that feeding of the anti-anaphylactically effective lipid together with an injection of the anti-allergic polysaccharide resulted in no

[1] R. MEIER, H. J. BEIN, and R. JAQUES, Exper. *12*, 235 (1956); Int. Arch. Allergy *11*, 101 (1957).

protection at all, i.e. in a mortality identical with that for non-treated controls. On the other hand, all the animals receiving the lipid by mouth and an antihistamine parenterally were fully protected.

The nature of the protective materials present in the lipids studied and the mechanism by which they exert their effect are as yet unknown. Since such lipids as egg-yolk, soy bean lecithin, or linoleic acid were found to be ineffective against anaphylactic shock, the type of lipid activity observed is not directly dependent on phospholipids or unsaturated fatty acids as such, nor is it related to the arachis oil factor described by D. A. LONG and MARTIN[2] or to the egg-yolk fractions active in the dietary experiments of COBURN *et al.*[3] or CHANG and FRENCH[4]. The anti-anaphylactic activity of sesame, cotton-seed oil etc. is furthermore clearly distinguished by the fact that one single oral dose is effective whereas in the experiments of the last-named authors the lipid had to be injected or fed over several weeks in order to suppress tuberculin or Arthus reactions in the guinea-pig.

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Zusammenfassung

Gewisse Lipide besitzen am Meerschweinchen nach einmaliger peroraler Verabreichung eine mehrstündige anti-anaphylaktische Schutzwirkung. Der anti-anaphylaktische Effekt von parenteral zugeführten Proteus-Polysacchariden wird durch perorale Zufuhr solcher Lipide aufgehoben, während Antihistaminica in ihrer Schutzwirkung nicht beeinflusst werden.

[2] D. A. LONG and A. J. P. MARTIN, Lancet *270*, 464 (1956).
[3] A. F. COBURN, C. E. GRAHAM, and J. HANINGER, J. exper. Med. *100*, 425 (1954).
[4] I. CHANG and C. E. FRENCH, Proc. Soc. exp. Biol. Med. N.Y. *93*, 366 (1956).

Organ Weights of TE Mice Bearing Ehrlich Ascites Carcinoma Growing in the Solid Form and of C3H Mice Bearing Spontaneous Mammary Carcinoma

In the course of our studies on the anaemia of cancer, we observed that the weight of the spleen and the liver of cancerous mice was higher than the weight of the spleen and the liver of healthy mice.

MÜLLER[1] reported that in humans who died from various carcinomas the weight of the spleen sometimes though not always was significantly higher than the weight of the spleen of non-cancerous individuals (cf. also CALO[2]).

In this communication we report observations on the weight of spleen, liver and kidneys of TE mice bearing Ehrlich ascites carcinoma in the solid growing form and of C3H mice bearing spontaneous mammary carcinoma.

Male TE mice, kindly supplied by the Animal Department of the British Medical Council, were inoculated intramuscularly with Ehrlich ascites carcinoma and killed as described elsewhere[3]. The spleen and liver were removed and weighed. In one series the dry weight of the organs was also determined.

[1] IRMA MÜLLER, Zbl. allg. Path. path. Anat. *55*, 180 (1932).
[2] A. CALO, Z. Krebsforsch. *37*, 151 (1932).
[3] G. v. EHRENSTEIN, Arkiv Kemi (1958), in press.

Table I
Fresh weight of spleen, liver and kidneys of female C3H mice bearing spontaneous mammary carcinoma and of healthy male C3H mice.

	Number of animals	Mean weight in g	Standard error	Range
Controls				
Body weight. .	11	28	± 1·7	21–36
Spleen weight .	11	0·183	± 0·016	0·125–0·269
Liver weight. .	11	1·654	± 0·086	1·243–2·026
Kidney weight.	11	0·548	± 0·047	0·332–0·791
*Tumours**				
Body weight. .	11	30	± 1·3	23–37
Spleen weight .	11	0·540	± 0·041	0·271–0·726
Liver weight. .	11	2·178	± 0·139	1·631–2·871
Kidney weight.	11	0·386	± 0·011	0·340–0·461

* Average tumour weight = 2·5 g.

The C3H mice were females of about 6 months of age all having spontaneous mammary carcinoma. In order to get controls of this strain we were obliged to take C3H males of the same age and body weight. In this series the weight of the kidneys was also determined.

The results are seen in Table I and II. The fresh weight of the spleen in both tumour groups is significantly higher than in the controls, the ratio between cancerous and control mice being 3·7 for the TE mice and 3·0 for the C3H mice. The enlargement of the spleen was proportional to the tumour weight. The corresponding figures for the liver are 1·4 and 1·3. For the dry weights essentially identical ratios were obtained. The weight of the kidneys of the cancerous C3H mice was found to be lower than that of the controls, the ratio being 0·7. When the C3H females were allowed to die spontaneously, the dispersion of the values was greatly increased, some animals were found to have a normal, some even a decreased liver and spleen weight. For these results cachexia was presumably responsible.

Tissue examination revealed no metastases. Histological examination showed the presence of massive infiltrations of plasma cells or lymphocytes in the spleen and periportal infiltrations of plasma cells or lymphocytes in the liver of the cancerous mice (cf. CALO[2]). Our radioiron studies suggest that there must also be an appreciable amount of erythropoietic tissue in the spleen of the cancerous animals (v. EHRENSTEIN[3], see also KELSALL[4] and ANTOPOL *et al.*[5]).

We have also injected healthy male TE mice intraperitoneally under aseptic conditions with 0·25 ml of whole blood of TE mice bearing Ehrlich ascites carcinoma in the solid growing form. The weight of the spleen of the healthy mice, which received the blood of the cancerous animals, was found to be increased to twice that of the controls which were injected intraperitoneally with saline. The weight of the liver and kidneys was not affected in these experiments. Intraperitoneal injection of 0·25 ml of whole blood of healthy mice did not produce splenomegaly.

Intraperitoneal injection of 0·2 ml of blood plasma of cancerous TE mice into healthy TE mice caused spleen enlargement to twice the normal weight as early as 120 h after the injection. Intraperitoneal injection of either 0·2 ml plasma or 0·1 ml packed red blood corpuscles of healthy TE mice, or of 0·1 ml of packed red corpuscles of cancerous TE mice, did not affect the spleen weight.

[4] M. A. KELSALL, J. nat. Cancer Inst. *10*, 625 (1949).
[5] W. ANTOPOL, S. GLAUBACH, and S. GRAFF, Proc. Amer. Assoc. Cancer Res. *2*, 276 (1958).