einander darstellen, eine reizkontrollierende und -regulierende Funktion (in beiden Richtungen) zugesprochen werden. Ähnlich könnten die morphologischen[9,10] und elektrophysiologischen[7,11] Befunde anderer Autoren gedeutet werden. Inwieweit die 4 den Desmosomen benachbarten Kristallkegelfortsätze daran physiologisch beteiligt sind und welche Bedeutung dem in allen Retinulazellen dicht an der Zellmembran gelagerten endoplasmatischen Retikulum (Figur 3) zukommt, sei zur Diskussion gestellt.

Summary. The granular material found in the 4 sectors of the crystalline cone of varying electron density possibly causes a different absorption of incident polarized light. As the quadrants of the crystalline cone are rotated against the quadrants of the rhabdom, we can conclude that each rhabdomere may be stimulated by light of different physical qualities consequently providing a 4- to 8-fold pattern in the rhabdom of the ommatidia.

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Release of Endogenous Pyrogen in Cats by Staphylococcal Enterotoxin B

Staphylococcal enterotoxins A and B exhibit pyrogenicity which is similar in many respects to that of bacterial endotoxins[1,2]. In fact, although totally different chemically, these toxins share to some extent the ability to produce a wide variety of effects[3]. Endotoxins (and a number of other agents) can cause fever by the release of an endogenous pyrogen[4,5], which can be demonstrated by transferring sera to normal recipients from donors given endotoxin. Such transfers cause fever with a rapid onset and short duration in either normal or endotoxin tolerant recipients. Tolerance does not develop with repeated transfers. The experiments reported below suggest the presence of such an endogenous pyrogen in the blood of cats during the peak of fever caused by enterotoxin B.

Materials and methods. Highly purified staphylococcal enterotoxin B was supplied by Dr. M. S. Bergdoll (Food Research Institute, University of Wisconsin, Madison, Wisconsin, USA). Commercial, nonpyrogenic saline was used for flushes. All containers, syringes, needles, etc. were either of the commercial, nonpyrogenic, disposable type or were sterilized in dry heat at over 175 °C for at least 2 h.

Temperature was recorded automatically in the retroperitoneal space of essentially unrestrained cats which were also prepared chronically with a jugular venous catheter[1,6]. All injections were made at 10.00 h. Room temperature was maintained at 75 ± 2 °F.

5 h after a donor cat was administered enterotoxin i.v., it was anesthetized with ether. A sterile, carotid-arterial catheter was implanted. Heparin (1000 units) was injected via a saphenous vein, and the animal was exsanguinated through the catheter. After centrifuging the blood, a portion of the plasma was tested for sterility, and the remainder was stored at 4 °C. (In some experiments heparin was omitted, and serum was collected.) Plasma from 2 donors was pooled when necessary to provide enough material for multiple injections. After incubating at 37 °C for 1 h, 10 ml/kg of plasma was given i.v. to an enterotoxin-tolerant recipient which had shown no pyrogenic response when tested 1–4 days earlier with the same dose of enterotoxin that had been given to the donor. Responses were plotted with time (1 in = 1 h) on the abscissa and temperature change from the (baseline) temperature at the time of injection (1 in = 1 °F) on the ordinate. The area, in square inches, between the curve and the baseline temperature for the 2-h period after transfer was measured with a planimeter to give a thermal response index (TRI). A negative TRI indicates a net fall of temperature after injection. Each sample of plasma was tested in 1–3 recipients, and the average TRI was determined for each sample.

Results. As controls, plasma samples were obtained from donors which had been made tolerant by repeated injections of enterotoxin. The results are summarized in the Table. As indicated, these donors had little or no fever at the time they were anesthetized. The recipients tended to develop small decreases in temperature. (Saline solution produces very similar responses under comparable conditions.) In contrast, non-tolerant donors

Pyrogenic responses of enterotoxin-tolerant recipients to plasma collected from donors 5 h after injection of 1.5–2.0 μg/kg enterotoxin B

Status of donors	No. of samples[a]	Donor fever °F[b]	Recipient fever TRI[c]
Enterotoxin-tolerant	4	0.5 (0.2 to 1.6)	−0.81 (−1.20 to −0.01)
Enterotoxin-sensitive	10	3.8 (1.5 to 4.9)	1.54 (−0.70 to 4.01)

[a] Each sample consisted of plasma from 1 or 2 donors. [b] Mean (range) of temperature change from baseline, immediately preceeding blood collection. [c] Mean (range).

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developed considerable increases in temperature after enterotoxin, and the recipients of their plasma responded with fevers having the characteristics ascribed to endogenous pyrogen. (Similar fevers were also elicited by transfer of sera from non-tolerant donors to tolerant recipients.) The recipients' temperatures typically began to rise 10–15 min after the transfer, and the responses were usually over after 2–3 h. These pyrogenic responses differed significantly from the responses to plasma from enterotoxin-tolerant donors ($P < 0.02$, Mann-Whitney U test[7]). Repeated injections of pyrogenic plasma did not result in tolerance development by the recipients.

Discussion. In accord with current concepts of the pathogenesis of fever[5], the most likely explanation for the fevers seen in these experiments is that they were due to transfer of endogenous pyrogen which was released into the plasma of the donor during enterotoxin-induced fever. The responses were typical of endogenous pyrogen when released by a variety of other agents and in other species. Circulating endogenous pyrogen has also been reported after enterotoxin administration in rabbits[8]. The results, however, do not eliminate the possibility that a metabolically altered form of enterotoxin is responsible for the fever. Such an explanation is perhaps favored by our inability to demonstrate an enhanced release of pyrogen from granulocytes (the most likely source of endogenous pyrogen in most experimental fevers) by *in vitro* incubation with enterotoxin.

The enterotoxin originally given the donors cannot account for recipient responses since the recipients were tolerant to much larger amounts of enterotoxin than can possibly be transferred in the 5-h plasma. Studies in a number of species, including the cat, indicate that enterotoxin is very rapidly removed from blood[9,10]. Neither can contamination with extraneous pyrogens such as bacterial endotoxin account for the results since the response pattern, latency, etc. were different than those expected for endotoxin; no tolerance could be demonstrated; no bacterial contamination was noted in sterility tests, and fevers were not caused by plasma from enterotoxin-tolerant donors handled similarly to the pyrogenic plasma from non-tolerant donors[11].

Conclusion. The presence of a pyrogen with the physiological characteristics of endogenous pyrogen was demonstrated in plasma (and serum) taken from cats 5 h after i.v. injection of staphylococcal enterotoxin B.

Résumé. On a montré la présence d'une substance pyrogène qui avait les caractéristiques physiologiques endogènes dans le plasma et dans le sérum sanguin de félin, pris 5 h après l'injection i.v. d'entérotoxine staphylococcique B.

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Cholecystokinetic Activity of a New Synthetic Caerulein-Like Heptapeptide in Man

It has recently been shown (ANASTASI et al.[1]) that the biological activity of caerulein and caerulein-like peptides is greatly reduced by de-sulphation. Since the tyrosyl-*O*-sulphate bond is rather unstable, particularly at pH < 7, the synthesis of analogues in which the tyrosyl sulphate residue is replaced by the stable *p*-sulphonylphenylalanine residue was undertaken. It was hoped to obtain peptides still retaining the biological activities of caerulein and which would be more stable and possibly longer acting.

In the present note, the cholecystokinetic activity of the new heptapeptide *p*-Phe(SO_3Na)-Thr-Gly-Trp-Met-Asp-Phe-NH_2 is reported. Experiments were carried out on 25 normal volunteers of both sexes, aged 20–60 years. The biliary system was filled by oral (15 subjects) or endovenous contrast medium (10 subjects). Iodopanoic or ioglycamic acid, respectively, were employed. However, no difference in the spasmogenic effect of the peptide was noted by changing the contrast medium or the route of administration.

The new synthetic peptide, supplied by Farmitalia Research Laboratories (Milan), (molecular weight 1004) in a 10% methanolic solution, was administered after removal of the solvent under air stream in a boiling water-bath and the remaining aqueous liquid was brought to the desired volume with physiological saline solution. Doses of 0.5, 1, 10 μg/kg body weight by i.m. injection and of 10 μg/kg by nasal insufflation were used. These doses were approximately 10-fold as high as doses used in the same experimental conditions in previous investigations (ORLANDINI and AGOSTI[2]). Indeed unpublished experiments performed in this Institute of Pharmacology (BERTACCINI, personal communication) showed that this heptapeptide has in different laboratory animals approximately $^1/_{10}$th of the activity of caerulein.

Radiographic serial exposures were obtained at 15, 30, 45, 60, 90 and 120 min after the beginning of the administration. The quantitative evaluation of gall bladder emptying was calculated either by measuring the largest transverse diameter according to BRODÉN[3] or by calculating the whole area of the gall bladder on the roentgenogram with a Salmoiraghi planimeter.

Results obtained are shown in Figure 1. Data represent reduction of volume of the gall bladder after synthetic peptide and caerulein administration in comparison with basal (pre-drug) values considered as 100. It is evident from the figure that the action of the synthetic peptide is more prompt and less lasting than that of caerulein. The 2 peak effects were practically equal identical.

The peptide produced an active cholecystic contraction and the effect on the evacuation was marked by a reduction in the gall bladder size and by filling of the biliary ducts.

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