mine in the mast cells of these species. The cheek pouch of the hamster, which showed a mast cell density similar to that of the swimbladder of *Salmo irideus*, was studied for comparison. The histamine content of the cheek pouch was 19.8–30.5 μg/g, and histamine could easily be histochemically localized in the mast cells. In the reptilian specimens, chosen from 2 species which compared to other reptiles generally have very low levels of histamine in their tissues[3,5], mast cells were searched for in tissue from mesentery, intestine and stomach (after staining with alcoholic thionin). Occasionally, a single or a few of these cells were encountered, but in most preparations they seemed to be completely absent. There is good reason to believe, therefore, that the histamine content of tissues from the digestive tract of all studied species of fish, amphibians and reptiles (Tables I and II) represents non-mast cell histamine.

The present study indicates that whereas the presence of histamine in the mast cells in confined to rather limited groups of vertebrates, the presence of high tissue levels of non-mast cell histamine in the digestive tract, and specifically in the gastric mucosa, is a general feature. The results support the view that non-mast cell histamine is intimately linked to the gastric secretory process, actively or passively.

Résumé. La teneur en histamine des divers segments du tube digestif a été mesurée chez les poissons, les batraciens et les reptiles. Les résultats indiquent la présence de dépôts d'histamine dans la muqueuse gastrique de tous les vertébrés, tandis que l'histamine de mastocytes n'existe que chez des groupes limitées de vertébrés.

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Site of Formation of Cx-Reactive Protein

The appearance of C-reactive protein (CRP) in human serum has been recognized for years as a common non-specific response to infection and other pathological processes. For this reason tests for its presence have joined the host of other laboratory aids used clinically for the evaluation of the status of patients. Interpretation of the human response is based on a body of empirical observation, since the function of the protein is unknown and its source is not established beyond some dispute.

MONTELLA and WOOD[1] showed that blockade of the reticuloendothelial system with ThO_2 severely depressed the ability of the rabbit to produce the analogous Cx-reactive protein (CxRP) and suggested it might arise from this cellular compartment. KUSHNER and KAPLAN[2] and KUSHNER et al.[3] found CxRP in necrotic muscle tissue but not in normal tissue following experimental injury. CxRP was detected by immunohistochemical methods. They interpreted their results to indicate CxRP arises as a product of tissue degeneration. GOTTLIEB[4], on the basis of labelling experiments with ^{14}C-glycine was led to the view that CxRP exists in some form in tissue prior to breakdown of a precursor molecule to give circulating CxRP. Finally, HURLIMANN et al.[5], using tissue culture technics, demonstrated CRP production by liver slices of man, monkey and rabbit, but not by kidney, lung, lymph node, intestine, salivary gland, mammary gland, bone marrow, spleen and peripheral leucocytes of Rhesus monkeys. We report here the behavior of CxRP in rabbits following total surgical removal of their livers to supplement the earlier observations on the source of CxRP.

New Zealand female rabbits were totally hepatectomized by a 2 stage procedure, to be described in detail elsewhere, based on the procedure first described by DRURY[6]. Briefly, the vena cava and the portal vein are partially occluded and some weeks later when collateral circulation has been established the liver is removed surgically. Rabbits were maintained subsequently by parenteral administration of glucose until death intervened. Serum CxRP levels were determined by the titration procedure of SWIFT et al.[7] using specific guinea-pig CxRP antiserum (CxRPA) of our own preparation[8].

Summary of CxRP responses before and after total hepatectomy

Rabbits studied during first stage preparatory surgery

Serum sample	No.	Serum CxRP	Mean titer
Preoperative	16	16/16 negative	–
Postoperative (24 h)	16	16/16 positive	1:11
Postoperative (48 h)	16	16/16 positive	1:16

Rabbits studied during second stage, total hepactectomy, which survived longer than 8 h

Serum sample	No.	Serum CxRP	Mean titer
Preoperative	15	11/15 positive	1:8
		4/15 negative	–
Terminal posthepatectomy			
Positive preoperative rabbits	11	6/11 negative	–
		5/11 positive	1:5
Negative preoperative rabbits	4	4/4 negative	–

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Blood samples were taken immediately before surgery and afterward at various times including an immediate post mortem sample.

The observations are summarized in the Table. First stage preparatory surgery was a strong stimulus to CxRP appearance in blood. All animals responded, 7 of 16 reaching a maximum response in 24 h and 9 in 48 h. Eleven had titers $\geqq 1:8$ at 24 h. Four rabbits tested repeatedly during the first 24 h had reached half their maximum response in 14 h, in essential agreement with the temporal sequence of response noted by others[1,3]. Over $^2/_3$ of the animals had remained CxRP positive until the time of total surgical removal of the liver, generally 4–6 weeks after the first stage. The extended response was somewhat unexpected and may be related to continuing vascularization in the abdominal area or to continuing inflammatory processes around the initial midline incision. The moderately high mean titer was caused by 2 rabbits with high titers, 7 of the 11 having titers of 1:4 or less. Titers of 10 of the 11 positive at surgery declined while 1 remained the same (1:16). The extent of the decline in titer was quite variable: titers of 2 rabbits surviving nearly 24 h declined from 1:4 to negative and 1:4 to 1:2 while 2 surviving 9 and 11 h dropped from 1:32 to 1:4 and 1:8 to 1:1 respectively. 4 rabbits were negative at the time of the second stage operation. All of these remained negative for the 9, 12, 18 and 35 h they survived. The mean survival time for all hepatectomized rabbits reported in the Table was 15 h. No relationship between survival time and serum CxRP status was observed.

These results support the view of HURLIMANN et al.[5] that CxRP is produced uniquely by the liver. They show, however, that CxRP can be eliminated from the blood stream without mediation of the liver and that the protein at times can disappear from the blood quite rapidly. It is conceivable, therefore, that a source other than the liver exists but with synthetic capabilities too small to keep up with elimination of the protein from the circulation. We feel this is improbable and what is seen in serum at any particular time in the intact animal represents a balance between the rate of synthesis by the liver and the rate of elimination from the serum, one mechanism of which appears to be binding to damaged tissues[2,3,9].

Zusammenfassung. Synthese und Stoffwechselfähigkeit von Cx-reaktiven Proteinen in hepatektomierten Kaninchen wurden untersucht. Diese Kaninchen konnten das Protein nicht bilden, sie behielten jedoch die Fähigkeit, es aus ihrem Blutkreislauf auszuscheiden.

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Brain Uptake of ^{3}H Noradrenaline in Normal and *Shigella dysenteriae* Exotoxin Treated Mice

Experimental evidence indicates that noradrenaline does not pass in a significant quantity into brain capillaries[1]. On the other hand, molecules of comparable size evidently cross the capillary wall quite easily, rapidly equilibrating with a space of about 1–2 ml/100 g of brain tissue[2–4].

In the present study, an attempt has been made to investigate the transcapillary passage of noradrenaline in the brain of normal and *Shigella dysenteriae* toxin treated mice. *Shigella dysenteriae* toxin has been shown to damage the capillary wall in the mouse brain[5].

We have measured simultaneously the space of ^{3}H noradrenaline, ^{14}C sucrose and ^{131}I albumin. ^{14}C sucrose was found to pass very rapidly out of brain capillaries and its penetration into the brain tissue is probably hindered by some of the pericapillary structures[4]. ^{131}I albumin was used as an indicator of approximate intravascular plasma volume.

Material and methods. DL noradrenaline-7-H^3-hydrochloride, specific activity 1,820 mc/m*M*, sucrose C^{14} (U) specific activity 10 mc/m*M*, ^{131}I-human serum albumin were used.

The experiments were carried out in female mice, weight range 20–22 g. To 1 group of the animals, 36 h before the administration of labelled compounds, 4 LD_{50} of *Shigella dysenteriae* exotoxin was injected i.v. The other group of mice received saline. To both groups of animals, 3 μc of ^{131}I-albumin and 25 min later, 3 μc of ^{3}H noradrenaline and 0.5 μc of ^{14}C sucrose were injected i.v. 30 min after the first injection the animals were killed and blood and brain tissue were handled as reported previously[4]. ^{3}H noradrenaline was isolated by absorbtion on aluminium oxide.

The γ-radioactivity was measured in a well scintillation counter. β-radioactivity of ^{3}H and ^{14}C was counted in a Packard liquid scintillation spectrometer, using the screening method.

The results are expressed in terms of the space of a substance in the brain tissue defined in the case of ^{131}I albumin as: (cpm per 1 g of brain tissue)/(cpm per 1 ml of plasma) × 100 in the case of ^{3}H noradrenaline and ^{14}C sucrose as: (dpm per 1 g of brain tissue)/(dpm per 1 ml of plasma water) × 100; water content of plasma was assumed to be 93%.

Results. The space of ^{3}H noradrenaline, ^{14}C sucrose and ^{131}I albumin in the brain of animals intoxicated with *Shigella dysenteriae* toxin is significantly increased. The values of the space of ^{3}H noradrenaline and ^{14}C sucrose are approximately equal in both, the normal and the toxin treated group (Table).

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