the temporal response observed with partially hepatectomized rats have been verified statistically by variance analysis.

A further experiment was carried out in order to answer the following questions: 1. Are the changes in element concentrations specific for liver regeneration or are they simply a result of the operation itself? 2. Can the very rapid changes in Na and Zn concentration observed after partial hepatectomy be correlated with the increase in DNA-synthesis (^{3}H-TdR incorporation)? 3. Are the changes observed the same for male and female animals?

110 male rats were randomly distributed into 2 groups, of which one was partially hepatectomized and the other sham operated (laparotomized). 2, 4, 8, 12, 16, 20, 24, 36, 48, 72 and 96 h after the operation, 5 rats from each group were killed and the ^{3}H-TdR incorporation and the concentrations of elements were determined. The average values obtained are shown in Figure 2. ^{3}H-TdR incorporation increases sharply after 16 h in partially hepatectomized rats, reaching its maximum around 24 h. No increase in incorporation was observed with laparotomized rats. The earliest change in element concentrations in partially hepatectomized rats is observed for Na, which reaches a maximum as rapidly as 4 h after the operation. The increase in Zn concentration also precedes the onset of DNA-synthesis. In both cases, the increases observed in partially hepatectomized rats are appreciably higher than in the corresponding laparotomized rats. For this reason, the elevated Na and Zn concentrations can only be partially attributed to a non-specific effect of the operation. In particular, the very early increase in Na concentration after partial hepatectomy could be of importance for liver regeneration. This early increase has also been reported by other authors[4].

A clear increase in K concentration between the 2nd and 4th days was observed only in partially hepatectomized animals. In addition, the large increase in Cu concentration after 36 h is only seen in hepatectomized rats. Shamoperated animals showed only a small increase in Cu concentration during the first day after the operation. The increase in copper concentration is temporally correlated with the increase in ^{3}H-TdR incorporation and therefore appears to be related to liver regeneration. It is noteworthy that in earlier investigations on various transplanted tumours, we demonstrated that changes in Cu concentration in blood plasma could be correlated with ^{3}H-TdR incorporation in the tumours[5,6]. The concentration of Fe in partially hepatectomized rats shows a clear decrease after 2 days. A similar decrease is observed for Mn. However, in laparotomized rats, this effect is even more pronounced. This observation can probably be explained by the overlapping of 2 different effects. During liver regeneration it could be expected that the Mn concentration is increased. (The microbodies were more numerous in regenerating liver – and Mn is located in the microbodies[7,8]). However, owing to the strong effect of the operation (see Figure 2), a small decrease in Mn concentration is observed rather than the expected increase.

For the elements Mo, Co, Rb, Se, As, Mg and Cs, no significant differences were observed which could be related specifically to partial hepatectomy. In addition, no fundamental differences in element concentrations could be detected between male and female rats.

Zusammenfassung. Während der Leberregeneration nach einer Teilhepatektomie lassen sich mit der Neutronenaktivierungsanalyse unspezifische und spezifische Erhöhungen bzw. Erniedrigungen der untersuchten Elemente nachweisen. Spezifische Erhöhungen finden sich bei Cu, Na, K, Zn, eine spezifische Erniedrigung bei Fe.

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Leukocytes and Prostaglandins in Acute Inflammation

Since the importance of prostaglandins (PG's) as mediators in acute inflammation was described[1–3], the source of these substances has remained a matter of speculation. Some have proposed the leukocytes as the cells responsible for the release of the inflammatory PG's (PGE_1, PGE_2 and $PGF_{2\alpha}$) because both these cells and the PG's appear early in the inflammatory tissue, and therefore inflammatory exudates rich in leukocytes, mainly polymorphonuclear (PMN), are often also rich in PG's[4–6]. In addition it has been found that suspensions of PMN-rich peritoneal exudates incubated together with bacteria release PGE_2 and $PGF_{2\alpha}$ in vitro[7]. On the other hand, it has been shown that acute inflammations can be elicited in leukopenic animals, and that therefore the release (if any) from these cells of PG's may not be relevant[8], but – to our knowledge – PG's have not been measured during leukopenic inflammation.

We observed two symptoms of inflammation; nociception and temperature-rise, to appear before PMN or even monocytes can be seen at the site of inflammation in the avian microcrystal arthritis[9]. Therefore we reasoned that

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PG's – if at all – could either be released synchronously with the appearance of the inflammatory symptoms or together with the invasion of PMN. Either result would be of interest, confirming the importance of PG's as mediators or the role of PMN as source of PG's in acute inflammation.

An acute inflammation was elicited by the injection of urate crystals in saline into the intertarsal joints of chicken. In the injected animals, either 2 symptoms of the resulting acute inflammation were recorded, i.e. nociception or temperature-rise, or joint washes were performed 40, 60, 120, 180, 240 or 360 min after urate injection. The joint washes were analyzed for their content of PMN and for the concentration of a (granulocytic) lysosomal marker enzyme (lysozyme 3.2.1.17) in the cell-free supernatant obtained by centrifugation.

Methodological details and results of such experiments have already been reported[9]. We have now assayed PGE_2 and $F_{2\alpha}$ in the cell-free supernatant of joint washes of normal chickens and chickens treated with colchicine 3 h before urate crystals were injected. Colchicine was administrated because it was found to delay the invasion of PMN completely for at least 3 h[10]. The PG's were assayed using a direct radioimmuno assay[11] and antisera, the specificity of which has already been described[12, 13].

The results are given in the Figures. Although in non-drugged animals, there were no detectable amounts of PMN present 1 h after urate injection when the inflammatory symptoms began, the highest levels for both PG's were found at that time. The same holds true for PMN/PG relationship 2 h after UC-injection in the colchicine-treated animals. Instead, as soon as PMN could be detected in the joints both PG's began to disappear. This disappearance was more rapid in the non-drugged than in the colchicine-treated animals, which is apparently related to the number of invading PMN. Therefore, the PMN, instead of being the source of PG's, might rather be responsible for the removal of these mediators in our model of acute inflammation. To test this hypothesis, joint washes obtained 4 h after urate injection were diluted with Hanks balanced salt solution and further incubated at 40 °C in vitro. Samples were removed after different time intervals and assayed for $PGF_{2\alpha}$.

As may be seen from the results given in the Table, there was no significant change in the $PGF_{2\alpha}$-content of the joint wash throughout incubation. Similar results were obtained for PGE_2. This further supports the in vivo findings ruling out PMN as a significant source of PGE_2 and $PGF_{2\alpha}$. On the other hand, these results, being in good agreement with the observation that white blood cells do not metabolize PG's[14, 15], do not support the idea that the PMN might remove inflammatory PG's. Instead the in vivo results showing disappearance of PG's synchronously with appearance of PMN might indicate an increased vascular permeability due to, for instance, the vasodilatory

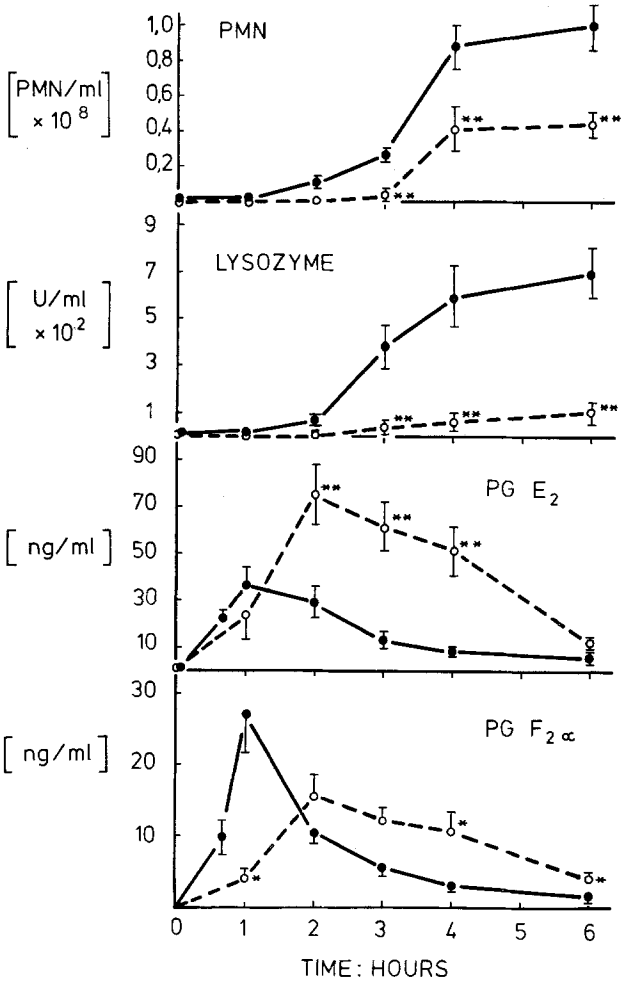

Fig. 1. Time course of PMN- and PG-appearance in joint washes. The intertarsal joints of chickens (of about 2 kg body weight) were washed by injecting 0.5 ml saline at different time intervals following the injection of 0.3 ml of 4% (w/v) suspension of urate crystals. Cell-counts and differential-counts wer done on the whole material. Lysozyme and PG's were assayed in the cell-free supernatant after centrifugation (2000 *g*/30 min). For PG-assays a direct radioimmunoassay was used, adapted from[11]. The values measured for $PGF_{2\alpha}$ were not influenced by the protein concentration in the joint washes. Also, the antiserum did not show cross-reactions with PG's of the E, A or B-type[13]. The specificity and accuracy of the PGE_2 assay was less good[12]. Therefore the values measured for PGE_2 in the presence of high concentrations of $PGF_{2\alpha}$ (> 20 ng/ml) can overestimate the real values up to 30%. Similar results were obtained using the method of JAFFE et al.[23]. •—•, non-drugged controls; ○--○, colchicin treated (3 mg/kg, 3 h before urate injection); means and S.E.M. from 6 and more experiments; **, significant $p < 0.01$; *, significant $p < 0.05$.

$PGF_{2\alpha}$ concentration in joint washes further incubated in vitro

Incubation (min)	0	30	60	90
Controls (ng/ml)	1.1 ± 0.1	1.1 ± 0.2	1.2 ± 0.3	1.0 ± 0.2
Colchicine-treated (ng/ml)	3.5 ± 0.3	3.3 ± 0.3	3.4 ± 0.4	3.4 ± 0.3

Joint washes were recovered 4 h after urate injection from non-drugged controls and colchicine-treated chicken (3 mg/kg, 3 h before UC-injection), diluted 1:2 with Hanks balanced salt solution containing 10 U Heparin (Liquemin, Roche), and further incubated in siliconized glass-tubes on a rotating disc at 40 °C. After the time-intervals given, samples were removed and $PGF_{2\alpha}$ assayed in the cell-free supernatant. (Means and S.E.M. from 5 experiments).

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activity of PGE_2[16], which in turn might facilitate the immigration of PMN due to the leukotactic stimulus of PGE_1[17,18] and E_2[19].

To test this assumption, the degree of vascular permeability and the resulting accumulation of plasma constituents was assayed using PVP (^{131}J)[20]. As may be seen in Figure 2, a more than 10-fold increase in vascular permeability was observed in the non-drugged animals 2 h after urate injection, whilst in the colchicine-treated animals the maximal increase in vascular permeability amounted to only 3 times the control values and was observed not earlier than 3 h after urate injection. Correspondingly the accumulation of plasma constituents in the joint fluid was smaller and appeared later in the drugged than in the non-drugged animals. Nevertheless, in both groups PMN invasion followed PG-release and increased vascular permeability, whilst the PG's disappear when vascular permeability reaches its peak.

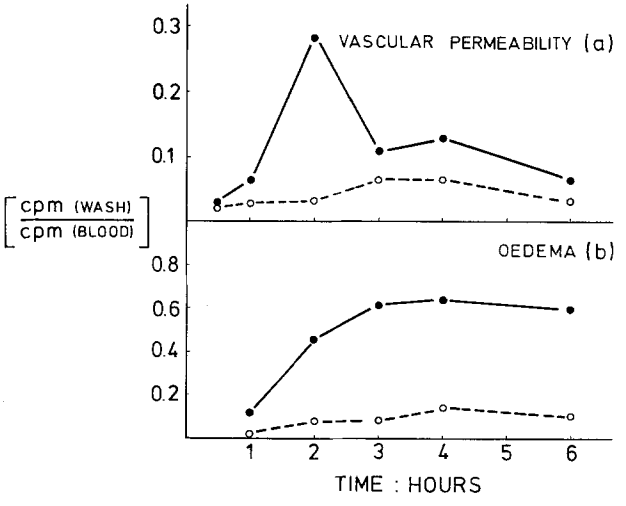

Fig. 2. Time course of changes in vascular permeability and oedema as measured with the PVP (^{131}J) method[20]. PVP (^{131}J) (rate constant of elimination, k_e in chicken = 0.1) was injected i.v. (10 µCi/kg) in chickens (2 kg weight) either 30 min before joint washes were performed or at zero time simultaneously with the intratarsal administration of urate crystals (details see Figure 1). At the times given, joint washes were performed with each animal and venous blood was obtained. The ratio cpm (per ml joint wash) to cpm (per ml blood) were taken as measure of the degree of vascular permeability during the preceding 30 min when PVP (^{131}J) was given 30 min before (a), or as a correlate of oedema when PVP (^{131}J) was given simultaneously with the urate crystals (b). The results are given for the urate injected joints of ● — ●, non-drugged and ○ --- ○, colchicine-treated animals (3 mg/kg, 3 h before urate injection). The ratios obtained from the saline-injected joints (not given in the figure) never exceeded 0.05. Each point in the figure represents a mean of 3 or more experiments.

In conclusion, it can be stated that PMN do not release significant amounts of PGE_2 or PGF_2 in the joint fluid in our model of acute inflammation. They could release these PG's while being trapped in the vessel wall before reaching the joint fluid. However, this appears unlikely because it implies that the PMN stop releasing PG's when they reach the joint fluid and start phagocytizing, a mechanism which is assumed to lead to cell breakage, enzyme release and PG's synthesis[5,7]. Instead we propose the thrombocytes as a more likely source of PG's in acute inflammation. These cells appear early enough in the joint fluid[9], they are well known to release PGE_2 and PGF_2[21] and in all experiments relating PG-synthesis in acute inflammation with PMN, thrombocytes (or platelets) were also present[4–7]. In addition it should be mentioned that the effect of colchicine on PMN invasion and on the vasculature response to inflammation is well compatible with the known impact fo this drug on microtubules[22,23].

Zusammenfassung. Bei einer akuten Entzündung wurde der zeitliche Verlauf der Prostaglandinfreisetzung, Granulozyteneinwanderung und Gefässpermeabilität verfolgt. Die höchsten Prostaglandinkonzentrationen wurden vor der Einwanderung von Granulozyten und vor einer massiven Steigerung der Gefässpermeabilität beobachtet. Dieser Befund spricht gegen die Behauptung, dass Granulozyten wesentlich an der Freisetzung von Prostaglandin beteiligt sind[24].

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Ethylene as a Plant Hormone and Anaesthetic

Ethylene is now well established as a naturally occuring plant hormone[1]. Because the first effects of applied ethylene to be discovered were inhibitions of plant growth which disappeared on removal of the ethylene[2], it became generally known as a plant 'anaesthetic' and this led Luckhardt and Carter[3] to test and demonstrate its true anaesthetic effect on animals. The action of ethylene in plants occurs at much lower concentrations than in animals, for example, the stimulation of stem elongation in *Callitriche platycarpa* by ethylene is saturated at 1 nl ml^{-1} (ref. [4]) while the alveolar concentration of ethylene required for surgical levels in man is 67×10^4 nl ml^{-1} (ref. [5], though no measurement has been made of the concentration at its site of action). Also, ethylene is by