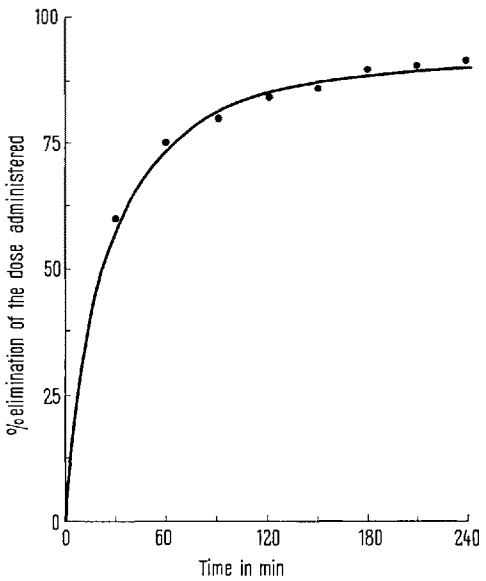
Group	No. of animals	mg of phenol administered mean (range)	mg of free[a] and total[b] phenols eliminated mean (range) First 30 min	First 60 min	First 120 min	First 180 min	First 240 min
Control	12	0	[a] 0.3 (0.0–0.6)	0.5 (0.1–0.9)	0.8 (0.4– 1.2)	1.0 (0.7– 1.5)	1.3 (0.8– 1.9)
			[b] 0.3 (0.0–0.6)	0.5 (0.2–0.9)	0.8 (0.4– 1.3)	1.1 (0.7– 1.6)	1.3 (0.8– 1.9)
Treated	12	12.8 (10.5–14.8)	[a] 6.8 (6.1–7.3)	9.6 (8.8–9.9)	11.1 (10.2–11.8)	11.8 (11.0–12.5)	12.7 (11.8–13.6)
			[b] 6.9 (6.2–7.3)	9.6 (8.9–9.9)	11.1 (10.2–11.8)	11.9 (11.0–12.6)	12.7 (11.8–13.7)

mined with the same reagent after hydrolysis with 0.5 N H_2SO_4 in sealed ampoules kept at 100°C for 1 h.

The Table shows that control animals normally eliminate, in discrete amounts, some compounds which react as free phenols; these basal values, like a blank, must be subtracted to obtain correct figures of the elimination rates of administered doses of phenols. It appears, then, that of the 200 mg/kg dose of phenol about 50% is eliminated within 30 min after the injection and almost 90% within the first 4 h. The excreted phenols have been found only in the free form, conjugated compounds appearing to be completely lacking. In the Figure is reported one individual excretion pattern of free phenols, corrected for basal elimination of phenols and expressed as % of the injected dose.



From these experiments it appears that goldfish are unable to conjugate phenol, while showing a high efficiency in excreting the drug unchanged. The latter peculiarity may help to explain the relatively moderate parenteral toxicity of phenol for fish, notwithstanding the fact that this animal species lacks the mechanism to detoxicate phenol by means of conjugation.

Riassunto. Nel ciprino la DLM del fenolo è di 230 mg/kg i.m. Il fenolo, iniettato i.m. a dose di 200 mg/kg, viene eliminato in media per quasi il 90% nelle prime 4 ore come fenoli liberi. Sotto il profilo della tossicità, la mancata capacità a detossicare mediante coniugazione sembra nel pesce compensata dalla elevata capacità escretiva degli organi emuntori.

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Stasis-Induced Changes in Platelet Adhesiveness

Previous studies suggest that abnormally low platelet adhesiveness is correlated more closely with increased bleeding tendency than mere reduction in the platelet count[1,2] and that abnormally high adhesiveness better reveals the predisposition to thrombosis than do coagulation tests or determinations of platelet count[2]. Circulatory stasis is a factor promoting thrombus formation, but, of the factors involved, increased platelet adhesiveness is regarded as being the most important. However, the effects of stasis on the platelet adhesiveness have not been studied, although the coagulation status seems to be affected thereby; besides fibrinolysis[3], stasis has been found to evoke hypercoagulability as reflected in a shortening of the plasma cephalin time and in a rise of the plasma AHG activity[4]. Because the formation of a platelet nidus must be regarded as the primary event of thrombosis, it was deemed useful to determine whether the platelet adhesiveness is altered by circulatory stasis, and whether the response, if demonstrable, is modified with increasing periods of stasis.

The tests were done on eight medical students. A control blood sample (9 ml in 1 ml of 3.13% citrate solution) was taken without stasis from an antecubital vein of one arm. Then a pressure cuff was placed above the elbow of the other arm and inflated to 100 mm Hg. Following stasis of 3 or 6 min, two successive samples of 9 ml were collected from an antecubital vein of the 'cuffed' arm. The first sample was considered to represent a large vein

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sample and the second a microcirculation sample. For assessing the platelet adhesiveness, the method developed by HELLEM[1] was used, with some modifications[5]. Each sample of citrated blood was drawn into a plastic syringe. This was then placed into an electrically driven device which expelled blood from the syringe at a constant rate. Four 1 ml samples were taken. The first and the fourth were taken directly from the syringe, while the middle two were forced through separate plastic tubings containing a standardized amount of minute round glass beads. From the four samples obtained, the platelet counts were made in duplicate using the direct method BJÖRKMAN[6]. Percentage values were reckoned for the adhesive platelets, for those adhered to the glass beads. Microhematocrit determinations were also made in duplicate in order to evaluate the hemoconcentration-dependent changes in the adhesiveness (adhesiveness corrected for hematocrit changes = observed percentage of adhesive platelets × 45/observed hematocrit)[1]. All the material coming in contact with blood was siliconized.

In response to stasis and independent of its duration, the platelet count did not exhibit any noticeable changes. Yet the hematocrit readings increased with increasing periods of stasis. At the same time the adhesiveness values corrected for hematocrit changes showed a biphasic response, notably in the microcirculation samples (see Table).

Following 3-min stasis, the mean values for uncorrected platelet adhesiveness in the microcirculation samples increased from 45 to 56%, the mean increment (9.9%) being statistically significant ($P < 0.001$). Meanwhile the hematocrit readings had increased less (from 45 to 47 Vol%; + 3.0 Vol%; $P < 0.01$) suggesting that a real elevation in the platelet adhesiveness had taken place. This was substantiated by the fact that the adhesiveness values corrected for hematocrit changes showed a rise from 46 to 53%, the mean increment (6.2%) still being statistically significant ($P < 0.01$). After 6-min stasis, too, the mean values for uncorrected platelet adhesiveness were significantly increased (from 45 to 53%; + 8.4%; $P < 0.01$). However, owing to a greater rise of the hematocrit readings after 6 min (from 45 to 53 Vol%; + 8.7 Vol%; $P < 0.001$) the corrected adhesiveness values presented no statistically significant deviation as compared with those obtained before stasis (from 46 to 45%; − 0.2%; NS).

In the large vein samples taken after 6-min stasis, the corrected and uncorrected adhesiveness values were distinctly less than in the microcirculation samples, and following 3-min stasis there was similar, though less striking, inequality in the adhesiveness readings.

The following mechanisms may be considered to be responsible for the initial rise observed in the platelet adhesiveness within the microcirculation, at least. It is well-established that adenosine diphosphate is capable of increasing the platelet adhesiveness in very minute concentrations[7,8]. Under conditions of stasis, this compound

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Platelet count (PC; thousands per mm³), hematocrit values (HC; Vol %) and platelet adhesiveness (%), uncorrected (PA) and corrected (PA_c) for hematocrit changes, in blood samples taken from an antecubital vein before and after 3 or 6 min stasis (100 mm Hg). I = first 9-ml sample, II = second 9-ml sample

Case	Before stasis				After 3-min stasis								After 6-min stasis							
	(I)				I				II				I				II			
	PC	HC	PA	PA_c	PC	HC	PA	PA_c	PC	HC	PA	PA_c	PC	HC	PA	PA_c	PC	HC	PA	PA_c
1a	165	49	40	37					155	53	53	45								
b	231	48	52	49													247	57	64	51
2a	261	43	43	45					247	45	67	67								
b	256	43	43	45													257	47	37	35
3a	221	48	50	47					225	49	54	50								
b	201	49	48	44									197	58	49	38	222	60	65	49
4a	248	45	53	53					233	47	60	57								
b	213	46	33	32									226	50	38	34	208	57	52	41
5a	176	47	50	48	165	48	51	48	165	48	55	52								
b	210	47	49	47					199	53	60	51								
c	216	48	46	43									206	54	39	33	213	61	49	36
6a	197	43	42	44	196	45	45	45	195	47	46	44								
b	228	44	42	43					236	46	52	51								
c	238	44	40	41									234	52	45	39	246	52	54	47
7a	216	40	49	55	212	44	51	52	234	45	58	58								
b	222	40	42	47													261	49	51	47
8a	178	41	53	58									220	48	55	51	222	48	58	54
b	169	42	43	46													211	48	46	43
Mean	214	45	45	46	191	46	49	48	210	47	56	53	213	52	45	39	232	53	53	45
Mean increments									− 3.7	+ 3.0	+ 9.9	+ 6.2					+ 16.8	+ 8.7	+ 8.4	− 0.2

may be liberated into the microcirculation from the tissues, including platelets and red cells, mainly as a result of hypoxia-induced degradation of intracellular high-energy phosphates. Some recent studies suggest that tissue epinephrine could promote this nucleotide release[9]. Also, owing to an increased coagulability of the blood in response to stasis[4], traces of thrombin may be generated in the platelet surfaces with a consequent release of adenosine diphosphate from the platelets[10]. A self-perpetuating mechanism increasing the platelet adhesiveness could be established thereby. Nevertheless, the apparent fall in the platelet adhesiveness by 6-min stasis suggests that mechanisms reducing the adhesiveness come into play during sustained stasis. An increased fibrinolytic activity may be proposed as a mechanism involved. TIGHE and SWAN[3] have demonstrated that, after stasis similar to that employed in the present tests and lasting 3.5 min or more, there occurs a steady increase in the fibrinolytic activity, and others have shown that the platelet adhesiveness is reduced by fibrinolysis through inhibition of the adhesiveness-increasing factors[11]. In case the platelets constitute the critical moiety in thrombogenesis, it would appear that fibrinolysis normally counteracts thrombus formation by its indirect, adhesiveness-reducing action on the platelets.

The unequal adhesiveness response in the large vein and microcirculation samples is compatible with the evidence suggesting that, in studies on thrombogenesis, it is hazardous to transfer observations made on large vessels to the microcirculation and vice versa[12]. Moreover, it points to the possibility that, whenever multiple blood samples are taken under stasis for hemostatic studies, quite uniform changes may not occur in various hemostatic indices in the successive samples[13].

Zusammenfassung. Stauung des Blutkreislaufs mit Hilfe einer Druckmanschette (100 mm Hg) am Oberarm verursachte eine Veränderung der Blutblättchenadhäsivität im distal davon gelegenen Bereich des Kreislaufs. Nach einer Stauung von 3 min nahmen die in bezug auf die Hämatokritzunahme korrigierten Adhäsivitätswerte zu. Nach einer Stauung von 6 min war eine Rückkehr der korrigierten Adhäsivitätswerte zur Ausgangslage oder auf noch niedrigere Werte feststellbar. Im Blut, welches hauptsächlich aus den grösseren Venen herstammte, und im Blut aus dem Kapillargebiet waren die Veränderungen der Adhäsivität gleichgerichtet, jedoch verschieden gross.

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Institute of Physiology, University of Helsinki (Finland), September 25, 1964.

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[13] This work was financially supported by the Sigrid Jusélius Foundation and the Finnish Medical Research Council.

Sur le rôle joué par l'atrophie du thymus dans l'inhibition de la lymphopoïèse provoquée par la carence alimentaire en protéines chez le rat mâle

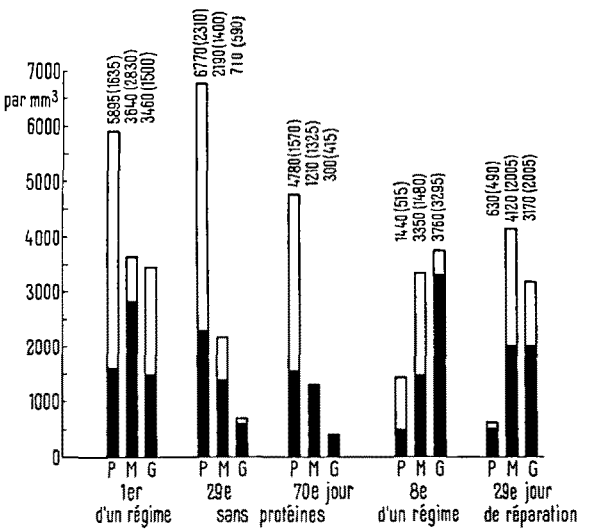
Etant donné la précocité de l'involution thymique dans la carence en protéines et le pouvoir stimulant exercé par le thymus sur la lymphopoièse, il nous a paru intéressant de voir jusqu'à quel point cette involution commandait la lymphocytopénie sanguine des rats carencés.

Technique expérimentale. 13 rats mâles (Wistar) intacts et autant de rats thymectomisés 3 à 4 semaines après le naissance, couplés avec les précédents, sont à l'âge de 70 jours soumis à un régime sans protéines (pour sa composition voir[1]). 7 couples sont sacrifiés après 28 jours. Les autres sont, après 70 jours de carence remis pendant 4 semaines à un régime à 18% de caséine[1].

Des numérations périodiques de leucocytes sont complétées par des mensurations des diamètres lymphocytaires. Selon leurs indices cellulaires (produits de deux diamètres perpendiculaires), les lymphocytes sont répartis en petits ($< 80\ \mu^2$), moyens ($80–110\ \mu^2$) et grands lymphocytes ($> 110\ \mu^2$).

Résultats. (1) Dès avant le régime carencé les rats thymectomisés ont à peu près deux fois moins de lymphocytes circulants que les rats intacts, la réduction portant surtout sur les petits, mais aussi sur les grands lymphocytes (Figure).

(2) Sous l'effet de la carence en protéines les deux groupes de rats intacts et thymectomisés accusent une chute élective du nombre des moyens et des grands lym-



Taux moyens de petits (P), moyens (M) et grands (G) lymphocytes chez des rats *mâles* intacts et des rats thymectomisés (segments foncés des colonnes et chiffres entre parenthèses) au cours d'un régime sans protéines et d'un régime de réparation à 18% de caséine. Dans les colonnes 8 et 9, les valeurs des rats thymectomisés dépassent celles des rats intacts.

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