(Standard B)/ml) have been injected i.v.. Controls and operated recipients have been sacrificed in groups of 4 rats, 0, 1, 2, 4 and 6 h after the injection of active plasma. Erythropoietin plasma level has been assayed on post-hypoxic polycythemic mice, receiving an additional transfusion (1 ml blood, 75% tc). Fe 59 incorporation into red cells has been measured 72 h after radioiron injection. Results have been expressed in international units, by reference to a dose response curve, constructed with standard B. The regression curves have been calculated considering the values of erythropoietin plasma titre at 0 time (10 minutes after injection) as 100%.

As shown in the Table, nephrectomy increases significantly the disappearance rate of erythropoietin. In the controls, the half life averages 2.0 h against 5.8 h in the nephrectomized groups ($p < 0.001$). 48 h and immediately after ureteral ligation, the half lives average respectively 3.8 and 2.4 h. The half lives after ureteral ligation, whatever the delay between surgery and injection of active plasma, are significantly different from the values in the nephrectomized groups. The values found in the controls and in the rats injected immediately after ureteral ligation are similar, and the slight difference observed is not statistically significant.

The significant difference observed between nephrectomized and ureteral ligated rats, shows that the T/2 increase is not imputable to the absence of urinary excretion of the hormone, or to decreased utilization related to uremic intoxication. It is inferred that renal tissue itself is implicated in the catabolic destruction of the hormone. The difference observed between the disappearance rates measured in ureter ligated groups 0 and 48 h after surgery, could be due to some alteration of renal tissue, consecutive to the severe hydronephrosis observed 48 h after ureteral ligation. However, an additionnal role of uremic intoxication cannot be definitely excluded. These experiments performed in vivo agree with results obtained in vitro and imply that the same organ producing erythropoietin is also involved in its catabolic destruction, a mechanism which is presently being investigated.

Effect of nephrectomy or ureteral ligation on the *T/2* of erythropoietin

Exp. groups	No experiments	Urea (mg/100 ml ± SEM)[b]	T/2 (h)	
Controls	4	0.33 ± 0.05	2.0	N.S.
Ligation 0 h	3	0.39 ± 0.03	2.4	
Nephrectomy 48 h	8	5.13 ± 0.24	5.8[a]	
Ligation 48 h	4	5.38 ± 0.44	3.4[a]	

[a] Significantly different from the other groups, $p < 0.001$. [b] Urea plasma level at 0 time.

Résumé. La néphrectomie bilatérale réduit de façon significative l'utilisation de l'érythropoïétine. Cet effet n'est pas dû à l'absence d'élimination par les urines ni à l'intoxication urémique. Ces résultats impliquent que le rein joue un rôle dans le catabolisme de l'hormone.

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The Influence of Hypothermia on Arthus-Phenomenon and Leucotaxis

In previous experiments it has been shown that hypothermia prevents both active and passive systemic anaphylactic shock of guinea-pigs[1,2], local Shwartzman phenomenon in rabbits[3] and anaphylactoid reaction in rats elicited by dextran or ovalbumin[4]. Recent investigations have demonstrated that passive cutaneous anaphylaxis and hypersensitivity induced by DNCB, as well as inverse passive Arthus reaction, can be considerably decreased or fully prevented by cooling the animals[5].

The present study gives an account of the effect of hypothermia on inverse passive Arthus phenomenon and on the Arthus-like reaction induced by the lysosomes of PMN leucocytes. In addition results are reported about leucocyte migration applying different leucotactic agents – to various body temperatures.

Material and method. Inverse passive Arthus reaction was induced in normothermic and hypothermic guinea-pigs. 2 mg of ovalbumin were given intrajugularly; then after a 15 min interval 200 µg antiovalbumin rabbit γ-globulin were intracutaneously injected. To elicit Arthus-like reaction, lysosomes were prepared from rabbit's leucocytes according to the method of Cohn and Hirsch[6] and injected into normothermic and hypothermic rabbits and guinea-pigs intracutaneously (50–70 µgN).

The following leucotactic agents were administered into the dorsal skin of normothermic and hypothermic rabbits: *E. coli* 0111 endotoxin, 1% casein, 0.1% glycogen and 1% Witte peptone. In order to induce hypothermia, the

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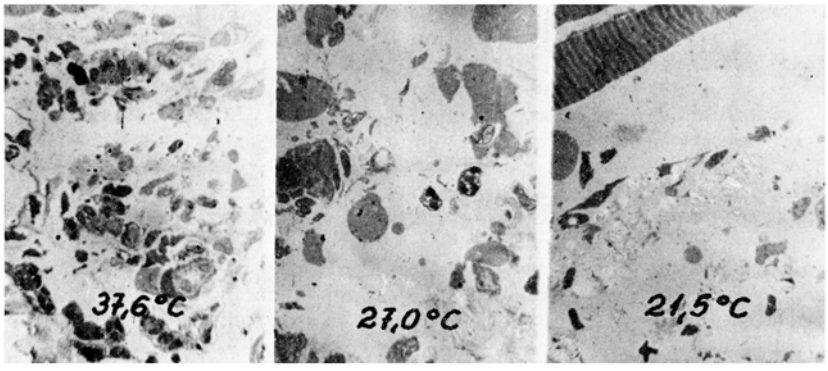

Fig. 1. Inverse passive Arthus reaction elicited in the skin of the guinea-pig at different body temperatures (6h after eliciting the reaction). Half thick section (1500 Å); toluidine-blue staining. ×900.

lightly anaesthetized animals were cooled with ice bags. Both colonic and skin temperature were subsequently taken by means of a thermistor thermometer. By taking excisions from the skin of the animals, histological investigations were also performed.

Results and discussion. According to our experiments in hypothermic animals, the size of the reaction area, as well as the intensity of the reaction, decreased with the lowering of the body temperature and at 20–22°C no inverse passive Arthus phenomenon developed[5]. According to the histological studies, in normothermic guinea-pigs the intensive PMN leucocyte accumulation—that is typical in inverse passive Arthus phenomenon—markedly decreased (at 25–30°C colonic temperature) or was totally absent (below 25°C) in hypothermic conditions (Figure 1).

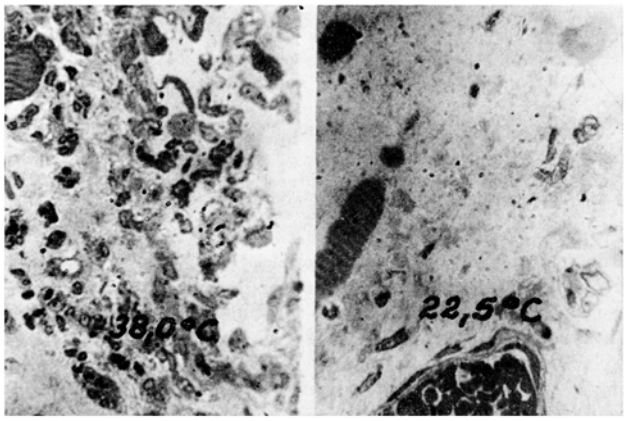

Fig. 2. Arthus-like reaction induced by lysosome preparation. Half thick section from the skin of normothermic and hypothermic rabbits. (6h after eliciting the reaction). Toluidine-blue staining. ×900.

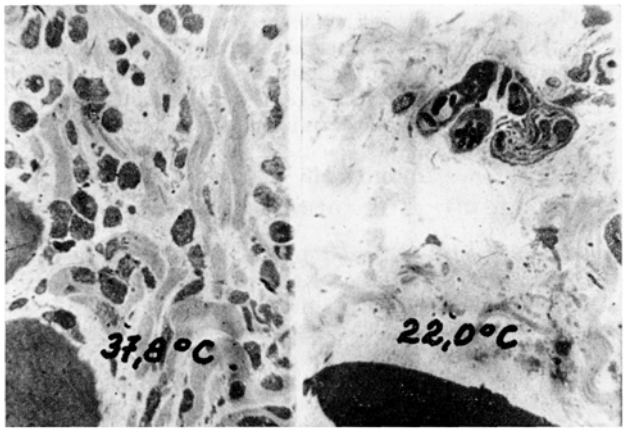

Fig. 3. Examination of the leucotactic effect of casein in the skin of rabbits at different body temperatures (6h). Half thick section, toluidine-blue staining. ×900.

GOLUB and SPITZNAGEL[7] could produce with lysosome granules of the isolated PMN leucocytes an Arthus-like phenomenon. The results of our experiments showed that in cooled guinea-pigs and rabbits the intensity of the Arthus-like reaction decreased with the lowering of the body temperature and at 20–22°C no reaction developed. The histological specimen proved that at the latter temperature the leucocyte migration totally failed to develop (Figure 2).

After studying the results, it is considered that they must be appreciated as a general phenomenon: hypothermia inhibits the leucotaxis of all types. In order to prove this assumption, various leucotactic agents were administered to rabbits. It was endotoxin and casein[8] that appeared as the most effective of all. As a result it was considered that at 20–22°C no leucocyte migration could be observed (Figure 3).

BRYANT et al.[9], by examining leucocyte migration in vitro, concluded that the process reaches its highest level at 40°C and with the lowering of the temperature the leucocyte migration considerably decreases in the capillary tube. Since WARD and BECKER[10] found that, in the chemotactic response of the neutrophils esterase, enzymes play an important role; it is evident that their activity depends on temperature.

Our experiments give a clearcut proof that hypothermia inhibits in vivo the effect of both complement dependent[11] (antigen-antibody complex, endotoxin, glycogen) and complement independent (lysosomal cation-protein, casein, Witte peptone) leucotactic agents.

Zusammenfassung. Es wurde an Kaninchen und Meerschweinchen festgestellt, daß Arthus-Phänomen und Leucotaxis durch Abkühlung verhindert werden können.

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