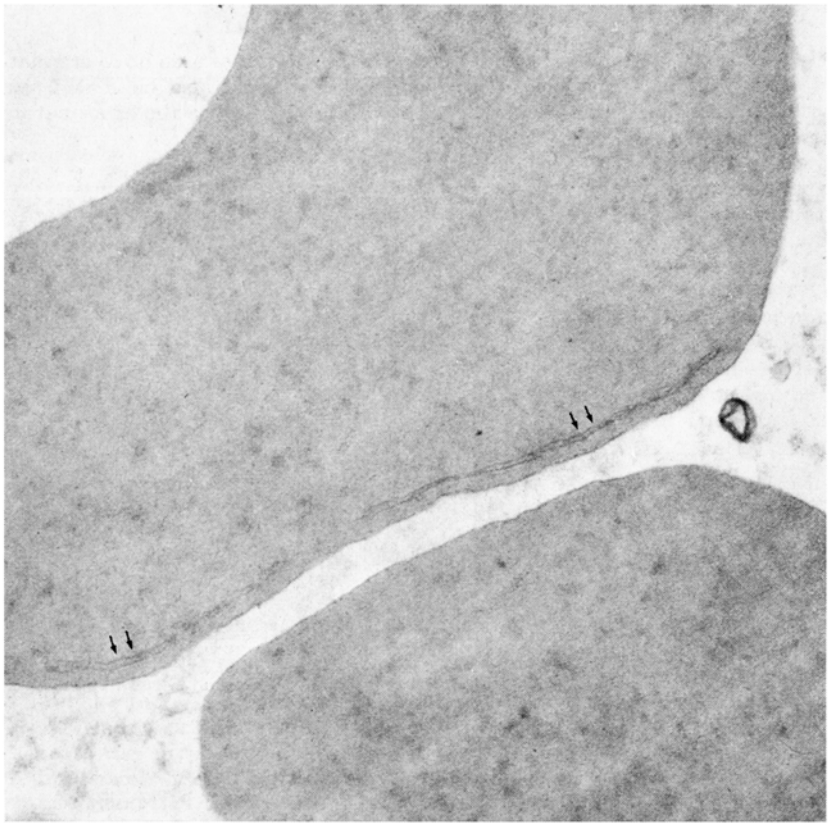

Fig. 3. Electron microscopic picture of an erythrocyte demonstrating stretches of the described anomaly. × 36.000.

of this structure. Abnormalities of the Hempas erythroblasts have recently been mentioned by HEIMPEL et al.[6] and by WONG et al.[7].

We suggest that the cell membrane anomaly, when it extends to a large part of the periphery in a late erythroblast, impedes postmitotic cell division or enucleation, this enucleation being a process similar to a cell division without a previous nuclear division[8]. This anomaly thus results in an intramedullar accumulation of the most affected erythroblasts and in ineffective erythropoiesis. The less affected erythroblasts can still pursue their maturation and appear in the peripheral blood as erythrocytes with stretches of the same abnormality.

Résumé. Description d'une anomalie de la membrane cellulaire des érythroblastes et des érythrocytes chez les malades atteints de «Congenital Dyserythropoietic Anaemia, type II». Les auteurs suggèrent que cette anomalie interfère avec la division cellulaire et est la cause de la binucléarité et de l'érythropoièse inefficiente rencontrées dans ce syndrome.

R. L. VERWILGHEN, P. TAN, C. DE WOLF-PEETERS, A. BROECKAERT-VAN ORSHOVEN and A. C. LOUWAGIE

Laboratorium voor Fisiopatologie-Hematologie, Laboratorium voor Histochemie en Cytochemie, Academisch Ziekenhuis Sint-Rafael, B–3000 Leuven (Belgium), 22 June 1971.

[6] H. HEIMPEL, J. FORTEZA-VILA and W. QUEISSER, Scientific Exhibition at the XIIIth International Congress of Haematology (Munich 1970), p. 391.

[7] K.Y. WONG, G. HUG and B.C. LAMPKIN, Abstract of paper presented at the XIIIth Annual Meeting of the American Society of Hematology (Puerto Rico, 1970), p. 135.

[8] E. SKUTELSKY and D. DANON, Expl. Cell Res. *60*, 427 (1970).

[9] We thank Prof. V.J. DESMET for the use of the electron microscope, Dr. H. VERHAEGEN for his help in the investigation of the patient under his care and Miss A. PINNOY for her skilful assistance.

The Kidney and Utilization of Erythropoietin

The metabolism of erythropoietin is poorly understood. Several studies have shown that the liver is probably implicated in the catabolism of the hormone[1,2] and utilization by the erythroïd marrow has also been incriminated[3]. However we have shown recently that neither hypoplasia nor hyperplasia of the erythroïd marrow modify the disappearance rate of erythropoietin in the rat[4]. On the other hand, it has been demonstrated that renal tissue or extracts are able to destroy erythropoietin in vitro[5,6]. This effect could be non-specific and not indicative of a physiological function of this organ. In order to precise this point, we have compared the effects of nephrectomy and ureteral ligation on the disappearance rate of exogenous erythropoietin in the rat.

Male Wistar rats, weighing from 180 to 200 g, have been submitted to bilateral nephrectomy or to ligation of both ureters. 48 h after nephrectomy and immediately after or 48 h after ligation of the ureters, 2 ml of plasma with high erythropoietic activity from hypoxic rats of the same strain (containing 2 to 4 units of erythropoietin

(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.

J. P. Naets and M. Wittek[7]

Laboratoire de Médecine Expérimentale and Laboratoire de Biologie Clinique de l'Hôpital Brugmann, Université Libre de Bruxelles and Fondation Médicale Reine Elisabeth, Bruxelles (Belgium), 1 June 1971.

[1] T. C. Prentice and E. A. Mirand, Proc. Soc. exp. Biol. Med. *95*, 231 (1957).
[2] W. T. Burke and B. S. Morse, in *Erythropoiesis* (Eds. L. O. Jacobson and M. Doyle; Grune and Stratton, New York, 1962), p. 111.
[3] F. Stohlman jr. and G. Brecher, Proc. Soc. exp. Biol. Med. *100*, 40 (1959).
[4] J. P. Naets and M. Wittek, Am. J. Phys. *217*, 297 (1969).
[5] Z. Kuratowska, Bull. Acad. pol. Sci. *13*, 385 (1965).
[6] A. J. Erslev and L. A. Kazal, Proc. Soc. exp. Biol. Med. *129*, 845 (1968).
[7] Grateful acknowledgment is made to Dr. P. Vereerstraeten, who performed the statistical analysis of the results. This work was performed under contract Euratom U.L.B. – Pise No. 063-4 Biac and supported by a grant of the F.R.S.M.

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

[1] T. Szilágyi, L. Kocsár and F. Gyulai, Acta physiol. hung. *8*, 393 (1955).
[2] L. Kesztyüs, T. Szilágyi, B. Csaba and H. Csernyánszky, Acta physiol. hung. *14*, 177 (1958).
[3] T. Szilágyi, L. Kocsár and H. Csernyánszky, Acta microbiol. hung. *3*, 327 (1956).
[4] T. Szilágyi, B. Csaba and E. Szabó, Acta physiol. hung. *20*, 145 (1961).
[5] T. Szilágyi, H. Csernyánszky, S. Imre and M. Went, Acta microbiol. hung. *16*, 363 (1969).