The electrical stimulation of the clot restores always a maximal clot retraction, even after a prolonged (8 or 10 min) previous in vitro platelet aggregation (figure 2, B); this result was constantly found in all the experiments.
The table reports all the results of clot retraction (following previous in vitro platelet aggregation prolonged of different times), occurring in clots submitted or not to electrical stimulation.
Discussion. Present results confirm that previous in vitro platelet aggregation inhibits spontaneous clot retraction. However, the degree of inhibition seems more dependent on the duration than on the degree of aggregation: 4 min after the addition of ADP, the degree of aggregation was the same as after 10 min, but the subsequent spontaneous clot retraction was inhibited only in the latter case. Moreover the electrical stimulation of the clot provokes clot retraction even after a previous prolonged (10 min) platelet aggregation, thus demonstrating that suitable condition (s), like electrical stimulation, can trigger off platelet modification leading to clot retraction.
These facts show clearly that the inhibition of spontaneous clot retraction, by previous in vitro platelet aggregation, is not related to the altered distribution of the platelets, nor to a diminution of the platelet surface available for fibrin fibres, as was supposed by de Gaetano et al.[2]; therefore it is possible that the previous in vitro platelet aggregation provokes an altered metabolic state of the platelets, which become unable to supply energy for spontaneous clot retraction, even if their responsiveness to the electrical stimulation is not decreased.
An earlier paper from our laboratory indicated that electrically induced retraction of reptilase clots is inhibited by aspirin and by indomethacine[5], which are ineffective on the reptilase clot retraction occurring in the presence of aggregating agents[6].
Present experiments showed clearly another difference between clot retraction occurring after electrical stimulation or in the presence of aggregating agents[6].

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Leukocyte mobilization by epinephrine and hydrocortisone in patients with chronic renal failure

G. Perescenschi, V. Zakouth, Z. Spirer and A. Aviram

Department of Nephrology and the Paediatric Immunology Unit, Rokach (Hadassah) Hospital, Tel-Aviv Medical Center, Tel-Aviv (Israel), 23 May 1977

Summary. The mobilization of WBC from the bone marrow, as judged from hydrocortisone-induced leucocytosis, is markedly impaired in dialyzed and nondialyzed uremic patients. The release of WBC from the marginal pool by epinephrine was found to be normal.

Uremia is commonly considered to be an acquired immune-deficiency state, but the exact mechanism(s) of this impaired immunity is still not clear[1-4]. As polymorphonuclear leucocytes play an important role in the first line defence in the immunological process, it seemed important to study their function in uremia. We investigated the mobilization of leucocytes from the bone marrow and the marginal pool in patients with chronic renal failure.
Material and methods. 16 patients with chronic renal failure treated conservatively participated in the study. They had creatinine clearance below 30 ml/min. All were well maintained and none was in the terminal stages of uremia. Additional 18 patients were treated by hemodialysis. They were well dialyzed in accordance with accepted criteria, 15–18 h a week on coil dialyzer. A group of volunteer medical students and hospital employees served as normal controls. Age and sex were equally distributed among the 3 groups. None of the patients received steroids or immunosuppressive drugs.
Epinephrine test: 0.01 mg/kg b.wt of epinephrine solution was injected s.c. Capillary blood samples were drawn before and at 5, 15, 20, 30 and 60 min following the injection, for total white blood counts[5]. This test was performed in 10 of the normal subjects, 13 uremic and 8 dialysis patients.

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Table 1. Mean leucocyte counts (± SE) following epinephrine injection*

	Min after epinephrine injection						
	0	5	10	15	20	30	60
Normal subjects (n = 10)	6 645 ± 518	9 435 ± 1 317	14 415 ± 1 921	15 333 ± 1 806	14 083 ± 1 105	11 485 ± 875	9 365 ± 898
Uremic patients (n = 13)	7 438 ± 593	9 020 ± 828	12 659 ± 1 744	12 938 ± 1 124	13 526 ± 1 274	12 065 ± 1 252	10 042 ± 800
Dialysis patients (n = 8)	7 206 ± 599	8 175 ± 394	11 762 ± 1 019	12 850 ± 1 128	14 512 ± 1 339	12 788 ± 1 273	8 781 ± 1 162

*Differences between the means of the 3 groups were not statistically significant at any time.

Table 2. Mean leucocyte counts (SE) following hydrocortisone injection

	h after hydrocortisone injection 0	1	2	3	4	5	6
Normal subjects (n = 14)	6 364 ± 402	7 585 ± 666	10 231 ± 1 092	11 993 ± 983	11 286 ± 726*	9 785 ± 575	8 497 ± 514
Uremic patients (n = 16)	7 131 ± 784	6 550 ± 617	8 337 ± 1 012*	8 437 ± 730*	8 837 ± 500*	7 168 ± 435*	7 334 ± 509*
Dialysis patients (n = 18)	7 019 ± 452	6 939 ± 478	7 505 ± 589*	7 552 ± 505*	7 797 ± 529*	7 597 ± 565*	7 075 ± 460*

*$p < 0.01$ (patients vs controls).

Hydrocortisone test: 100 mg of hydrocortisone-Na-succinate (Solu-Cortef, Upjohn) were injected i.v. Capillary blood samples were taken just before the injection and then at hourly intervals for 6 h. All subjects of the above-mentioned groups participated in the hydrocortisone test. No adverse reactions were noted in either test, except for transient and mild tremor after the epinephrine administration.

Results. Table 1 summarizes the rise in WBC counts in response to epinephrine injection. There is no significant difference in this response between the normal subjects and the 2 groups of chronic renal failure patients. When the rise in WBC is depicted relative to the basic count (time 0), it seems that there is a slight delay in the maximal response of the patients when compared with the healthy subjects (figure 1), but this is of no statistical significance. In the hydrocortisone test, the rise in WBC counts was markedly diminished in both dialysed and nondialyzed uremic groups when compared to the normal subjects (table 2). This impairment is even better demonstrated when the response is expressed relative to counts at time '0' (figure 2).

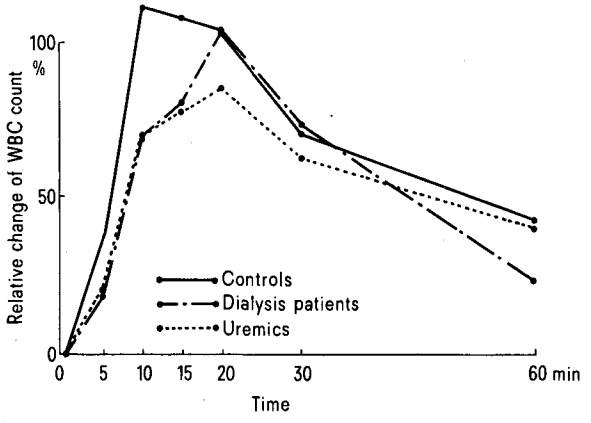

Fig. 1. Mean change in leucocyte counts induced by epinephrine.

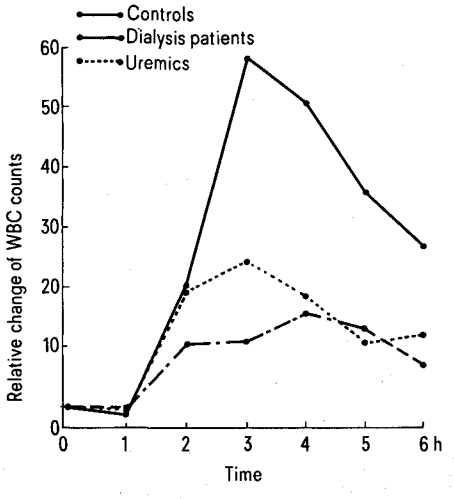

Fig. 2. Mean change in leucocyte counts induced by hydrocortisone.

Discussion. It is accepted that peripheral leukocytosis induced by epinephrine is due to mobilization of WBC from the marginal pool[6] while the hydrocortisone releases leukocyte from the bone marrow[7,8].

Our results show that there is no defect in the mobilization of leukocytes from the marginal pool in patients with chronic renal failure. On the other hand, there is a marked impairment in the recruitement of leucocytes from the bone marrow as evidenced by the decreased response to hydrocortisone injection in both uremic groups. It is noteworthy that dialysis does not improve this abnormal response. Our findings suggest that impaired WBC mobilization in uremia may play an important role in the abnormal immunological responses related to uremia. This could also explain the lack of leucocytosis during systemic bacterial infection seen in dialyzed patients[9].

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