Reduced Bactericidal Capacity of Polymorphonuclear Leucocytes in Nephrotic Syndrome and Effect of Steroid Therapy

Patients with nephrotic syndrome have an increased susceptibility to infections, many of which run a fulminant course. The mechanisms underlying such processes are not clear, but probably they touch more than one facet of immunocompetence. We have looked at the intracellular bactericidal capacity of polymorphonuclear leucocytes (PMNs) of children suffering from nephrosis, and evaluated the effect of corticosteriod therapy on such function.

Methods. The diagnosis of nephrotic syndrome was based on generalized edema, massive proteinuria and hypoalbuminemia. The bacterial test was essentially as described by QUIE et al.[1] using surface counting of *Staphylococcus aureus* colonies on nutrient agar plates. The bactericidal capacity of PMNs was calculated by the ratio : number of viable intracellular bacteria at 140 min/number at 20 min of the culture. The test was also done on nephrotic patients receiving prenisolone in a dose of 60 mg/m^2 body surface area, per day.

Results and discussion. There was a marked reduction in intracellular bacterial killing by PMNs of nephrotic children as shown in the Table ($P < 0.001$). The exact cause for this defect is not clear. There are at least 4 possible mechanisms for killing organisms inside macro- and microphages: Lysosomal phagocytin system involving arginine rich cationic proteins, hydrogen peroxide system, muramidase activity and hydrolases. In nephrotic syndrome, changes in protein metabolism (loss through proteinuria, reduced intake due to anorexia, increased catabolism, and impaired absorption due to edema of the gut wall) might reduce the availability of amino acids, thereby adversely affecting the synthesis of lysosomal enzymes. This simulates the state of malnutrition in which bactericidal capacity of PMNs is significantly impaired.[2]

The values in nephrotics receiving prednisolone overlapped those of patients not on such a therapy. The log mean for the former was, however, significantly lower ($0.05 > P > 0.02$). The administration of glucocorticosteroids suppresses inflammatory response and increases susceptibility to infection. On macrophages, the chief effect is a diminished influx of such cells from the blood to the site of inflammation.[3] The suppressed reduction of nitroblue tetrazolium by PMNs of patients receiving steroids[4] and the in vitro inhibition by hydrocortisone of NADH oxidase[5] are apparently incongruous with our data. The dichotomy between reduction of nitroblue tetrazolium and bactericidal capacity is well known in children with chronic granulomatous disease[6,7]. The improved bacterial killing by microphages of nephrotics on steroid therapy could be due to an actual or impending amelioration in the underlying renal disease and its consequences on protein metabolism, or it might be the result of stabilization of lysosomal membranes inside the cells[8].

Zusammenfassung. Es wird der Nachweis erbracht, dass die bakterizide Wirkung der polymorph-kernigen Leukozyten bei Patienten mit nephrotischem Syndrom vermindert ist und dass Prednisolon einen günstigen Einfluss auf die Bakterizidie polymorph-kerniger Leukozyten beim nephrotischen Syndrom hat.

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Intracellular bacterial killing by PMNs expressed as the ratio-number of viable intracellular bacteria at 140 min/number at 20 min of the culture

Group	Number	Bactericidal capacity		
		Range	Geometric mean	S.D.
Healthy subjects	24	0.02–0.21	0.07	0.03
Nephrotic syndrome	12	0.10–0.54	0.33	0.11
Nephrotics receiving prednisolone	16	0.03–0.64	0.25	0.12

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Effect of Serum from Tumor-Bearing Mice on the in vitro Migration of Thymocytes

The growth of a transplanted syngeneic tumor is known to induce a marked atrophy of the thymus[1–3]. Bilateral adrenalectomy reduces this phenomenon[4] and corticosteroid hormones are thus probably involved. Yet, another factor must operate since the total number of circulating lymphocytes increases during the course of tumor development[2]. It can be postulated that an increased migration of the thymic lymphocytes to the periphery might also account for the depletion of the thymus in this situation. One could further imagine that some changes in the properties of the serum might mediate the phenomenon.

The present work was undertaken in order to examine this last possibility. We have studied the migration of normal mouse thymus cells out of capillary tubes onto glass in culture chambers containing diluted syngeneic serum[5]. This technique allowed us to compare the effect