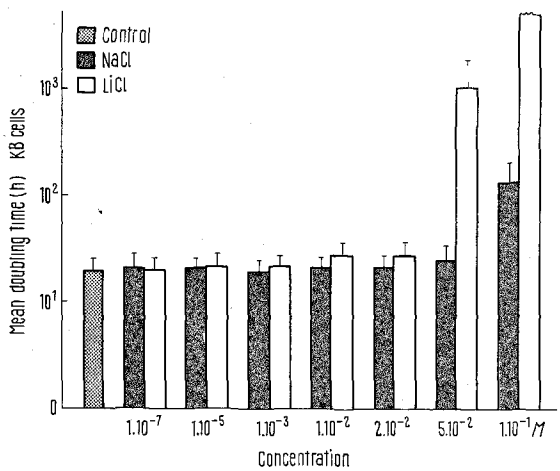
The data presented in the Figure show the effects induced on the mean doubling time of neoplastic KB cells by equimolecular concentrations of LiCl and of NaCl. These are expressed by means of groups of 2 adjacent columns. The first column of each group presents the effects exerted by NaCl while the second shows comparatively those induced by an equiconcentration of LiCl. The osmotic pressure on the cultures is thus the same for 2 adjacent columns of the same group.

As compared to the control column (stippled), the results obtained show that increasing concentrations of LiCl added to the medium progressively reduce and inhibit the proliferation of the cells during the logarithmic phase of growth. The induced increase in the mean doubling time of treated cells is not significant for concentrations of LiCl $\leqslant 1.10^{-3}M$ but highly significant ($p < 0.001$; t-test) for $5.10^{-2}M$ LiCl. Concentations of LiCl $\geqslant 1.10^{-1}M$ are toxic even for the cells in interphase, causing their degeneration as shown here by the broken column. For NaCl, a significant effect is observed only at concentrations of $1.10^{-1}M$ (2.3 mg/ml Na^+). Furthermore, even at this concentration, the corresponding mean doubling time is still significantly lower ($P < 0.01$; t-test) than that observed with $5.10^{-2}M$ LiCl (0.346 mg/ml Li^+). This selectivity would be in accordance with the data of SAMOILOV[5] who has shown in vivo that the toxicity of lithium is 10 times higher than that of sodium.

In addition, for exposure higher than 24 h, LiCl $5.10^{-2}M$ would induce a decrease in cytoplasmic RNA as suggested by our cytochemical studies which showed that the intensity of the RNA characteristic reddish-orange fluorescence was reduced in LiCl-treated cells. This effect appears to be in general agreement with the recent results of DEWAR and READING[6].



Effects of LiCl and NaCl on the mean doubling time of neoplastic KB cells.

With the normal RMK cells the results are grossly similar to those obtained with KB cells. However, more studies are needed to evaluate quantitatively the differences between these two cell types with regard to their reactivity toward lithium.

The mechanism of the antimitotic action of lithium ions is still unknown. However, it could be related to some known effects of this cation (SCHOU[7]) such as extrusion of intracellular potassium or interference with oxydative phosphorylation and amino acid metabolism. An action through catecholamines should also be considered since lithium activates the desamination[7] of these mitogenic substances[8]. In addition, it is not impossible to assume an intranuclear accumulation of lithium and its eventual combination with the anionic chromatin, as suggested for high concentrations of sodium[9]. The observed effect could also be partially related to the lithium-induced decrease of cytoplasmic RNA we have noted, here or to its blocking effect on DNA polymerase[10]. Moreover, it would be of interest to investigate the effect of lithium on the mitotic spindle. Indeed, lithium is known to interfere with ciliary movements[7] while antimitotic agents such as colchicine which act by impeding spindle formation also block many kinds of ciliary motility processes.

Nevertheless, whatever is the mechanism, in agreement with the recent work of PEDERSON and ROBBINS[11], our results emphasize the important role of electrolytes in the physiological control of cell division and the need for further investigations concerning their effects at this crucial level.

Résumé. L'action du lithium (LiCl) a été étudiée comparativement sur des cellules néoplasiques humaines KB et normales de rein de singe. Les résultats obtenus démontrent que le LiCl en concentrations égales et supérieures à $5.10^{-2}M$ entraîne une inhibition significative de la prolifération des deux types cellulaires. D'autre part, pour des temps d'exposition supérieurs à 24 h, cet effet cytoinhibiteur s'accompagne d'une diminution de la quantité des RNA cytoplasmiques. Ces effets du LiCl apparaissent sélectifs par rapport à ceux du NaCl utilisés en concentrations équimoléculaires.

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Natural Antibody Production in Human Tonsils

The tonsils, as lymphoepithelial organs, are known[1] to play an important role in the defence mechanism against invading bacteria and viruses. However, the actual function of tonsils has not been elucidated as yet. Recently[2,3], functional similarities between palatine tonsillar tissue and thymic tissue have been demonstrated. SURJAN and SURJAN[4] found antibody production in tonsils of parenterally immunized animals, showing a functional similarity between nonregional lymph nodes and tonsils.

Table I. 19S natural antibody forming cells in tonsils

Antigen[a]	No. of tonsils investigated	Tonsils producing antibody	Tonsils non-producing antibody	PFC count/10^6 cells mean ± SE
SRBC	13	13	∅	0.40±0.12
RRBC	12	12	∅	0.21±0.11
ChRBC	11	11	∅	0.18±0.10

[a] SRBC, sheep red blood cells; RRBC, rabbit red blood cells; ChRBC chicken red blood cells.

Table II. 7S natural antibody forming cells in tonsils

Antigen[a]	No. of tonsils investigated	Tonsils producing antibody	Tonsils non-producing antibody	PFC count/10^6 cells mean ± SE
SRBC	10	5	5	0.54±0.20
RRBC	9	0	9	—
ChRBC	8	2	6	0.18±0.08

[a] See footnote to Table I.

In the present studies, the natural antibody-producing cells were investigated in human tonsils to collect further evidence of its participation in the lymphoid defence mechanism.

The tonsils were removed 'à froid' from 4- to 10-year-old children. The tonsillar cells were separated in Parker's TC 199 medium, according to PIFFKÓ, KÖTELES and ANTONI[5]. The total cell number was counted and the living cell count was determined by means of Eosin Y dye exclusion test (0.1% Eosin Y reinst; Serva 21,005-solution was prepared in physiological saline at pH 7.0, the cell suspension was diluted 1:200 in the dye solution and counted). The living cell population ranged from 60 to 80% of the total cell count.

The direct, presumably 19 S natural antibody-producing cells were investigated according to JERNE[6] with a slight modification[7]. The indirect, probably 7 S (IgG) antibody-producing cells were counted[8], using anti human IgG sheep serum (Lot L. 47 B, HUMAN, Budapest) for development. The plaque-forming cells (PFCs) were determined against sheep, rabbit and chicken red blood cells (RBC). The plaque-forming cell count was expressed as PFC count per 10^6 cells.

All the tonsils investigated contained natural antibody-producing cells of IgM type (Table I.). The highest values were obtained against sheep RBC.

Some of the tonsils contained indirect PFCs, too (Table II). The results of different authors on indirect PFC are not comparable because of the different immune sera used. Some sera have only developing action while others also inhibit the IgM plaques[9, 10].

In our experiment we could not prove the inhibitory action of the anti IgG immune serum used, since with the exception of a single tonsil, all tonsils showed at least as many indirect PFCs as direct ones. On the basis of this consideration, the direct PFC count was substracted from the indirect ones and only the differences qualified as real 7 S antibody-producing cells.

There are at least two alternatives to explain the presence of natural antibody-forming cells in the tonsils. It is most likely that invading bacteria or other environmental antigens exert their action in situ and the PFCs represent a local antibody response. The other possibility is that the antigen stimulus originates from the intestinal bacterial flora, and specifically committed cells transfer the antibody-forming capacity to tonsils. We could not find antibody-forming cells against *E. coli* 0 26 antigen in tonsils, though almost all of human sera contain antibody against this bacterium[11]. This finding seems to support the significance of local antigen stimulus. However, experiments on the immune response of rabbits[4] proved that the PFCs in tonsillar tissue are the probable consequences of messenger lymphocytes reaching the tonsils by the lymphoid circulation. Irrespective of the origin of the natural antibody-producing cells present in the tonsils, their existence and possible participation in the immune reactions should be reckoned with when the tonsils are investigated in in vitro cultures[12].

Zusammenfassung. Es konnten in den aus den Tonsillen gewonnenen Lymphozyten natürliche, Antikörper bildende Zellen nachgewiesen werden.

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