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The Proliferation of Prostatic Epithelium in Chronic Prostatitis

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Summary. The labelling index in chronic nonspecific prostatitis ranges from 0.7 - 2.1%. This value is markedly higher than in nodular hyperplasia (0.4%) as well as in differentiated adenocarcinomas (0.6%). Increased labelling index could only be determined in glands adjacent to inflammatory foci. In recognition of these findings we believe that a correct evaluation of the cell proliferation in chronic prostatitis is only possible if each single cell can be evaluated, whether it is altered by inflammation or not. Therefore, solid tissue biopsies appear to be more suitable in autoradiographical studies than cytological material alone.

Key words: Prostatitis, cell proliferation.

Analysis of tumour cell proliferation has become of considerable importance in clinical therapy since a more effective cytostatic or radiation treatment can be instituted if the kinetics of tumour cells are known. However, autoradiographic investigations in human beings have been limited to in vitro methods till now. The results of such in vitro studies have shown that an exact determination of some proliferative parameters of tumour cells is possible (4, 7, 9, 11, 13).

Using a tissue incubation method, which has been described in detail in another paper (8), we examined prostatic needle biopsies in order to analyse the proliferative pattern of hyperplastic and carcinomatous epithelial tissue. Since it was found during these investigations that inflammation can influence the proliferative pattern in the prostate, therefore biopsies from patients with prostatitis were specially examined autoradiographically.

Methods

About 1 mm thick prostatic tissue biopsies, obtained with the Travenol^{R}-needle were incubated in autologous plasma at 37°C and 2,2 atm Carbogen pressure (95% O_2 and 5% CO_2). During the first incubation hour 0,5 µCi/ml C^{14}-thymidine (spec. activity 56 mCi/mMol, NEN Chemicals, Boston, Mass. U.S.A.) was added to the plasma. The biopsies were incubated during the second hour in a H^3-thymidine plasma solution (5 µCi/ml, spec. activity 20 Ci/ mMol). The biopsies were then fixed in formalin and embedded in paraffin. After exposure times of up to 50 days the autoradiograms obtained from 3-5 µ thick serial sections were stained with haemalaun. The percentages of pure C^{14} labelled and of pure H^3 labelled as well as those of double labelled (C^{14} and H^3) cells were determined. From these data the H^3 and C^{14} labelling indices were calculated. The mitotic index and DNA synthesis phase (S-phase) for steady state conditions were also measured. (For further details of autoradiographic technique and calculations see 7, 14).

Results

Prostate biopsies from 104 patients were examined. In 12 cases (11%) a chronic nonspecific prostatitis and in 1 case a granulomatous prostatitis was found adjacent to hyperplastic or atrophic and

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carcinomatous tissue changes. Cytological changes such as hyperchromasia and polymorphism of the cell nuclei as well as basophilic cytoplasm were also observed in the glandular epithelium adjacent to focal round cell stromal infiltration. The most extensive histological changes were observed in the case of chronic granulomatous prostatitis (Fig. 1). Occasionally squamous metaplasia occurred although none of the cases was hormonally treated. There was no case of acute prostatitis.

In the autoradiograms the average labelling index in nodular hyperplasia was 0.4% and in no case did it exceed 0.7% (labelling index of normal glands 0.01 - 0.3%). In contrast the values were clearly higher (0.7 - 2.1%) in chronic prostatitis. The average mitotic index was 0.03% and the S-phase ranged from 10-15 hrs. The labelling indices in chronic prostatitis also exceed the values obtained from the majority of the different-

Discussion

Investigations on the influence of an inflammation on the proliferative pattern of the prostatic tissue have obviously not been performed previously. However, there are many reports that an inflammation can lead to an increase in cellular proliferation in other tissues such as bronchus (12), larynx and pharynx (3) and stomach (15).

Castrup et al. (1) using similar methods, examined stomach biopsies and could show markedly increased labelling index in cases of chronic atrophic gastritis. It was striking that the average generation time was reduced by almost half and this was due above all to a considerably shortened G_1-phase, whereas the S-, G_2 and M-phase were essentially not altered. Since in our own material no labelled mitoses were observed - which was not surprising considering the low labelling and mitotic

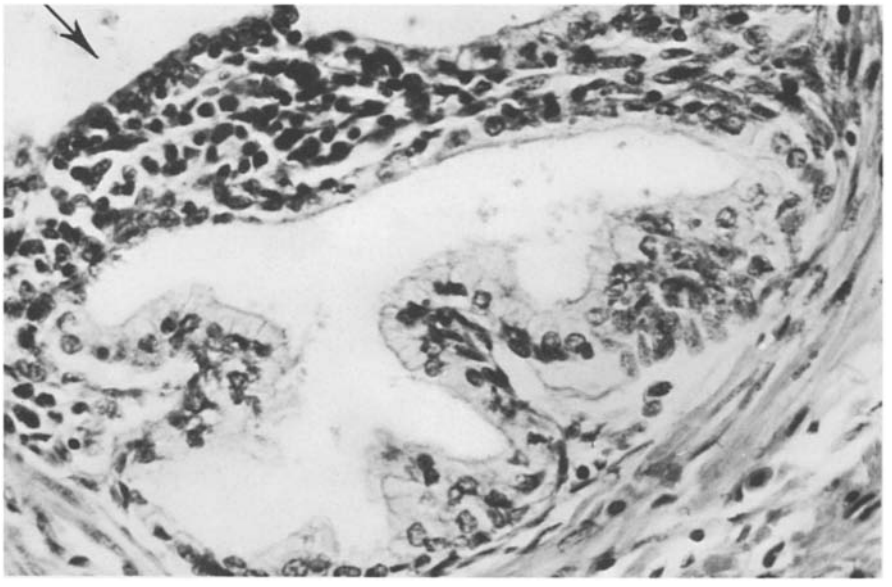

Fig. 1. Epithelial dysplasia of prostatic gland in chronic prostatitis. H.E.

iated adenocarcinomas, which have shown an average labelling index of 0.6% (8). The highest labelling index was recorded in chronic granulomatous prostatitis (2.1%). Figures 2a and b show autoradiograms of nodular hyperplasia in comparison to that of chronic prostatitis.

In 5 cases inflammatory areas could be compared with noninflammatory areas of the same prostatic gland. The results are shown in Table 1. The labelling indices in areas free of inflammation ranges from 0.12% and 0.56% and therefore correspond well with values obtained in nodular hyperplasia. The values in areas showing chronic prostatitis are 5 to 10 times higher.

indices - we could not determine the generation times. Assuming steady state conditions the length of the S-phase could be calculated. These values are not essentially different from those in nodular hyperplasia.

In contrast to factors such as age, state of nutrition, hormones and diurnal rhythms, which can influence the proliferative pattern of a whole organ, an inflammation in the prostate produces a locally active proliferative stimulus. This has also been observed in other organs (liver, kidneys, skin) after nonspecific resorptive inflammation following traumatic injuries (2, 5, 6, 10).

The cellular proliferation in chronic prostatitis

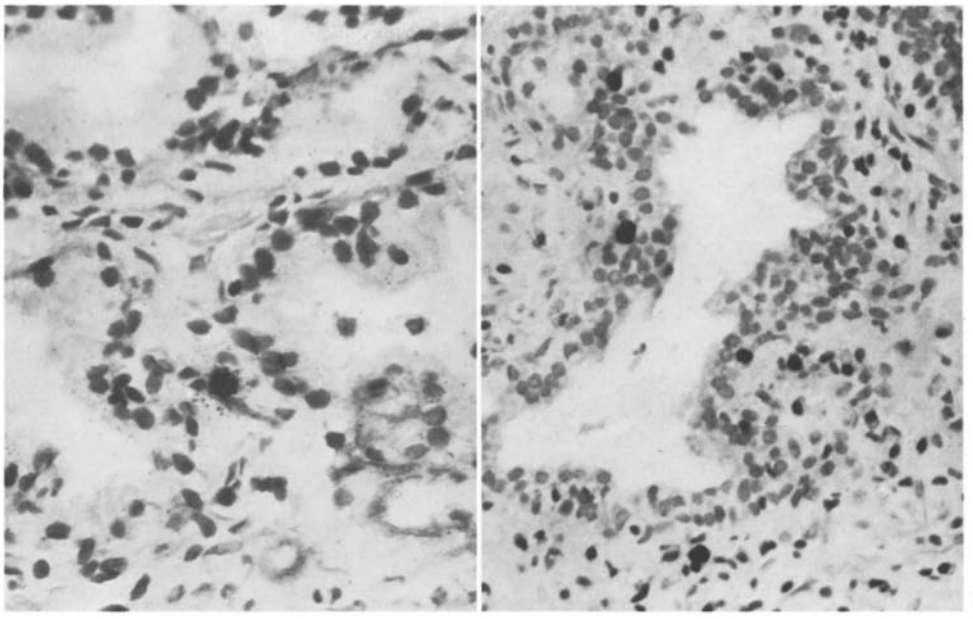

Fig. 2. a) Only one labelled epithelial cell in a hyperplastic prostate gland. b) Many radioactively labelled cells in chronic prostatitis. Stripping film autoradiogram

Table 1. Comparison of labelling indices of prostatic epithelium in inflammation and hyperplasia

No.	Prostatitis (L. I.)	Hyperplasia (L. I.)
920	1.2%	0.20%
938	1.2%	0.12%
744	1.5%	0.28%
740	1.7%	0.26%
746	2.1%	0.56%

clearly suggests that a reliable evaluation of cell kinetics in the prostate is only possible if sufficient material is available allowing a detailed examination of the surrounding tissue. In quantitative studies, especially in autoradiography, each single cell must be evaluated. In our opinion, therefore, solid tissue biopsies appear to be more suitable in autoradiographical studies than cytological material alone, since it is well known that difficulties often arise, especially in the differential diagnosis between granulomatous prostatitis and carcinomas in cytological aspiration material (16, 17).

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