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MICRONUCLEUS

- MN experiments with buccal cells were developed by Stich in 1982; in the following years a standardized protocol of the **MN cytochrome assay** and scoring criteria were published [1].
- Biomarkers of breaks and/or loss of chromosomes.
- **Chromosomal damage leads to neoplastic transformation.**

MN AND GENOMIC INSTABILITY

- Analysis of 19 studies showed high **correlation** between MN rates in **lymphocytes** and **buccal cells** [2].
- MN in buccal cells could reflect the **chromosomal instability** of other organs.
- MN frequencies are increased in **cancer patients (head-and-neck, breast, cervix uterus)** and patients with some **other pathological states** (diabetes, renal diseases, arthritis, colitis, neurodegenerative diseases) [3].

EXFOLIATED BUCCAL CELL TYPES

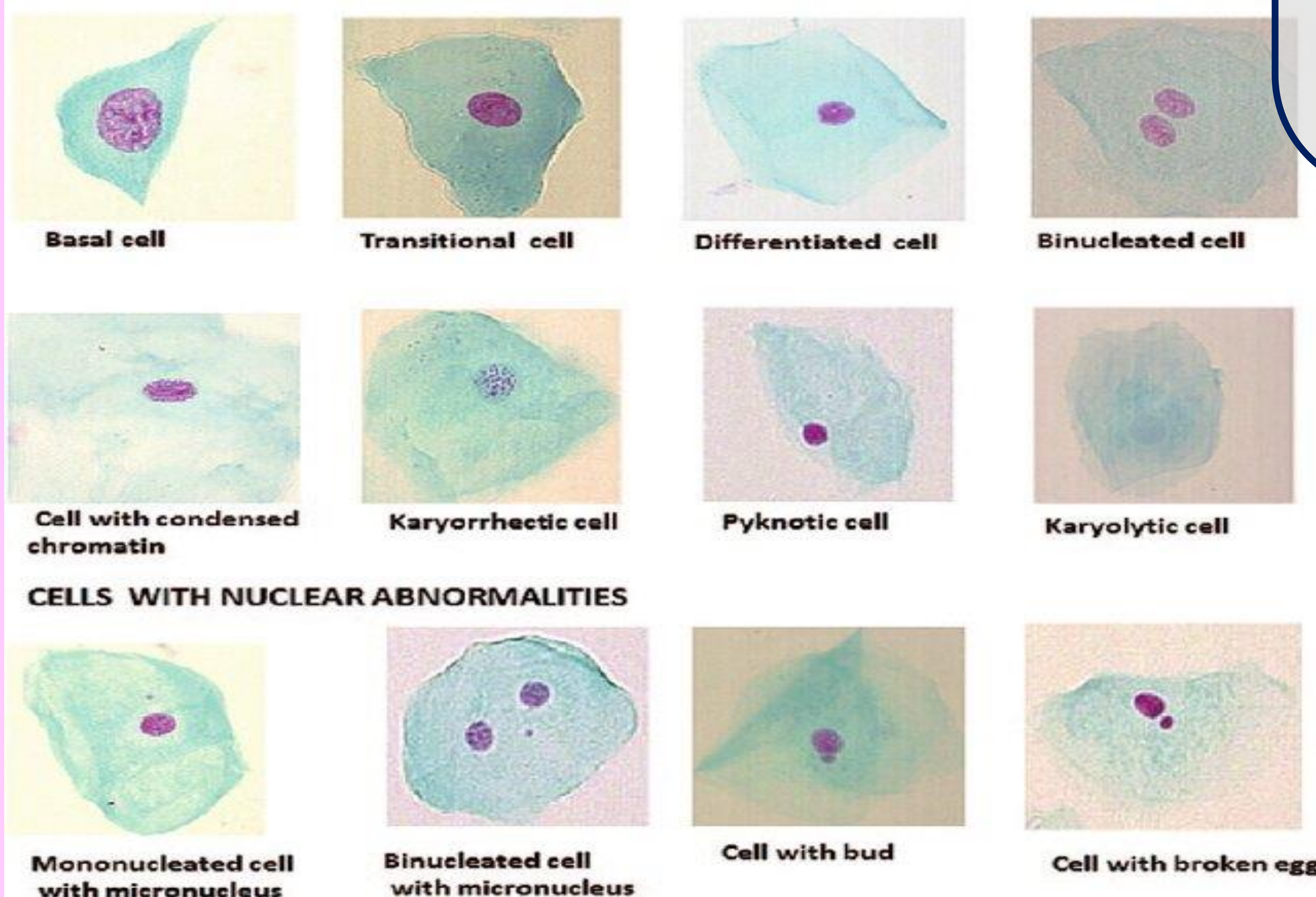


Figure 1. Different cell types and nuclear anomalies evaluated in the buccal micronucleus cytochrome assay [4].

BUCCAL MICRONUCLEUS CYTOME ASSAY

- Additional nuclear anomalies can be scored [4]:
- Nuclear buds
 - Disturbed cell division
 - Pyknosis
 - Karyorrhexis
 - Karyolysis
 - Cells with condensed chromatin
 - It is also possible to evaluate the number of **intact basal cells** which provides information about the **mitotic activity** of the oral mucosa.

ORAL CANCER AND PREMALIGNANT LESIONS [4]

Several studies indicate that MN formation is increased in individuals with **oral cancer** and in patients with **pre-malignant lesions (leucoplakia, erythroplakia, lichen planus, oral submucous fibrosis)**.

OCCUPATIONAL AND ENVIRONMENTAL STUDIES [5]

This assay was used in ~ 570 studies for occupational and environmental biomonitoring to detect exposure of **humans to genotoxic carcinogens**.

TOBACCO CONSUMPTION AND ORAL CANCER [6,7]

Evidence that **higher MN rates** as well as increased cytotoxicity is found in humans that **consume certain drugs (tobacco via smoking and chewing, khat and betel)** which cause **oral cancer**.

CONSIDERATIONS AND SEEKING NEW COLLABORATIONS:

These findings indicate that **cytochrome MN assays with oral cells** can be used to **identify individuals which have increased risks for oral cancer**. To further substantiate this assumption, a **collaboration of different laboratories** is suggested aimed at evaluating the available literature, to **train interested scientists** and to **realize a collaborative study**.

REFERENCES: 1-Thomas, P. et al. Buccal micronucleus cytochrome assay. *Nat Protoc* 4, 825–837 (2009); 2-Ceppi M, Biasotti B, Fenech M, Bonassi S. Human population studies with the exfoliated buccal micronucleus assay: statistical and epidemiological issues. *Mutat Res*. 2010 Jul-Sep;705(1):11-9. 3-Bolognesi C, Bonassi S, Knasmueller S, Fenech M, Bruzzone M, Lando C, Ceppi M. Clinical application of micronucleus test in exfoliated buccal cells: A systematic review and meta-analysis. *Mutat Res Rev Mutat Res*. 2015 Oct-Dec;766:20-31; 4- Bolognesi, C. et al., Buccal micronucleus cytochrome assay: results of an intra- and inter-laboratory scoring comparison, *Mutagenesis*, Volume 30, Issue 4, July 2015, Pages 545–555; 5-Nancy B. Hopf, Claudia Bolognesi, Brigitta Danuser, Pascal Wild, Biological monitoring of workers exposed to carcinogens using the buccal micronucleus approach: A systematic review and meta-analysis, *Mutation Research/Reviews in Mutation Research*, Volume 781, 2019, Pages 11-29. 6-Kokila S, et al. Evaluation of Micronuclei and Cytomorphometric Changes in Patients with Different Tobacco Related Habits Using Exfoliated Buccal Cells. *Asian Pac J Cancer Prev*. 2021 Jun 1;22(6):1851-1855. 7-Salih, D., Salih, S., Abdo, R., Rasool, C., & Alassady, A. (2022). Micronucleus assay of buccal mucosa cells in cigarette and waterpipe smokers in Duhok, Iraq. *Annals of Medical Research*, 29(5), 454–457.