



## Question of the Etiology of Malignant Neoplasms\*

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### ABOUT ARTICLE

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### ABSTRACT

#### Purpose.

To determine the severity of potentiometric parameters in patients with malignant neoplasms of the oral mucosa and the presence of metal inclusions in the form of non-removable dentures made of dissimilar metals and their alloys.

#### Methods.

We examined of potentiometric parameters in 39 patients with metallic inclusions in the oral cavity, in which malignant tumors of the mucous membrane of the oral cavity (tongue, palate, mucous membrane of the alveolar process and the bottom of the oral cavity) were detected. All subjects were between the ages of 40 and 68 years.

#### Results.

High potentiometric indicators were revealed in patients with non-removable metal dentures, which are made of dissimilar metals and their alloys. The presence of defects in the lining of dentures, as well as metal parts of a non-removable structure or metal protective coating ("bald zones") increase the potentiometric parameters and increase the risk of malignant neoplasms of the mucous membranes.

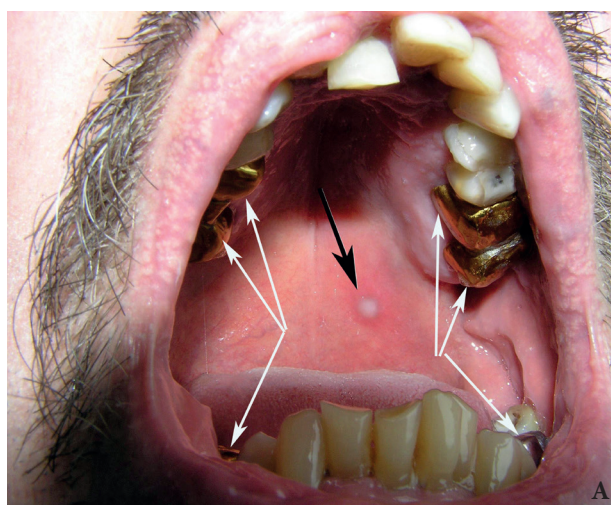
#### Conclusions.

The presence of metal inclusions in the oral cavity in the form of permanent dentures can be one of the reasons for the development of malignant neoplasms of the mucous membranes. A significant increase (more than 3 times higher than the normal values) of potentiometric parameters in patients with malignant tumors of the mucous membranes with metallic inclusions in the oral cavity is observed not only between the metals of immovable dentures, but also between the metal denture and the mucosa of the alveolar process of the jaw, between different parts of the mucous membranes of the alveolar process.

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### Introduction

Unity of views on the significance of previous diseases and pathological processes in the development of malignant tumors of the oral mucosa is not present. It is known that these or other precancerous diseases or malignant tumors of the oral mucosa arise on the background of various factors contributing to their development. One of these factors is the electrochemical effect [1-12]. The most typical example of this can be galvanic currents arising in the oral cavity, which are caused by the presence in the oral cavity of orthopedic structures made of different metals and their alloys. In these cases, on the mucous membrane in the oral cavity (Fig 1) and



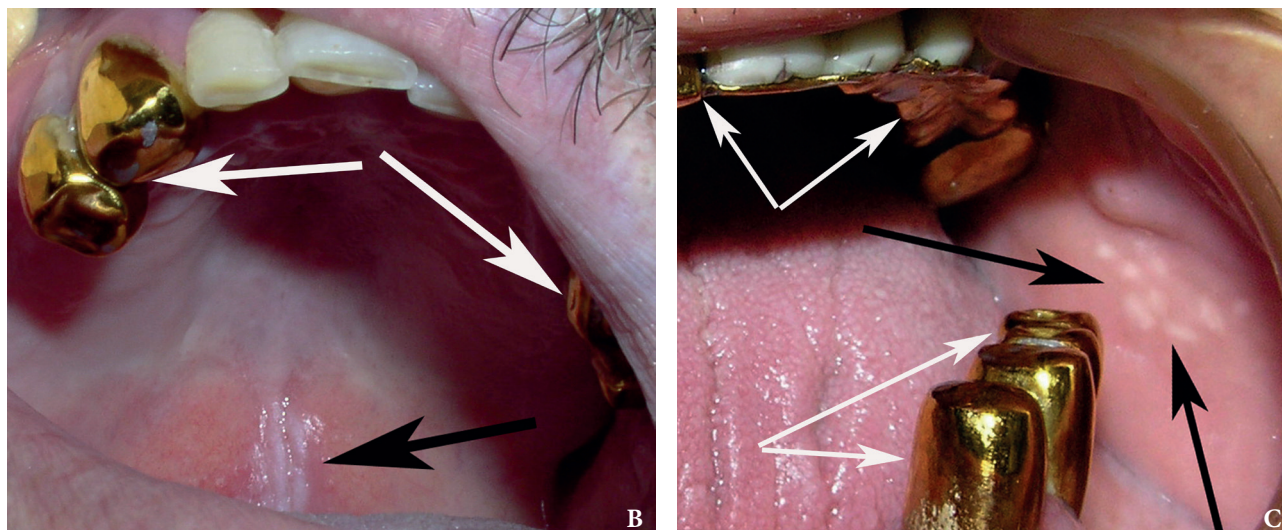
**FIGURE 1.** Black arrows (A-C) indicate foci of leukoplakia on the mucous membranes in the mouth. Metal inclusions are indicated by white arrows. (Fig 1 continued on the next page.)

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**FIGURE 1. (cont'd).** Black arrows (A-C) indicate foci of leukoplakia on the mucous membranes in the mouth. Metal inclusions are indicated by white arrows.

on the red border of the lips (Fig 2), leukoplakia, hyperplasia and hyperkeratosis appear which serves as a background for the development of malignant tumors.

We found that in many patients with malignant tumors of the oral mucosa, the previous diseases were leukoplakia, which were detected in them for a long time (more than one year). Leukoplakia on the mucous membranes of the oral cavity (cheeks, retro-molar regions, tongue, alveolar process, etc.) in these patients

appeared on the background of their high galvanic potentials caused by the presence in the oral cavity of dissimilar metals from which non-removable dentures were made.

The purpose of the study is to determine the severity of potentiometric parameters in patients with malignant neoplasms of the oral mucosa and the presence of metal inclusions in the form of non-removable dentures made of dissimilar metals and their alloys.



**FIGURE 2.** Precancerous diseases (arrows) of vermilion border of the lower lip in patients with metallic inclusions located in the oral cavity (A, B).

## Materials and Methods

From 2008 to 2010, we examined 39 patients with metallic inclusions in the oral cavity, in which malignant tumors of the mucous membrane of the oral cavity (tongue, palate, mucous membrane of the alveolar process and the bottom of the oral cavity) were detected. All examined patients underwent general clinical examination (history, examination, palpation, radiography, etc.). The diagnosis of a malignant tumor, established by us, was necessarily confirmed by pathohistological examination [13-17]. All subjects were between the ages of 40 and 68 years.

To conduct potentiometric methods of examination, an automatic digital potentiometer (Pitterling Electronic GmbH  $\mu$ g-potential, Munchen, Germany) with 32 memory cells and a pair of measurement electrodes from the chromium-nickel alloy in fluoroplastic holders (manufactured in Germany). The device automatically detects a potential difference in the range of 0 to 999 mV, current power in the range of 0 to 99  $\mu$ A and electrical conductivity in the mouth in microsimens ( $\mu$ S). In the established measurement mode (10-20 seconds after switching on the device), when one of the electrodes contacts the metal surface (the tooth surface) and the second one – mucous membrane in the hyoid area, the digital values of the potential difference, current and electrical conductivity of the oral liquid are displayed on the screen. All subjects underwent measurements of potentiometric parameters (potential differences, current power, electrical conductivity of oral fluid) in the following areas (points):

- between metallic inclusions (M-M);
- between metallic inclusions and the mucosa of the alveolar process of the same jaw (M-APM);

– between the mucosa of the alveolar process of one and the other side of the jaw (APM-APM).

Contact thermometry was carried out using a TPEM-1 electrothermometer (Medtekhnika, Kharkiv, Ukraine) with point thermocouples (sensors) with a measuring range from 16 to 42 °C. The accuracy of registration is 0.2 °C. The contact time of the sensor with the oral mucosa was 20 seconds, the intervals between repeated examinations were 2 to 5 seconds. Touching the sensor was done with approximately the same pressure force. The local temperature was measured three times and the arithmetic mean was calculated. We measured the temperature on the investigated and healthy side. According to the recommendations of Tymofeiev (2002), the basis of the contact thermometry being conducted is not the measurement of absolute temperatures over the pathological focus, but the detection of the temperature difference at symmetrical sites ( $\Delta T$ ). Control has always been thermal asymmetry ( $\Delta T$ ) in symmetrical areas, found in practically healthy people of the same age and sex.

All the data obtained in the course of the study were processed mathematically with the Student's test. The parameters were considered reliable at  $p < 0.05$ .

## Results and Discussion

From the anamnesis of 39 patients with malignant tumors [18-22] of the oral cavity (Fig 3), we found out that prosthetics with non-removable metal dentures was performed in the period from 1.5 to 7 years before the appearance of a premolar disease (leukoplakia, chronic erosion or ulcers) or the tumor first clinical symptoms. 8 patients (20.5%) had a period of 1.5 to 2 years, 10 (25.6%) had 2 to 3 years, and 21 (53.9%) had more than 3 years.



**FIGURE 3.** Squamous cell carcinoma of the mucous membrane of the alveolar process of the mandible, which appeared under the metal non-movable denture. Appearance of the tumor after removal of the denture.

Before the denture, according to all the examinees, dentists did not reveal any pathological changes from the mucous membranes of the oral cavity.

In all 39 subjects (100%) with malignant neoplasms of the oral mucosa, we found non-removable metallic inclusions in the oral cavity (crowns and/or bridges of stainless steel, chromium-cobalt (chromium-nickel) alloy, nitride-titanium coating, cermet prosthesis). In 31 subjects (in 79.5%) in the oral cavity there were constructions made of different types of metals and their alloys.

When visual inspection of the surface of non-removable metal structures (dentures), which were in the area of the pathological focus, we found: the fractures in places of soldering – in 16 people (41.0%), cracks or complete violation of the integrity (fracture) of the fixed design of dentures in the place of soldering – in 12 people (30.8%), a dark oxide film at the location of the solder – in 17 people (43.6%), areas of corrosive lesions – in 12 people (30.8%), uneven distribution of the metal protection coating (MPC) from titanium nitride over the denture surface, i.e. found “bald” areas – in 14 people (35.9%). In 19 subjects (48.7%), these clinical symptoms were combined with each other, i.e. there were two or even three of these disorders (changes from a non-removable denture). In all examined patients with malignant tumors of the oral mucosa, we found metal dentures with defects.

Values of galvanic potentials between metallic inclusions (M-M) of the oral cavity (crowns and bridges) were  $187.9 \pm 21.2$  mV and ranged from 140 mV to 330 mV (Table 1). Values of potentials from 140 to 150 mV were detected in 5 out of 39 subjects (12.8%). Values of galvanic potentials from 160 to 200 mV were observed in 6 patients (15.4%), from 210 to 300 mV in 20 patients (51.3%), from 310 to 330 mV in 8 patients (20.5%).

The magnitude of the current between the metallic prostheses of the oral cavity (M-M) was  $18.5 \pm 3.6$   $\mu$ A and was in the range from 5  $\mu$ A to 39  $\mu$ A (Table 1). Current intensity less than 10  $\mu$ A was detected in 8 patients (20.5%), from 11 to 19  $\mu$ A – 18 patients (46.2%), from 20 to 29  $\mu$ A – in 10 patients (25.6%), more than 30 MA – in 3 subjects (7.7%).

The electrical conductivity of the oral liquid in the patients under examination between the metallic prostheses (M-M) was  $24.9 \pm 2.8$   $\mu$ S and was in the range from 8 to 53  $\mu$ S (Table 1). The electrical conductivity of the oral liquid was less than 10  $\mu$ S in 2 patients (5.1%), from 11 to 19  $\mu$ S in 15 patients (38.5%), from 20 to 29  $\mu$ S in 16 patients (41.0%), from 30 to 39  $\mu$ A in 2 patients (5.1%), from 40 to 49  $\mu$ S for 3 patients (7.7%) and more than 50  $\mu$ S for 1 patient (2.6%).

Values of galvanic potentials between metallic inclusions of the oral cavity (crowns and bridges) and mucosa of the alveolar process (M-APM) were  $176.8 \pm 16.3$  mV and ranged from 130 mV to 300 mV (Table 1). Values of potentials from 130 to 150 mV were detected in 7 out of 39 subjects (18.0%). Values of galvanic potentials from 160 to 200 mV – in 7 patients (18.0%), from 210 to

300 mV – in 25 patients (64.0%).

The magnitude of the current between the metallic prostheses of the oral cavity and the mucosa of the alveolar process (M-APM) was  $16.9 \pm 2.9$   $\mu$ A and ranged from 6  $\mu$ A to 33  $\mu$ A (Table 1). Current intensity less than 10  $\mu$ A was detected in 8 subjects (20.5%), from 11 to 19  $\mu$ A – 19 patients (48.7%), from 20 to 29  $\mu$ A – in 12 patients (30.8%).

The electrical conductivity of the oral fluid in the patients under examination between metallic prostheses and the mucosa of the alveolar process (M-APM) was  $23.4 \pm 2.6$   $\mu$ S and was in the range of 7 to 38  $\mu$ S (Table 1). The electrical conductivity of the oral fluid was less than 10  $\mu$ S in 3 patients (7.7%), 11 to 19  $\mu$ S in 16 patients (41.0%), and 20 to 29  $\mu$ S in 19 patients (48.7%), from 30 to 38  $\mu$ A – in 1 patient (2.6%).

Values of galvanic potentials between the mucous membranes of the alveolar processes (APM-APM) of the oral cavity were  $179.1 \pm 18.3$  mV and ranged from 130 mV to 360 mV (Table 1). Values of potentials from 130 to 150 mV were detected in 6 out of 39 subjects (15.4%). Values of galvanic potentials from 160 to 200 mV – in 6 patients (15.4%), from 210 to 300 mV – in 19 patients (48.7%), from 310 to 330 mV – in 8 patients (20.5%).

The magnitude of the strength of the current between the mucous membranes of the alveolar processes (APM-APM) of the oral cavity was  $18.9 \pm 2.8$   $\mu$ A and was in the range from 9  $\mu$ A to 35  $\mu$ A (Table 1). Current intensity less than 10  $\mu$ A was detected in 6 subjects (15.4%), from 11 to 19  $\mu$ A – 20 patients (51.3%), 20 to 29  $\mu$ A – in 8 patients (20.5%), more than 30 MA in 5 subjects (12.8%) The value of the electrical conductivity of the oral fluid in the patients under examination between the mucous membranes of the alveolar processes (APM-APM) was  $23.8 \pm 2.7$   $\mu$ S and was in the range from 7 to 46  $\mu$ S (Table 1). The electrical conductivity of the oral liquid was less than 10  $\mu$ S in 1 patient (2.6%), from 11 to 19  $\mu$ S in 14 patients (35.9%), from 20 to 29  $\mu$ S in 15 patients (38.5%), from 30 to 39  $\mu$ A in 2 patients (5.1%), from 40 to 46  $\mu$ S in 7 patients (17.9%). All the arithmetic mean values obtained during the survey are presented in Table 1. In the same table, the reliability of the obtained indices was measured at different places of measurement with respect to each other.

Based on the analysis of Table 1, we found that in patients with malignant tumors of the mucous membranes of the oral cavity (Fig 3), when there were non-removable metallic inclusions in the oral cavity, the levels of potentiometric parameters between the metallic inclusions increased significantly ( $p < 0.001$ ) (potential differences –  $187.9 \pm 21.2$  mV, current strength – up to  $18.5 \pm 3.6$   $\mu$ A and electrical conductivity of the oral liquid –  $24.9 \pm 2.8$   $\mu$ S), between metallic inclusions and the mucosa of the alveolar process (the potential difference is  $176.8 \pm 16.3$  mV, the amperage – about  $16.9 \pm 2.9$   $\mu$ A and the electrical conductivity of the oral fluid –  $23.4 \pm 2.6$   $\mu$ S) and between the mucous membranes of the alveolar processes (potential differences –  $179.1 \pm 18.3$  mV, current – up to  $18.9 \pm 2.8$   $\mu$ A and the electrical conductivity of the oral fluid is  $23.8 \pm 2.7$   $\mu$ S).

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TABLE 1. Potentiometric indicators in patients with malignant tumors of the mucous membranes of the oral cavity.

Observation Group		Number of Subjects	Indicators of Potentiometry		
			Potential Difference (mV)	Current Intensity (μA)	Electric Conductivity of Oral Liquid (μS)
Patients with malignant tumors of the oral mucosa	Between metallic inclusions M-M	39	187.9 ± 21.2 p < 0.001	18,5 ± 3.6 p < 0.001	24.9 ± 2.8 p < 0.001
	Between metallic inclusions and the mucosa of the alveolar process (M-APM)	39	176.8 ± 16.3 p < 0.001 p <sub>1</sub> > 0.05	16.9 ± 2.9 p < 0.001 p <sub>1</sub> > 0.05	23.4 ± 2.6 p < 0.001 p <sub>1</sub> > 0.05
	Between the mucous membranes of the alveolar process (APM-APM)	39	179.1 ± 18.3 p < 0.001 p <sub>2</sub> > 0.05	18.9 ± 2.8 p < 0.001 p <sub>2</sub> > 0.05	23.8 ± 2.7 p < 0.001 p <sub>2</sub> > 0.05
Control group (healthy people)		27	32,6 ± 2,9	2,9 ± 0,2	2,7 ± 0,2

p – reliability of differences compared to healthy people (control group);  
 p<sub>1</sub> – reliability of differences between M-M and M-APM;  
 p<sub>2</sub> – reliability of the differences in the indicators between the M-APM and the APM-APM.

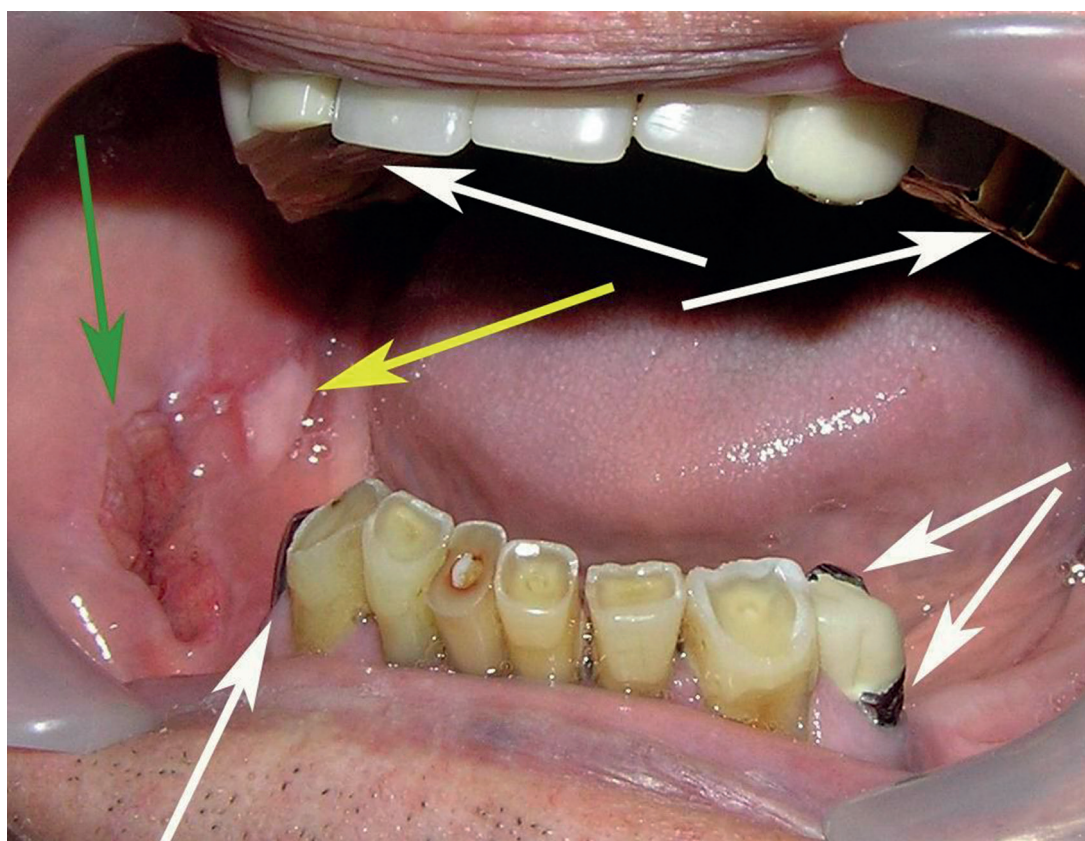


FIGURE 4. Erosive-ulcerative form of squamous cell carcinoma of the mucous membrane of the cheek (green arrow), flat form of leukoplakia (yellow arrow), metallic inclusions (white arrows).

The revealed indices of potential difference, current strength and electrical conductivity of the oral fluid in all patients with metallic inclusions in the oral cavity and malignant tumors of the mucosa of the bottom of the cavity and tongue exceeded the maximum values in healthy people by more than 2-3 or more times (the potential difference of 20- 60 mV, the current strength is from 2 to 5  $\mu$ A, the electrical conductivity of the oral liquid is from 2 to 6  $\mu$ S). It is necessary to pay special attention to the fact that potentiometric indicators, which were detected between metallic inclusions between (M-M); Between metallic inclusions and mucous membrane of the alveolar process of the same jaw (M-APM); Between the mucosa of the alveolar process of one and the other side of the jaw (APM-APM) significantly ( $p > 0.05$ ) did not differ. The latter indicated that high galvanic potentials were already detected in the thickness of the mucous membranes of the oral cavity.

Measurement of the thermoasymmetry of the mucosa of the alveolar processes of the upper and lower jaws (on the side of the tumor location and the healthy side) showed that the temperature difference (thermoasymmetry) was significantly ( $p < 0.05$ ) different from healthy people and was  $1.4 \pm 0.1$  °C (on the upper jaw) and  $1.3 \pm 0.1$  °C (on the lower jaw). In those places where the inflammatory phenomena were more active, the thermoasymmetry reached 1.6 °C.

Thus, based on our survey, it was found that high rates of galvanic currents in the oral cavity (with their prolonged existence) can be one of the factors that can cause the formation not only of premalignant diseases of the oral mucosa and the red border of the lips, but also promote the development of malignant tumors of the oral mucosa. More than 3 times higher than normal values (characteristic for healthy people) potentiometric

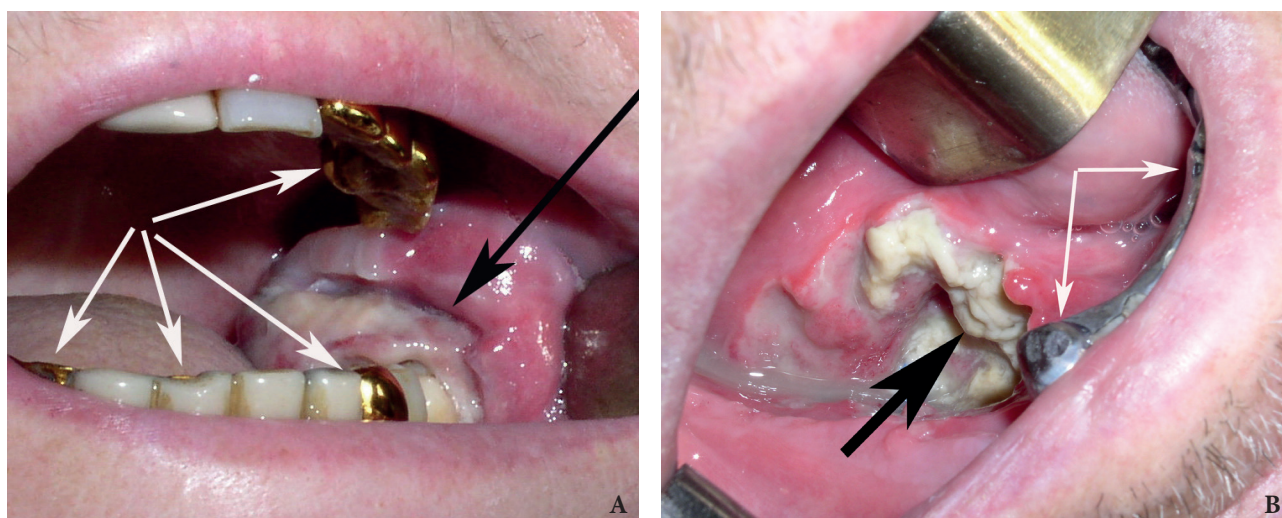
parameters in patients with malignant neoplasms of mucous membranes, in which metal inclusions are located in the oral cavity, differ. A significant increase in the potentiometric parameters not only between the metals of immovable dentures, but also between the metal denture and the mucosa of the alveolar process of the jaw, was found between the different sections of the mucous membranes of the alveolar process.

### Conclusions

The presence of metal inclusions in the oral cavity in the form of permanent dentures can be one of the reasons for the development of malignant neoplasms [23-31] of the mucous membranes (Fig 5). A significant increase (more than 3 times higher than the normal values) of potentiometric parameters in patients with malignant tumors of the mucous membranes with metallic inclusions in the oral cavity is observed not only between the metals of immovable dentures, but also between the metal denture and the mucosa of the alveolar process of the jaw, between different parts of the mucous membranes of the alveolar process.

High potentiometric indicators were revealed in patients with non-removable metal dentures, which are made of dissimilar metals and their alloys. The presence of defects in the lining of dentures, as well as metal parts of a non-removable structure or metal protective coating ("bald zones") increase the potentiometric parameters and increase the risk of malignant neoplasms of the mucous membranes.

A survey of patients with malignant tumors showed that one of the factors of their development can be high galvanic currents that cause the appearance of cancer of the mucous membranes.



**FIGURE 5.** Different forms of squamous cell carcinoma (black arrows) of the mucous membranes (A-D), which are caused by the presence of metallic inclusions (white arrows) in the oral cavity. (Fig 5 continued on the next page.)



**FIGURE 5. (cont'd).** Different forms of squamous cell carcinoma (*black arrows*) of the mucous membranes (**A-D**), which are caused by the presence of metallic inclusions (*white arrows*) in the oral cavity.

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### Conflict of Interests

None.

### Role of Authors

Oleksii O. Tymofieiev (concept of the paper, material collection, and editing)

Oleksandr O. Tymofieiev (material collection and writing)

Natalia O. Ushko (material collection and writing)

Mariia O. Yarifa (material collection and writing)

### Ethical Approval

Approval was obtained from the Medical Ethics Committee of the Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine.

### Patient Consent

Written patient consent was obtained to publish the clinical images.

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