Monoclonal Antibodies: Exploring the Impact, Possibilities, and Adverse Effects in Dentistry

Anna Matthews, RDH MS

New York City College of Technology, CUNY, 285 Jay Street, Dental Hygiene Department A-702, Brooklyn NY 11201

ABSTRACT:
Comprising a large and fast-growing group of medications with diverse therapeutic targets, monoclonal antibodies (mAbs) have a wide-ranging variety of current and potential therapeutic applications. The first monoclonal antibody was generated in 1975 and since then progress in biotechnology allowed for development of these biologic drugs that lessen the risk of immune response and permit much wider use. The field of mAbs has progressively grown since its introduction. Despite their specificity and generally good tolerability, mAbs are not without adverse effects, including oral and peri-oral – some severe enough to warrant therapy discontinuation. As the variety, number, and therapeutic indications for mAbs continue to increase, the chance of encountering patients using these biologics in the dental settings will correspondingly grow.

PURPOSE:
This review of literature was conducted to facilitate dental professionals' knowledge of the conditions managed with mAbs, their therapeutic and adverse effects, as well as interactions with other drugs and supplements, which is vital to providing safe dental treatment. Growing use of the various mAbs in management of many conditions necessitates oral health providers' awareness about these therapeutics.

REFERENCE: Matthews, A. (2021). Considerations for monoclonal antibodies in oral healthcare. *Decisions in Dentistry* 7(3):32-35.

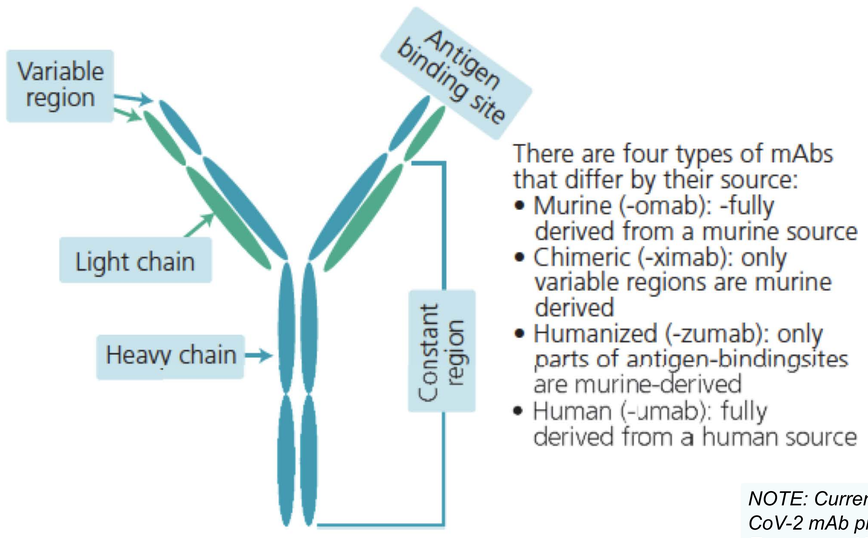


Fig.1. Structure and types of monoclonal antibodies

Monoclonal antibodies: BACKGROUND

Antibodies are immunoglobulin (Ig) molecules which are proteins of 5 different classes (IgA, IgD, IgE, IgG, and IgM) produced by the B-lymphocytes as a defense mechanism against foreign substances (*e.g. microorganisms, allergens*) and those produced by the host (*such as cancer cells or normal healthy cells in case of autoimmune reactions*). mAbs are IgG proteins (Fig.1), produced by a single B-lymphocyte clone, having identical structure and antigen-binding characteristics. mAbs are "biologics" produced by complex biotechnological methods.
Like typical chemotherapeutic agents, biological products undergo the rigorous process of approval, monitoring and post-market surveillance, ensuring their safety and effectiveness and helping to detect adverse reactions not identified during the clinical trials. And, despite their specificity to the intended cells and tissues defined as 'targeted therapies' and generally good tolerability, mAbs are not without adverse effects, including oral and peri-oral – some severe enough to warrant therapy discontinuation.
Variety, number, and therapeutic indications for mAbs continue to increase (Table 1).

Therapeutic indication	Examples of mAbs and their action
Cancer	• bevacizumab • cetuximab, panitumumab • rituximab
Inflammatory/immune-mediated conditions • *RA* • *Crohn's disease* • *Psoriasis*	• adalimumab • vedolizumab • secukinumab
Rejection of transplant	• muromonab-CD3 • basiliximab
Asthma	• omalizumab • reslizumab
Reversal of drug effects	• idarucizumab
Post-menopausal osteoporosis	• denosumab
Migraine	• erenumab, galcanezumab, eptinezumab • fremanezumab
Infectious diseases	• ibalizumab • raxibacumab • rmab
Drug delivery	• inotuzumab ozogamicin • ibritumab tiuxetan

NOTE: Currently, three anti-SARS-CoV-2 mAb products have received Emergency Use Authorizations from the Food and Drug Administration for the treatment of mild to moderate COVID-19. They are:
- *Bamlanivimab plus etesevimab*
- *Casirivimab plus imdevimab*
- *Sotrovimab*

https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/anti-sars-cov-2-monoclonal-antibodies/

Table 1. Selected therapeutic indications and examples of monoclonal antibodies used in treatment

MECHANISM OF ACTION:

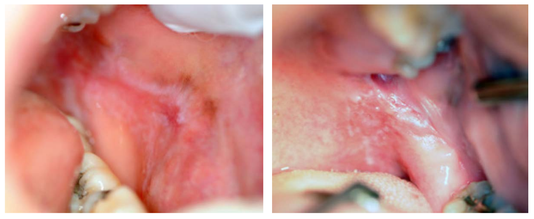
- *Blocking or neutralization of the target* can be accomplished by mAbs blocking action against the receptor or its binding molecule, referred to as receptor- or ligand-antagonism
- *Blocking the target signaling pathway:* upon binding to the target tumor cell receptor, mAb will affect the downstream signaling and intracellular messaging resulting in inhibition of cell growth or proliferation, or induction of the programmed cell death (apoptosis)
- *Antibody-dependent cell-mediated cytotoxicity (ADCC)* and *immune-mediated complement-dependent cytotoxicity (CDC)* reaction: leading to the death of the target cell via its lysis

Key references:
- Castelli MS, McGonigle P, Hornby PJ. The pharmacology and therapeutic applications of monoclonal antibodies. Pharmacol Res Perspect. 2019;7(6). doi:10.1002/prp2.535
- Suzuki M, Kato C, Kato A. Therapeutic antibodies: their mechanisms of action and the pathological findings they induce in toxicity studies. J Toxicol Pathol. 2015;28(3):133-139. doi:10.1293/tox.2015-0031
- Chmielauskaite M, Stojanov I, Saraghi M, Pinto A. Oral adverse events associated with targeted cancer therapies. Gen Dent. Published online 2018:6.

ADVERSE REACTIONS:

Generally, due to their high specificity to the intended targets, mAbs, especially humanized and fully-human mAbs with reduced immunogenicity, are well tolerated and adverse effects are typically mild, ranging from skin reactions at the site of injection to flu-like symptoms. However, some patients can experience severe adverse reactions, including life-threatening complications and even fatal outcomes.

- Severe acute reactions following mAbs administration:
  - immediate or delayed-onset anaphylaxis (type I hypersensitivity),
  - serum sickness (type III hypersensitivity reaction),
  - tumor lysis syndrome (TLS),
  - cytokine release syndrome (CRS)
- Infectious diseases (re-activation of latent TB, Progressive Multifocal Leukoencephalopathy – PML)
- Thrombocytopenia
- Auto-immune conditions
- Development of cancers



Pictures 1,2: Erosive Lichen Planus

Courtesy of Dr. Gwen Cohen-Brown, DDS and the Dental Hygiene Department/NYCCT

ORAL ADVERSE EFFECTS:

Some mAbs have been implicated in development of less frequent but very concerning complications:
- oral lichenoid drug-induced reactions or eruptions (OLDRs or LDEs)
- medication-related osteonecrosis of the jaw (MRONJ)

Clinically OLDR lesions are indistinguishable from idiopathic lichen planus (LP) (Pic.1,2) and histological differences are not definitive and therefore not diagnostic.
Clinical presentation of MRONJ related to various mAbs, is no different from that due to other drugs (such as bisphosphonates). Necrotic lesions most frequently appear on the mandible, following surgery, tooth extractions, implant placements, or spontaneously, from a few weeks to over a year after beginning of mAb therapy.