

New Medicines in Breastfeeding

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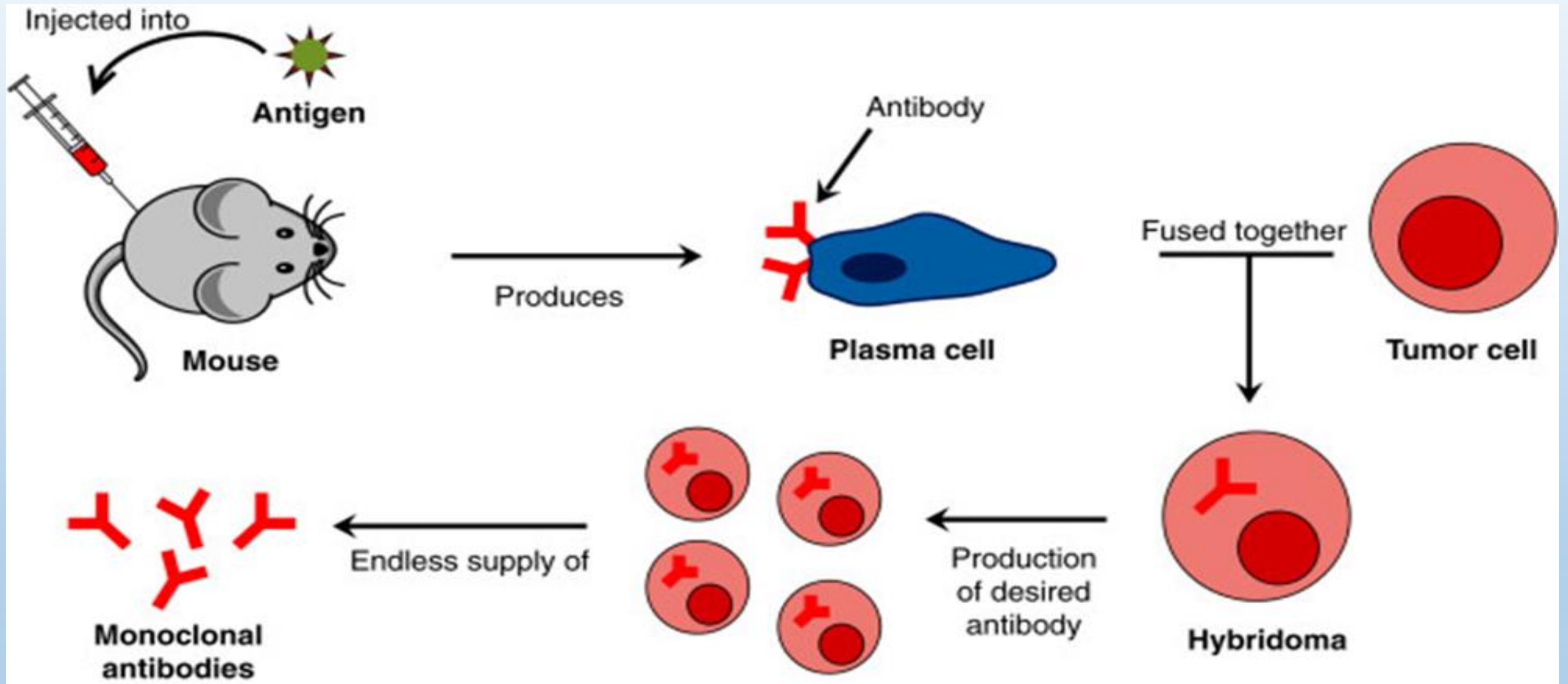
Rodney at work



MABs

- Therapeutic, diagnostic and preventive monoclonal antibodies are clones of a single parent cell. When used as medicines, the International Nonproprietary Names (INNs) end in –mab .
- There are now over 500 approved and investigational agents (Wikipedia)
- Mabs are used not only as drugs for treating various diseases, but are also used as powerful tools for a wide range of medical applications. They are routinely used in hospitals for diagnostic, blood and tissue typing
- Today, the growth and profitability of Mabs are outstripping those of earlier types of biotechnology drugs and more traditional pharmaceutical ones.
- Mab expansion is among the fastest in the global pharmaceutical world

MAB Production



Therapeutic Applications of Monoclonal Antibodies

Mabs are capable of specifically recognizing and binding to many molecules, mainly those of protein nature.

Properties used in diagnosis for the detection of hormones, vitamins, cytokines, allergens, numerous tumor markers, and a wide range of markers associated with many diseases, including microbial infections.

Mabs may be used directly in therapeutics, but also as vehicles or carriers of other drugs.

Monoclonal antibody therapy is used to treat a wide range of conditions, depending on the antigen it is targeting. These conditions include:

Many types of cancers including breast cancer, leukemia, lymphoma, & cervical cancer etc

Autoimmune disorders, such as rheumatoid arthritis, multiple sclerosis, and lupus

Organ transplant rejection, Psoriasis

Osteoporosis, Chronic Migraine

Infections, such as Covid-19, Alzheimer's

Asthma, by preventing allergic reactions to the allergens,

List of monoclonal antibodies

Drug name	Description
Dupixent (dupilumab)	Dupixent is used to treat eczema, asthma, and nasal polyps.
Taltz (ixekizumab)	Taltz is used for psoriatic arthritis and ankylosing spondylitis in adults and plaque psoriasis in children 6 yrs and older.
Tremfya (guselkumab)	Tremfya is used to treat plaque psoriasis and psoriatic arthritis in adults.
Avastin (bevacizumab)	Avastin is used to treat many forms of cancer including colorectal, lung, kidney, liver, cervical, and ovarian cancer.
Keytruda (pembrolizumab)	Keytruda is used to treat a range of cancers such as melanomas, lung, bladder, stomach, cervical, liver, and uterine.
Erbbitux (cetuximab)	Erbbitux is used to treat colorectal cancer as well as cancers in the head, neck, and rectum.
Yervoy (ipilimumab)	Yervoy is used to treat cancers of the colon, kidney, and liver as well as to prevent skin cancer from reoccurring after surgical removal.
Opdivo (nivolumab)	Opdivo is used to treat melanoma as well as other advanced forms of cancer.
Portrazza (necitumumab)	Portrazza is used in combination with other meds to treat metastatic squamous non-small cell lung cancer.
Empliciti (elotuzumab)	Empliciti is used to treat multiple myeloma, a type of bone marrow cancer.

Why breastfeeding women?

- If no evidence of safety? the default is often to assume a drug may cause harm
- Many neurologic diseases disproportionately affect women, particularly during their reproductive years.
- mAbs are becoming widely available as a treatment option
 - eg - migraine, multiple sclerosis, myasthenia gravis, psoriasis, RA,
- There is a paucity of research on the short/long term safety of prescription medications, including mAbs, during the peripartum period

In the Real (clinical) World...

massive molecules, heavily protein bound, tiny penetration into breastmilk

negligible oral bioavailability

no evidence of any harm to baby

(BUT American authors / others advise CAUTION (esp with preemies / newborn))

Commonly prescribed ADHD medications include:

Stimulants

Methylphenidate (Concerta, Ritalin)

Dexmethylphenidate (Focalin)

Dextroamphetamine (Dexedrine, Zenzedi, ProCentra)

Dextroamphetamine-amphetamine (Adderall, Mydayis)

Lisdexamphetamine (Vyvanse)

Non-stimulants

Atomoxetine (Strattera)

Bupropion (Wellbutrin, Zyban)

Clonidine (Catapres)

Guanfacine (Intuniv)

Modafinil (Provigil)

ADHD Medicines

ADHD in adulthood is associated with significant impairment in occupational, academic, and social functioning

Mechanism of action of stimulants (methylphenidate and amphetamines) in reducing ADHD symptoms is not fully known

Likely involves the improvement of daily functioning via increased neurotransmission of dopamine and norepinephrine

Stimulants have a higher potential for misuse and dependence than other ADHD medications

- Wilens, et al. "Misuse and Diversion of Stimulants Prescribed for ADHD: a Systematic Review of the Literature." *Journal of the American Academy of Child and Adolescent Psychiatry*, U.S. National Library of Medicine, pubmed.ncbi.nlm.nih.gov/18174822/.
- Cortese, et al. "Comparative Efficacy and Tolerability of Medications for Attention-Deficit Hyperactivity Disorder in Children, Adolescents, and Adults: a Systematic Review and Network Meta-Analysis." *The Lancet. Psychiatry*, U.S. National Library of Medicine, pubmed.ncbi.nlm.nih.gov/30097390/

ADHD medications when breastfeeding

ADHD Medications & Breastfeeding			
Medication	Relative Infant Dose	Pediatric Concerns	Infant monitoring
Methylphenidate	0.2% to 0.4%	None reported via milk.	Agitation, irritability, poor sleep, changes in feeding, poor weight gain.
Dexmethylphenidate	Enantiomer of methylphenidate No RID data	None reported via milk.	Agitation, irritability, poor sleep, changes in feeding, poor weight gain.
Dextroamphetamines	2.5% to 7.3%	None of the infants in the studies were affected.	Agitation, hyperactivity, insomnia, decreased appetite, weight changes, tremor.
Lisdexamphetamine	1.8% to 6.2%	None of the infants in the studies were affected.	Agitation, irritability, poor sleep patterns, poor weight gain.
Atomoxetine	No RID data	None reported via milk. Atomoxetine is a lipophilic, neuroactive drug. Caution about its use during breast feeding.	Not recommended during lactation. Irritability, poor sleep, tremors, weight gain.
Bupropion	0.1% to 2%	Two cases of seizure reported, other causes for seizure not ruled out.	Sedation or irritability, seizures, not waking to feed, poor feeding, poor weight gain.
Clonidine	0.9% to 7.1%	None reported via milk. May reduce milk production by reducing prolactin secretion.	Drowsiness, lethargy, pallor, dry mouth, poor feeding, constipation, weight gain.
Guanfacine	No RID data	Low molecular weight, likely to penetrate milk at significant levels.	Not recommended during lactation.
Modafinil	5.3%	None reported. Observe for reduced milk supply.	Agitation, irritability, poor sleep patterns, poor weight gain.

The Usual Suspects

Methylphenidate (Ritalin / Concerta) is excreted into BM in miniscule amounts no adverse effects of methylphenidate have been reported in breastfed infants monitor for agitation, irritability, poor or altered sleep, changes in feeding.

Amphetamines have a variable RID that remains under 10%

The lowest effective dose should be used to manage the mother's symptoms Even at maximum recommended doses for ADHD, the RID of amphetamines is generally safe for the recommended duration (6-48 months) of breastfeeding and, if necessary, medication can be adjusted accordingly—use a lower dose as tolerated by breastfeeding mother

Monitor the infant with respect to the Big 3 **Mood, Sleep, Appetite**

Effects on Milk Production

Clonidine and guanfacine are not commonly used in adults with ADHD, but may be prescribed for persistent symptoms

Guanfacine is likely to penetrate milk at significant levels.¹

Both clonidine and guanfacine have an impact on [prolactin](#) may reduce milk supply, especially prior to established lactation

Adjust medication if milk production levels are not sufficient to maintain [adequate nutrition](#) for the infant.

Conclusion (ADHD meds)

We recommend infant safety and monitoring when mothers taking ADHD drugs wish to breastfeed.

First-line ADHD medications are often compatible with breastfeeding

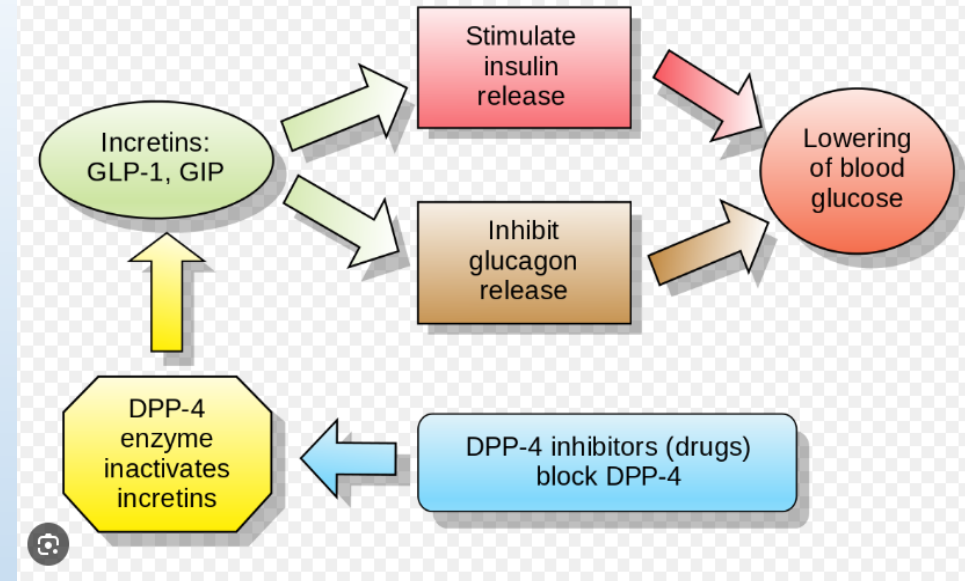
Atomoxetine and guanfacine have much less data for lactation

Using the above, consider the **benefits and risks** for both **mother and infant** before making an informed (?) decision.

GLP1 (and GIP) agonists

List of Glucagon-Like Protein-1 agonists

- Dulaglutide (Trulicity®) weekly inj
- Liraglutide (Saxenda, Victoza®) daily inj
- Semaglutide injection (Ozempic®, Wegovy) weekly inj
- Semaglutide tablets (Rybelsus®) tablet



Glucose-dependent insulinotropic polypeptide (GIP) Dipeptidyl peptidase-4 (DPP-4) inhibitors

There are also a class of medications called dual GLP-1/GIP receptor agonists

- Tirzepatide (Mounjaro® Zepbound)

Coming soon...

- Retatrutide – triple mechanism
- Orforglipron, Danuglipron – oral GLP1 ag
- CagriSema – combination cagrilintide + semaglutide – twin mechanism

Breastfeeding women?

Why would you?? YOU guess 😊

Safety in breastfeeding??

No/ltd information is available on the clinical use of GLP-1 ags during breastfeeding

But... peptide molecule with a huge molecular weight & over 99% protein bound
so amount in milk is likely to be very low

And... only 0.4% to 1% orally absorbed (destroyed in gut)
so it is very unlikely to adversely affect the breastfed infant

Thus.. use with **caution** especially while nursing a newborn or preterm infant
(adult adverse effects inc loss of appetite, nausea, diarrhoea, headache, itch
rare – mood (doom), pancreatitis, thyroid ca, renal infection, retinopathy)

Caution with new **ORAL** treatment options (with enhance oral bioavailability)

Botox in Breastfeeding

The onabotulinumtoxinA injection, commonly known as Botox, was approved in the United States in 1989

Botox works by preventing muscle contraction. Specifically, the toxin blocks the release of a contraction signal called acetylcholine, causing the muscle to remain relaxed

There has not been much investigation into the safety of Botox while breastfeeding

manufacturer neither recommends against nor encourages it

analysing limited data and resources, the risk of Botox entering breastmilk and harming your baby is low

“Ultimately, the decision must be made with your doctor’s guidance based on your own comfort level and necessity for Botox”

<https://www.infantrisk.com/content/botox-injections-and-breastfeeding>



Botox in breastfeeding

Patients may opt to receive intramuscular injections for management of:

[facial wrinkles](#), migraine, spasm, sweating, overactive bladder, tmj, incontinence

Side effects vary and are dependent on the location at which the drug is injected.

Cosmetically, headache along with droopy or swollen eyelids are reported

Warnings in the package indicate the “risk of distant spread of toxin effect.”

“there is no known mechanism by which such a process can directly affect bmilk”

“it is unlikely that Botox would enter your milk or harm a breastfed baby. Some women choose to wait up to 48 hours to provide their breast milk after injections, but there is no evidence to support that this helps reduce the already low risk to the infant”

<https://www.infantrisk.com/content/botox-injections-and-breastfeeding>

New(er) Antidepressants & Antipsychotics

Antidepressants inc

- duloxetine (Cymbalta), desvenlafaxine (Pristiq), agomelatine (Valdoxan)

Antipsychotics

- quetiapine (Seroquel), asenapine (Saphris)

Maternal quetiapine doses of up to 400 mg daily produce doses in milk that are less than 1% of the maternal weight-adjusted dosage.

Limited long-term follow-up of infants exposed to quetiapine indicates that infants generally developed normally.

- aripiprazole (Abilify), Limited information indicates that maternal doses of aripiprazole up to 15 mg daily produce low levels in milk.
- Asenapine (Saphris)

No information is available on the use of asenapine during breastfeeding. If asenapine is required by the mother, it is not a reason to discontinue breastfeeding

Most newer antidepressants = low/undetectable plasma concs in nursing infants
Highest infant plasma levels are for fluoxetine, venlafaxine, citalopram. [Lactmed](#)

Suspected adverse effects have been reported in a few infants

Expectations in the next 5-10 years?

- New vaccines (RSV), regenerative medicine options, chemotherapy (lymphoma, NHL)
- **Zuranolone** - the first oral medication designed specifically to treat PPD (&MDD)

Considered a neuro-active steroid (GABA receptors)

Addresses the biological & chemical imbalances in postpartum depression
more precise and effective treatment option

Works within 3 days!! (and available in the US now)

NK3R antagonists (Neurokinin 1/3 antag eg Fezolinetant) for “Hot Flushes”(VMS)*

by disrupting a signalling pathway in the brain

Mirikizumab – Crohn’s dis, UC (IL-23 p19 subunit)

Pegcetacoplan – Geographic Atrophy (AMD) anti-C3 agent (30-50 million people)

CRISPR Clustered Regularly Interspaced Short Palindromic Repeats genetic manipulation technique

Wearable devices eg smart watch (rhythm, BP, Sleep, Menstrual Cycle, ovulation)*

And most anticipated/dangerous of all **Artificial Intelligence** : humanity will be the judge

Appendix – Reference List

Pregnancy...

ADEC – Medicines in Pregnancy 4th ed (99) – being removed

Drugs in Pregnancy and Lactation 3rd ed (2018) Weiner

Briggs GG et al – Drugs in Preg & Lactation 12th ed 2021

Pregnancy and Breastfeeding- Medicines Guide RWH 2020

Mothertobaby.org (consumer medication “fact sheets”)

micromedex-reprorisk

Mothersafe <https://www.seslhd.health.nsw.gov.au/royal-hospital-for-women/services-clinics/directory/mothersafe>

perinatology.com (www) otispregnancy.org (www)

Lactation...

Hale – Medication & mother’s milk 2023 (19th ed)

google “lactmed” <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>

infantrisk.com (Prof Thomas Hale – Texas Uni) and an app available

Breastfeeding and Medication 2nd ed 2018 – Wendy Jones

https://www.breastfeedingnetwork.org.uk/wp-content/dibm/EntireDrugPack_BfN%20FINAL%20090217.pdf

Hale - Clinical Therapy in Breastfeeding Patients 2013 (3rd ed)

Lawrence- Breastfeeding, a Guide for the Medical Profession

www.adf.org (Australian Drug Foundation – Fact sheets!)

<http://www.thewomens.org.au/Methadone> (eg) and State Specialist Centres