NHS
Sussex Partnership
NHS Foundation Trust

Pharmacokinetics and administration of oral and IM RT medicines

Jules Haste

CMHP
College of Mental Health Pharmacy

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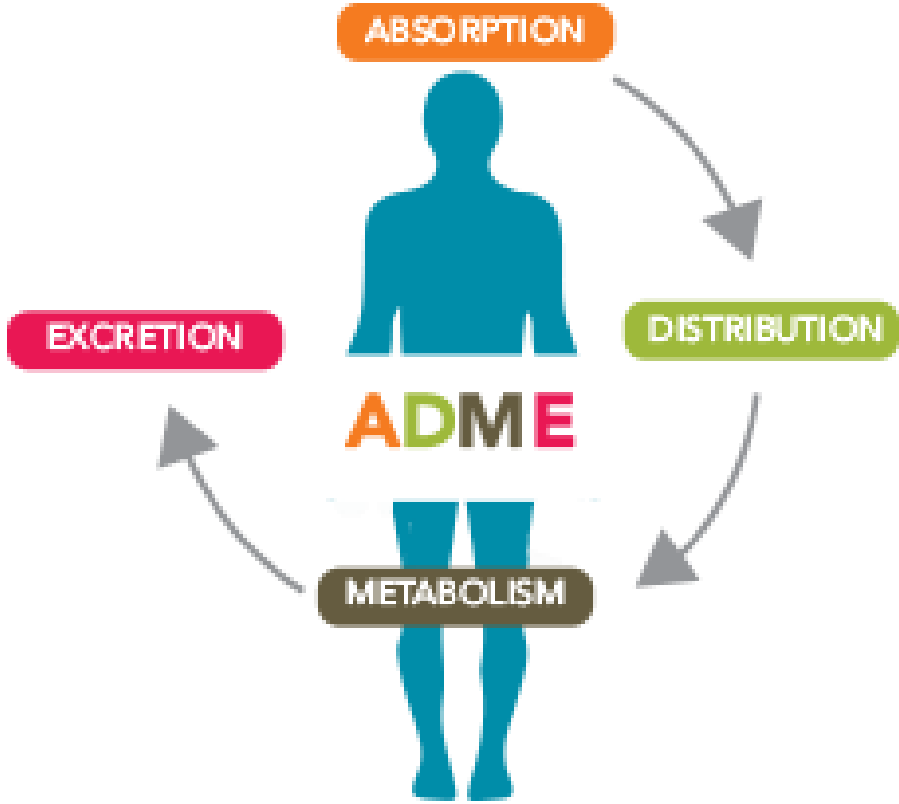
Pharmacology

- Pharmacodynamics
  - Mechanism of action
  - Receptors - agonists or antagonists



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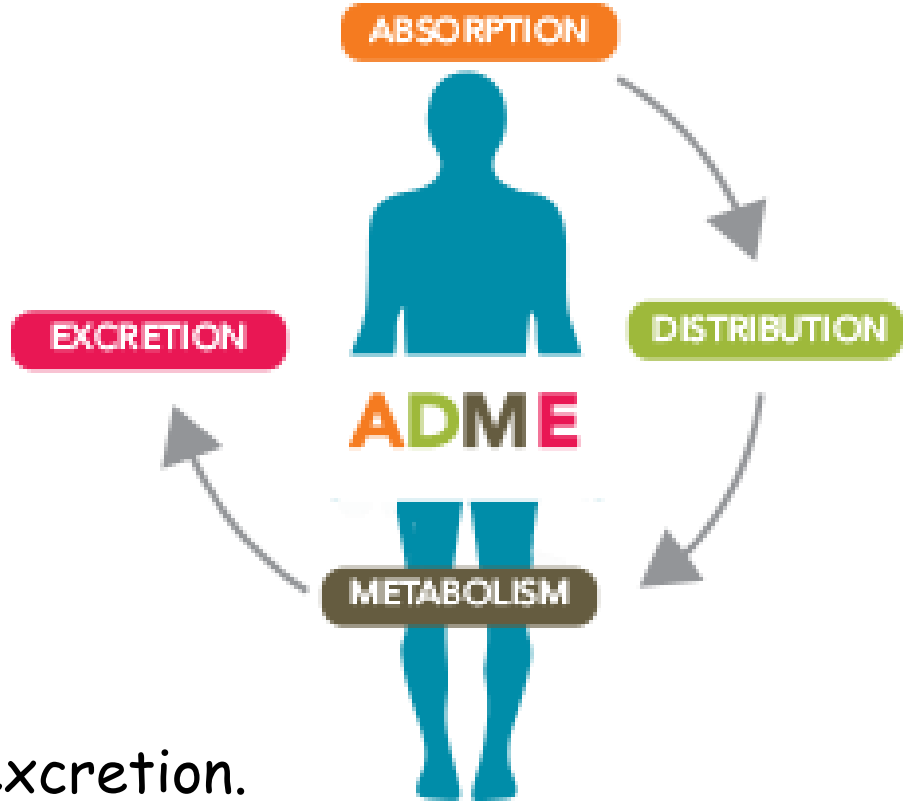
  - Absorption, distribution, metabolism and excretion.
  - Including peak plasma and half lives (T $\frac{1}{2}$)



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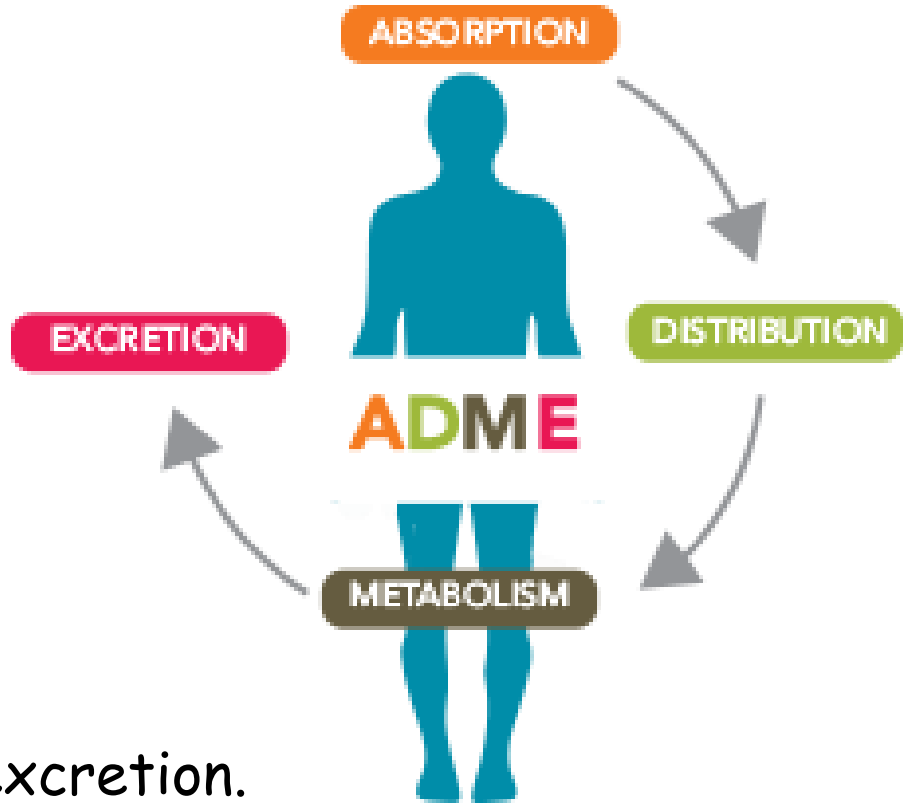

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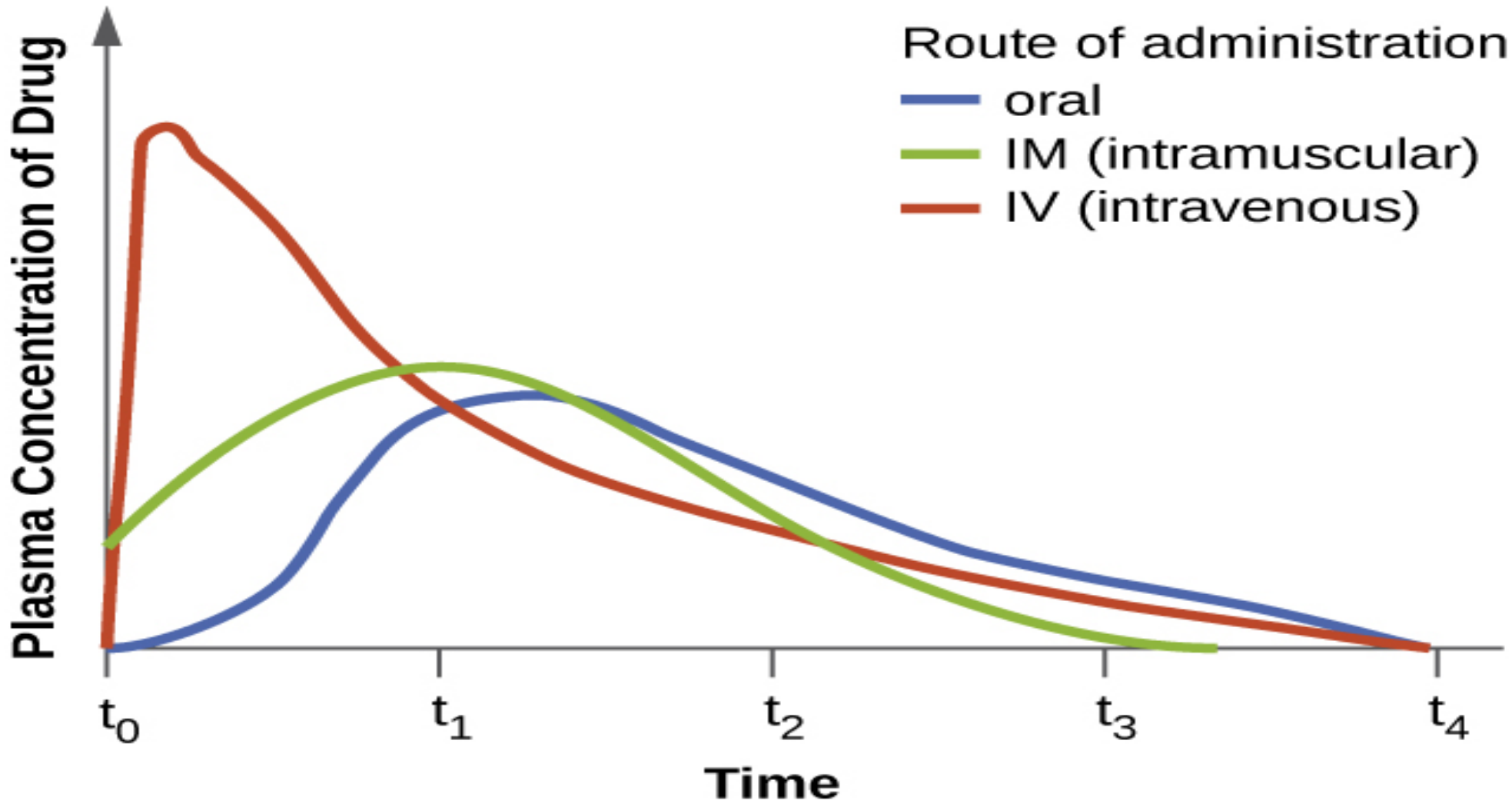
www.medicines.org.uk

American Hospital Formulary Service (AHFS) and Martindale

Plasma Concentration of Drug as a Function of Response Time



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Pharmacokinetics

Different formulations of the same drug can vary markedly in their pharmacokinetics

Complex interplay between absorption, Tmax, time to onset of action, duration of effect, $t\frac{1}{2}$ and risk of acute side effects

Time to peak plasma effect (Tmax)

- Peak levels in the blood
- Onset of effect? Usually some level of sedation
- Oral preparations absorbed by GIT have longest Tmax
  - Also can be affected by food
- IV considerably quicker than IM or oral
- Buccal, sublingual and inhaled formulations comparable to IM
- Orodispersible has no Tmax benefit over oral.
  - Bioavailability is the same as oral.
- Dose related side effects more likely at peak plasma levels

Pharmacokinetics

Bioavailability

- The % of absorption of a medicine
- Hepatic first pass metabolism
- IV will be 100%
- Haloperidol 60%-70% for oral

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Elimination half life ($T\frac{1}{2}$)

- Time taken for the plasma concentration of a drug to reduce to half its original value.
- Estimate how long it takes for a drug to be removed from your body.
- Effected by interacting medicines/food/smoking, age, ethnicity or genetics, hepatic and/or renal function, obesity and co-morbidity.
- Accumulation

Medicine	Route	Onset of effect	Time to peak effect	Bioavailability	Duration of action	Elimination half life
Aripiprazole	Oral	NR	3-5 hours	87%	18-24 hours	75-146 hours
	IM	30-45 mins	1-3 hours	100%		
Diazepam	Oral	NR	30-90mins	76%	12-24hours	1-5 days (biphasic)
	IV	5-10 seconds	<1 min	100%		12-24 hours
Haloperidol	Oral	1-2 hours	2-6 hours	60-70%	18-24hours	13-40 hours
	IM	15-30 mins	20 mins	100%		
	IV	seconds/minutes	seconds/minutes	100%		
Lorazepam	Oral	20-30 mins	2 hours	100%	6-8hours	12 -16 hours
	IM	15-30 mins	60-90 mins	100%		
Midazolam	Buccal	NR	30 mins	75%	? Few hours	30mins – 3.5hours
	IM	<15 mins	30 mins	100%		4 hours
Olanzapine	Oral	≈ 2 hours	5-8 hours	None	24 hours	31-52 hours
	IM	15-30 mins	15-45 mins			
	IV	5-10 mins	seconds/minutes			
Promethazine	Oral	≈ 2 hours (15-30 mins)	2-3 hours	None	2-8 hours	5-14 hours
	IM	30-60 mins	1-2 hours			

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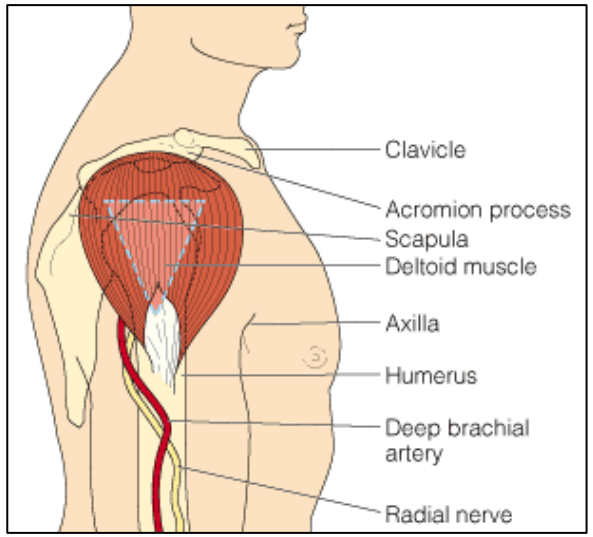
Administration - sites

- 5 main sites
  - **Deltoid, ventrogluteal, dorsogluteal,** vastus lateralis and rectus femoris

Deltoid



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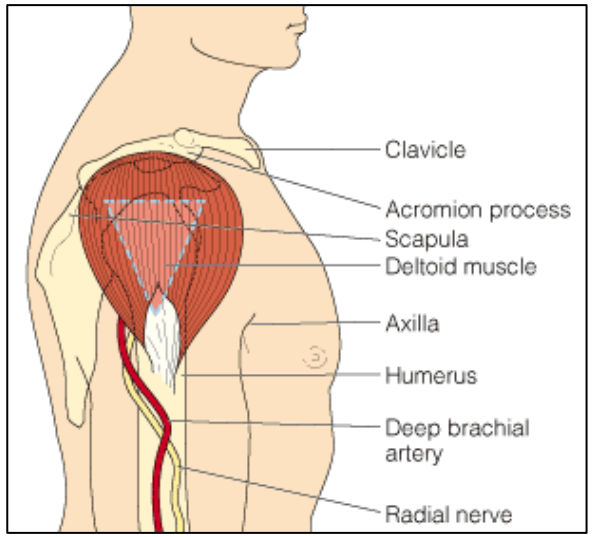
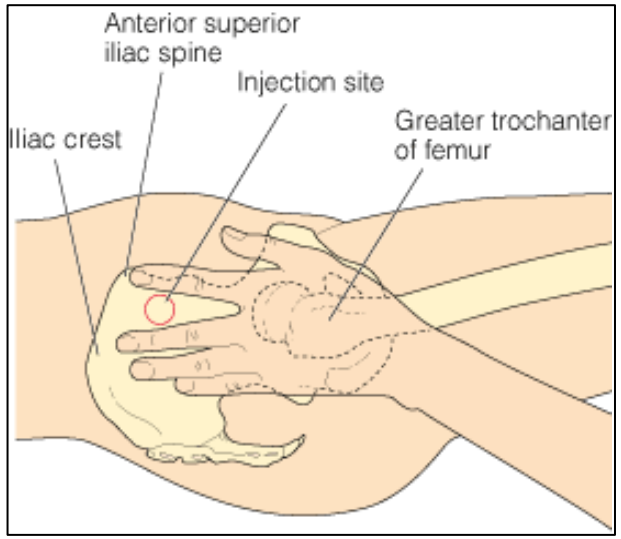


Ventrogluteal



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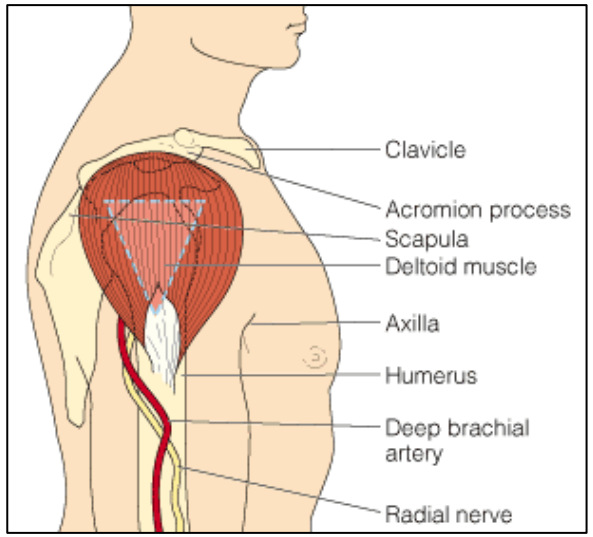

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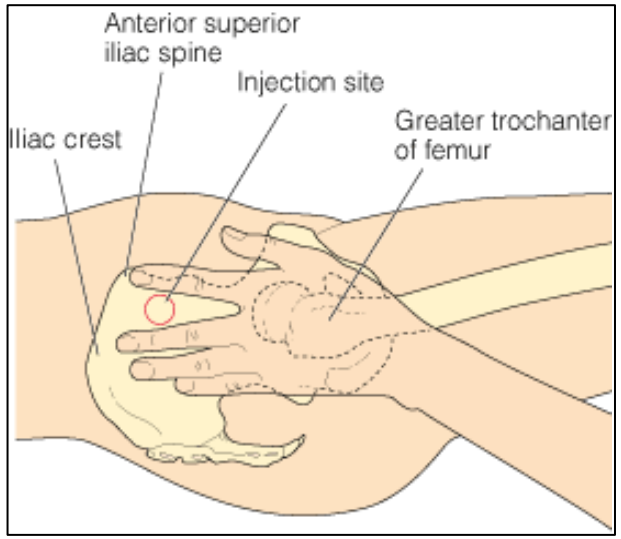
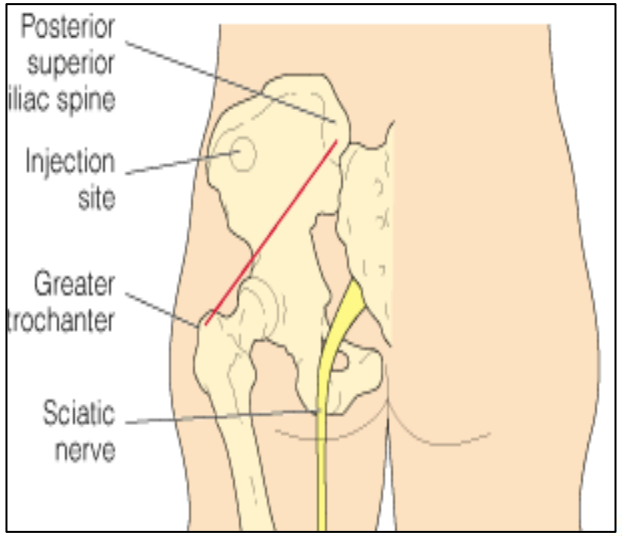


Dorsogluteal



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Prone position

How would you give RT under restraint?

When using manual restraint NICE (2015), avoid taking the service user to the floor, but if this becomes necessary:

- use the supine (face up) position if possible **or**
- if the prone (face down) position is necessary, use it for as short a time as possible.

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- Deltoid administration is rare as administration requires a stationary arm for correct injecting technique.

Administration – Z-tracking

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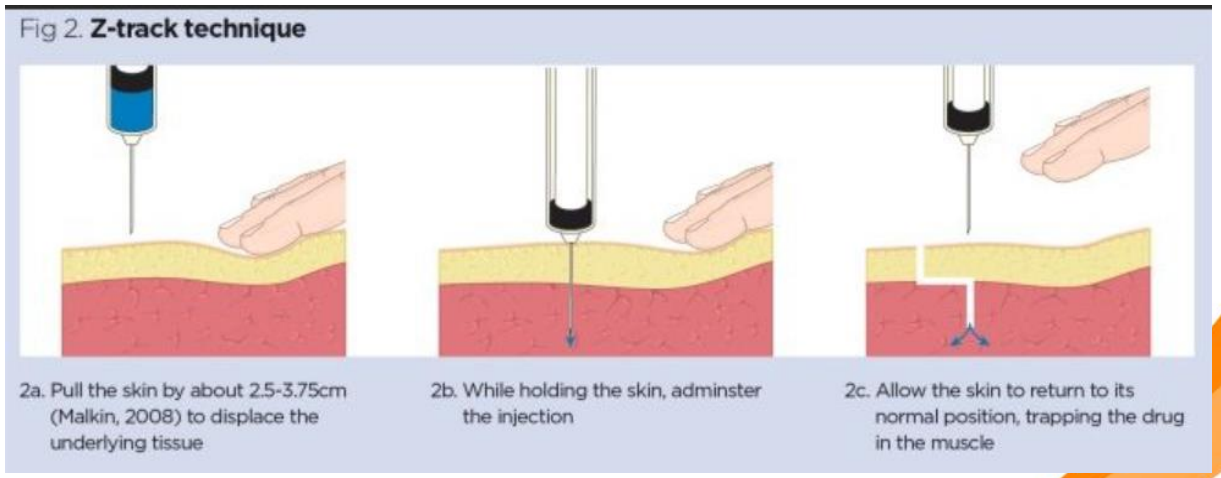
2. Stretch/displace the skin by pulling it laterally away form the intended point of injection.



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Administration – Z-tracking

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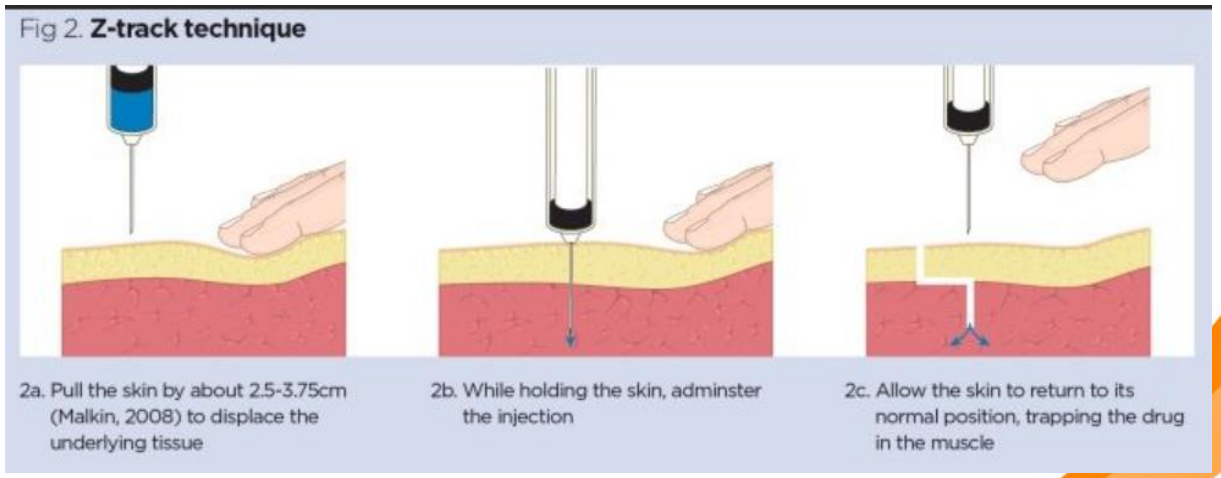
2. Stretch/displace the skin by pulling it laterally away form the intended point of injection.
3. Insert the needle into the site at a 90° angle, *aspirate by pulling back on the plunger for 5 seconds, allowing time for any blood to travel from a penetrated vessel up the bore of the needle. If blood is aspirated withdraw the needle, seal the wound and repeat the procedure at another site with new equipment and medication. If no blood is aspirated administer the injection.*



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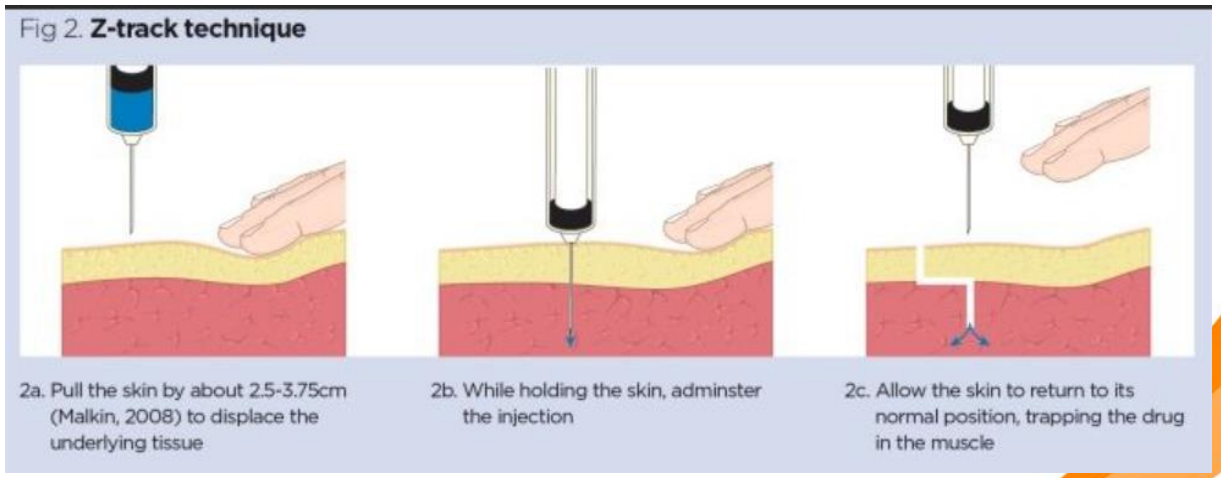
4. Wait 10 seconds then withdraw the needle and release the skin allowing the displaced tissue to seal the needle track.



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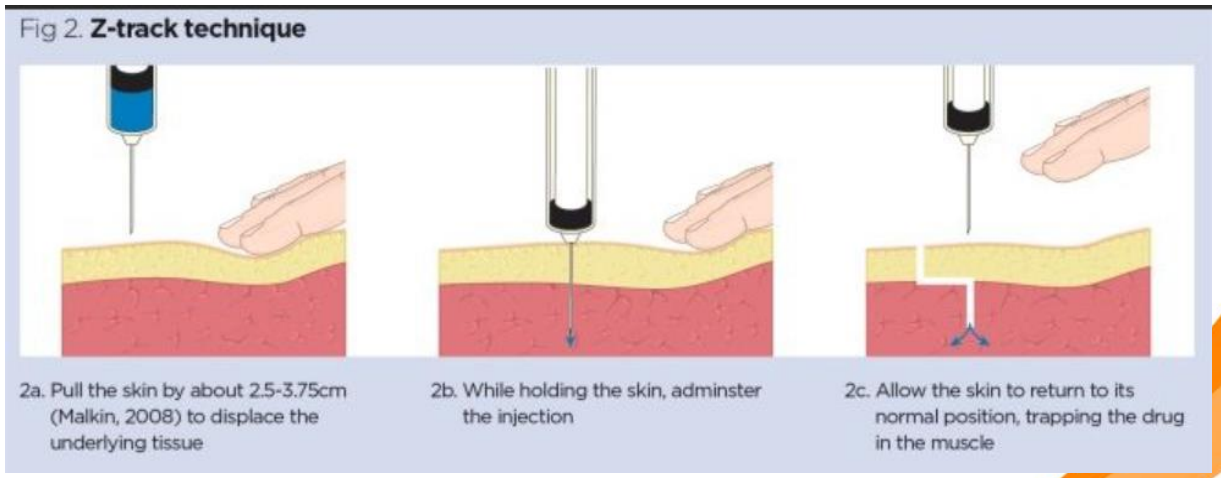
Incorrect administration may lead to reduced effectiveness.



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Administration

- It is common practice to draw back on a syringe after the needle is inserted to check whether it is in a blood vessel. While it is important to aspirate if the dorsogluteal muscle site is used – because of proximity to the gluteal artery – it is not required for other IM injection sites.

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Note

- Olanzapine pamoate must be aspirated for several seconds.

- Correct needles in pack must be used e.g. Consta see SmPC or Medusa for details

Administration

Lorazepam injection 4mg/mL – Macure ampoules

- Slightly viscous when cool.
- Dilution with an equal volume of diluent is recommended. The diluent should be 0.9% sodium chloride or water for injections. 5% glucose can also be used in SmPC.
- Oversized ampoules to aid dilution, add 1mL dilute = 2mg/mL
- To be kept in the fridge (2-8°C) as it is unstable.
- Lorazepam Macure (from SPS)
  - In the event of an inadvertent temperature excursion the following data may be used: The product is stable when exposed to the following conditions:
    - 48 hours at temperatures up to 25°C.
    - 3 repeated excursions of 24 hours at 25°C.
    - 7 days at freezing temperatures.

  The product can be returned to the fridge and no change in expiry date is required if exposed to the conditions above.

Administration

- In general, no more than 2-3mL of oily injection should be administered per site. If volumes above this are to be given then given in divided doses.

- Injecting an IM injection slowly into a site can reduce pain and therefore some volumes may be larger than the amounts quoted above. For example Trevicta long-acting injection which is licensed for deltoid use but it's volume is over 1mL.

- Needle length is important to ensure the injection is administered into the muscle and not subcutaneously
    - Site of injection
    - Female or male
    - BMI

Note

- Many of depot injections require very precise shaking of the syringe prior to administration, or if the syringe has been allowed to stand for a certain amount of time.

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Administration - volumes

- Historically the maximum volumes of fluid which can be administered intramuscularly for each of the recommend muscle group (for adults) are:

    - Deltoid = 1mL
    - Dorsogluteal = 4mL
    - Ventrogluteal = 2.5mL
    - Rectus femoris = 5mL
    - Vastus lateralis = 5mL.

Administration - anticoagulants

- There is no clear evidence-based guidance for Intramuscular injections for people taking oral anticoagulants.
    - Avoid IM injections if possible and consider an alternative route or therapy if necessary
    - Do not administer if INR is above the therapeutic range.
        - If a small volume injection is necessary
            - Consult SmPC for the IM product
            - Evaluate the risk-benefit ratio for the individual
            - Injection into an upper extremity
            - Use a fine needle and apply firm pressure for at least 2 minutes post injection.
            - Advise patient to watch for signs of bleeding or haematoma.

- If there is any doubt consult with the clinician responsible for prescribing or monitoring the individual's anticoagulant treatment

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