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European Metrology Research Programme
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Multi infusion E-learning

Understanding physical characteristics of infusion systems for patient-safe application

MEDD
Drugmetrology.com

University Medical Center Utrecht

Multi infusion E-learning

This E-learning is intended to create awareness on the risks of multi-infusion. Our aim is to improve your understanding of the physical characteristics of infusion systems. We discuss both pumps and disposables. We focus on their influence on the dose rate and potential dosing errors that can be clinically relevant.

Disclaimer

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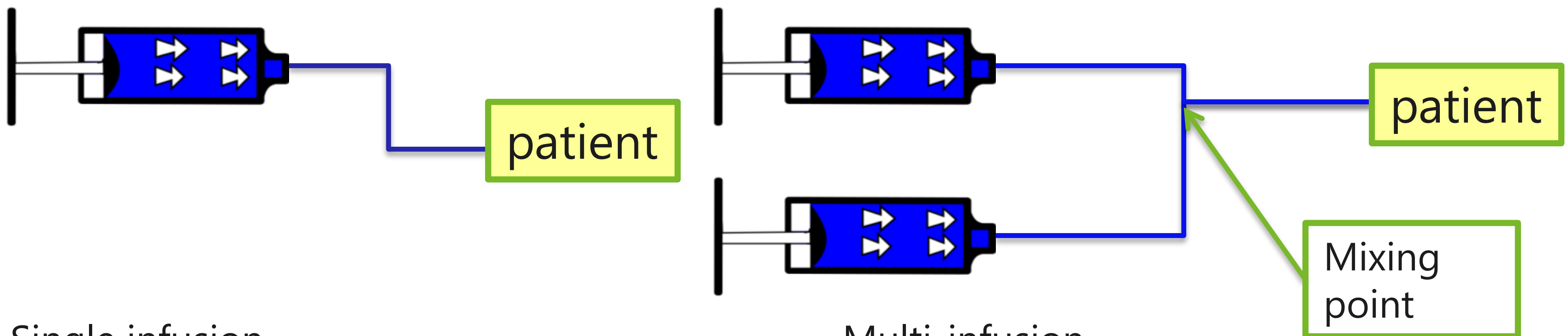
Contents

- Infusion medication characteristics
- What is multi infusion and why is it difficult?
- The most important physical effects
  - dead volume
  - system mechanical compliance
  - free flow

- Cases
  - clinical case OR
  - start-up arterial line
  - vertical displacement of pumps
  - occlusion

What is multi infusion?

- Let’s start by defining the term multi-infusion:
  - Administering **more than one** substance directly into the veins of a patient over **one** access point



Single infusion

Multi-infusion

- As we will see, the main problems with multi-infusion arise by the fact of administering multiple drugs over one access point.

Principle of multi-infusion

- A drug solution is inserted in an infusion pump, for example a syringe pump

- We set the flow rate of the pump such that the correct amount of drug is adminstered per time

- If, for some reason, the actual drug administration differs from the setpoint of the pumps: we make a dosing error

Dosing error: deviation from the intended dose.

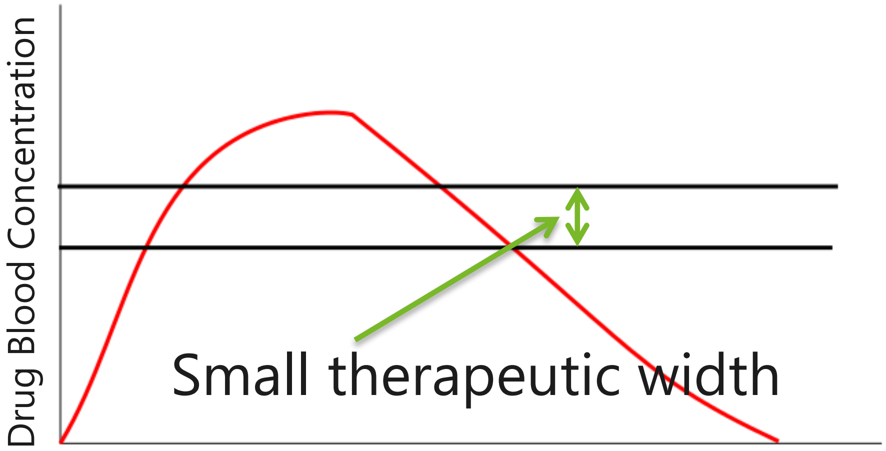
Why is multi-infusion difficult?

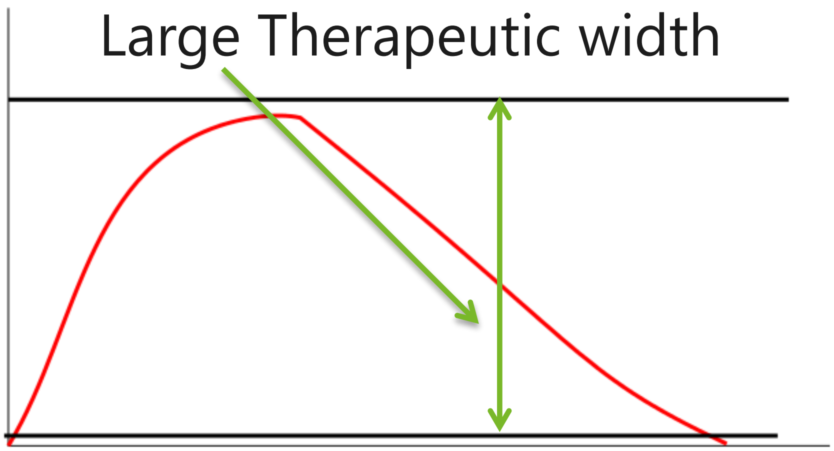
When is it hard to administer right amount of drug?

- Conditions of the patient:
  - Some patients can handle only a restricted fluid intake (especially on the NICU)
- Some of the drugs used are:
  - Fast acting
  - Potent (strong effects on vital signs)
- Some drugs have a small therapeutic range:
  - Too low or too high dosage is dangerous

Why is multi-infusion difficult?

- Some drugs have a small therapeutic range:
  - An under dosage does not have the desired effect
  - An over dosage leads to increased side effects and can be dangerous





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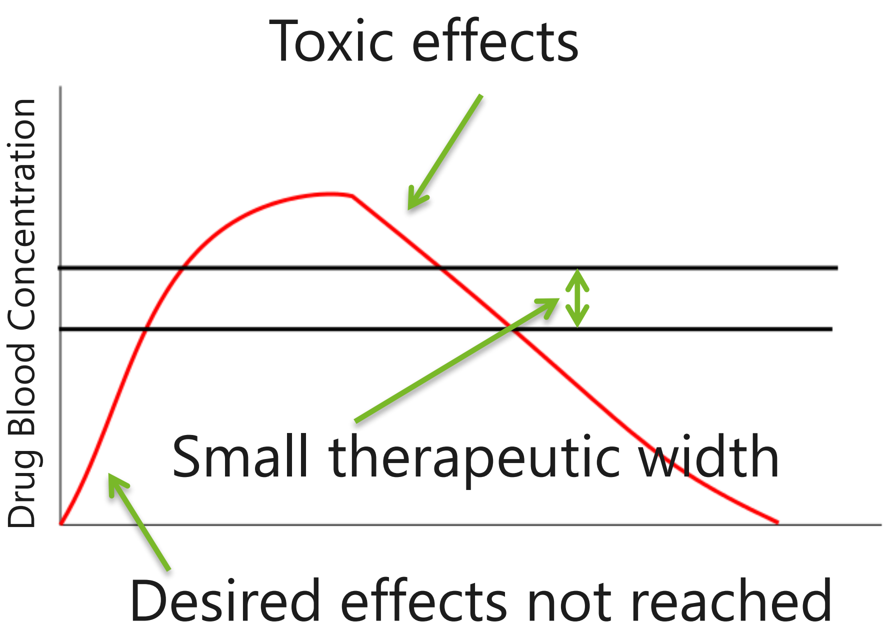
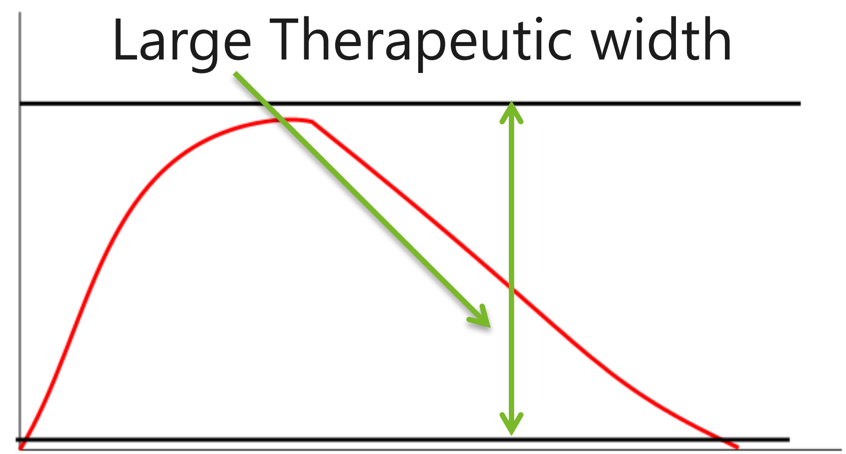
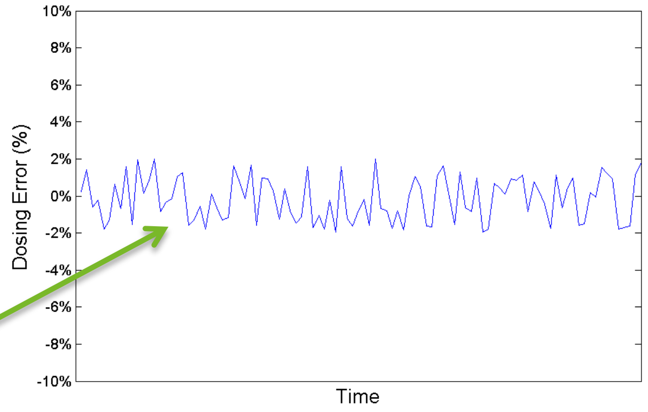




Dosing errors

- When do dosing errors occur?

- **Dosing error at steady state:**



- ISO standards demand 2% accuracy
  - Pumps are calibrated to test their accuracy

- 2% accuracy is not always met:
  - At low flow rates (≤0.5 ml/h) measured errors in drug delivery are larger and also the spread is larger
  - The accuracy changes when using different disposables

- Measurements help to assess performance of syringe pumps

Dosing errors

- When do dosing errors occur?

- **Dosing error during a change in flow rate:**

- This can occur when we change the flow rate of **any** pump in our infusion system.

- The severeness of dosing error depends on:
  - System components
  - The change in flow rates

Dosing errors

More information can be found in the Best Practice Guide:

http://drugmetrology.com/images/2015_05_13_Best_Practice_Guide.pdf

Dosing errors

- As we will see, both effects occur each time we change the flow rate of an infusion pump

- Let’s start with a clinical case where can see the dead volume effect

Typical dosing errors are caused by two effects:

- ❖ Dead Volume effect
- ❖ Compliance effect

A clinical case

- Clinical case:
  - Female patient, 62 years of age, no history of disease, had a subarachnoid hemorrhage yesterday
  - She is operated for clipping of an aneurysm
  - An arterial line and central venous pressure device are inserted
  - Blood pressure has lowered too far after induction: Noradrenaline therapy (3ml/h) is started using a saline carrier flow (10 ml/h)

Onset of blood pressure increase only starts after approximately 15 minutes!

What causes this delay?

A clical case

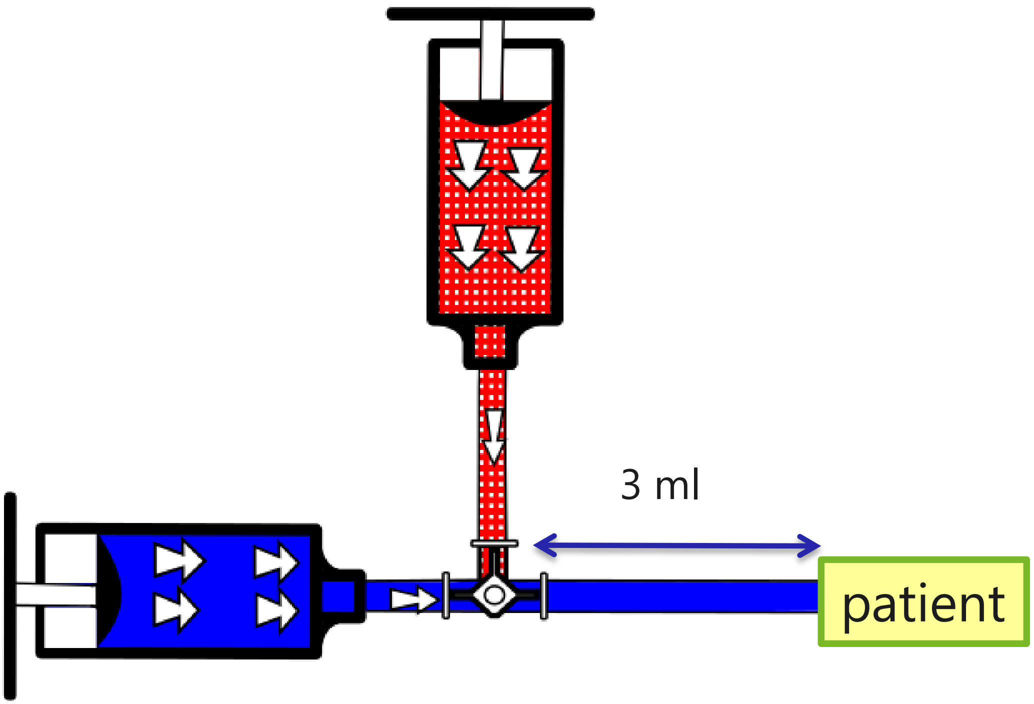
- In our case:

  Flow rate Noradrenaline: 3ml/h

  Flow rate Saline carrier flow: 10 ml/h

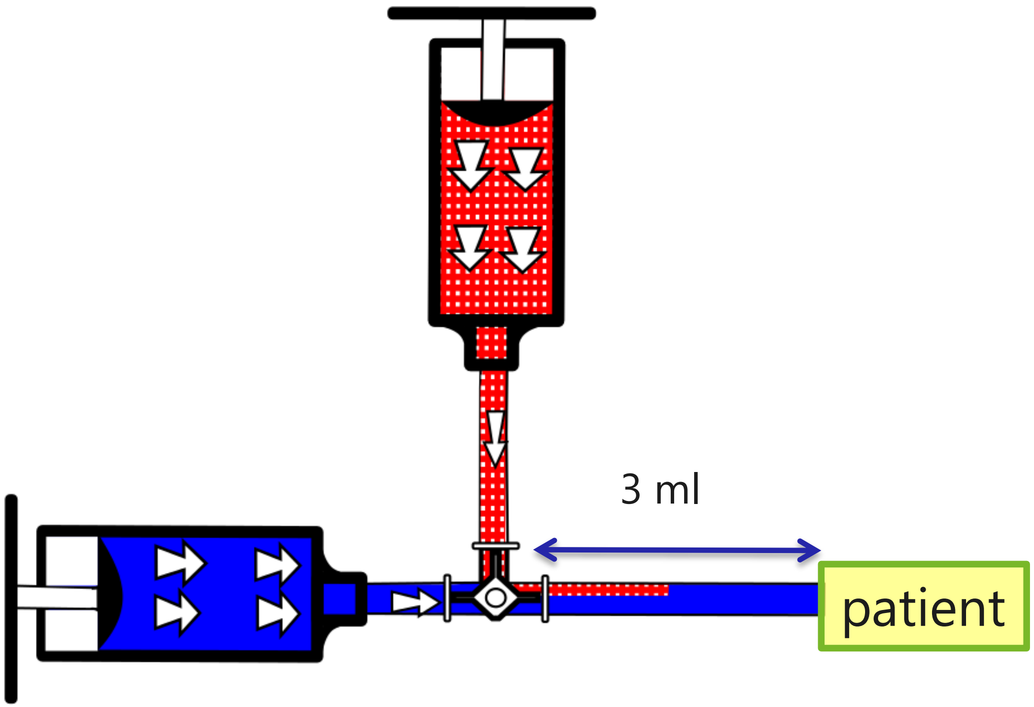
Volume from three way stop cock to patient is 3 ml

Total flow = 13 ml/h



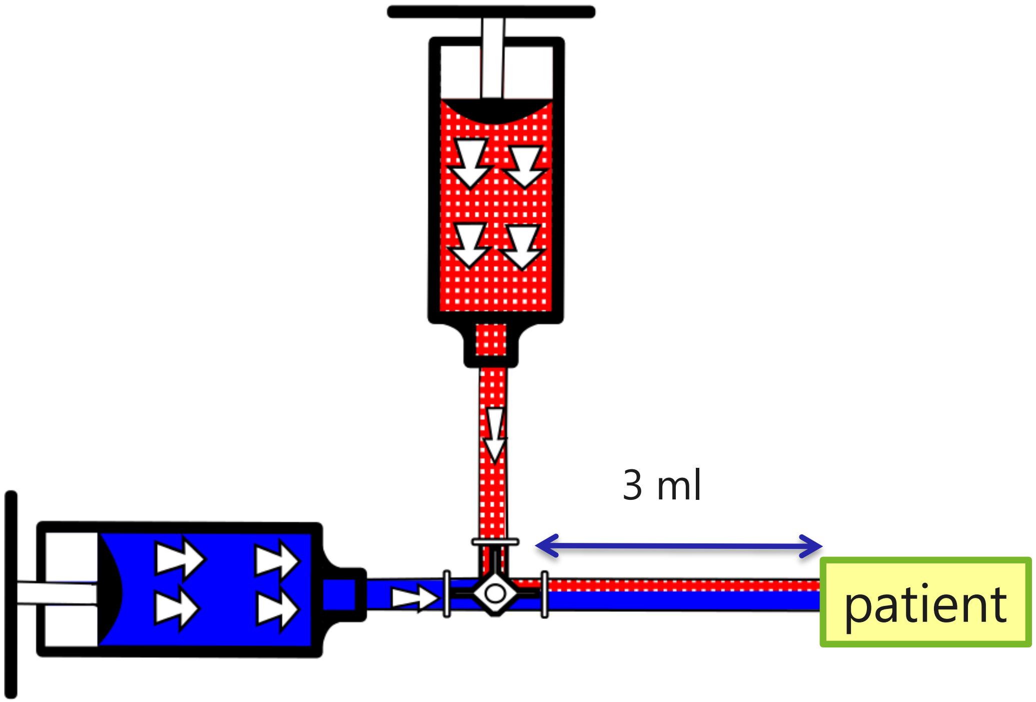
A clinical case

- The noradrenaline has to travel the 3 ml to reach the patient.
- With a flow rate of 13 ml/h: after 7 minutes the noradrenaline is halfway



A clinical case

- In our case:
  - After 14 minutes noradrenaline reaches the patient!



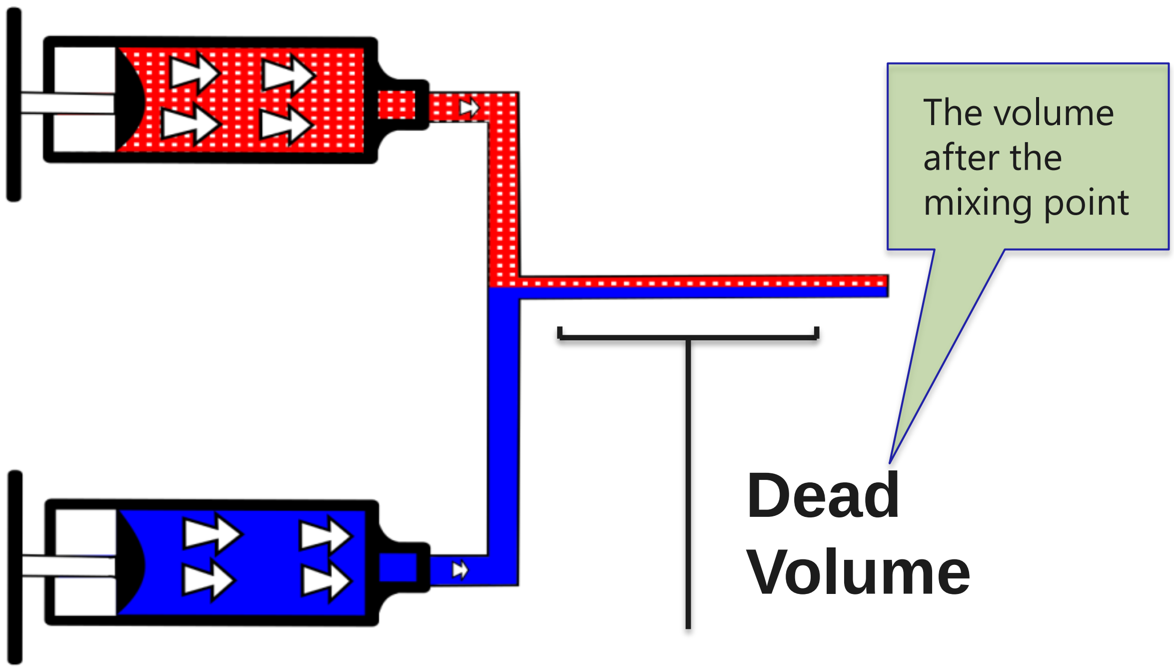
Dead volume

- This delay effect is called the dead volume.
  - The dead volume is the shared volume
    - In our case: 3 ml
  - The delay depends on:
    - The amount of volume
    - The flow rates

Besides delay in start of drug administration dead volume effects can also lead to other types of dosing errors

Dead Volume effect

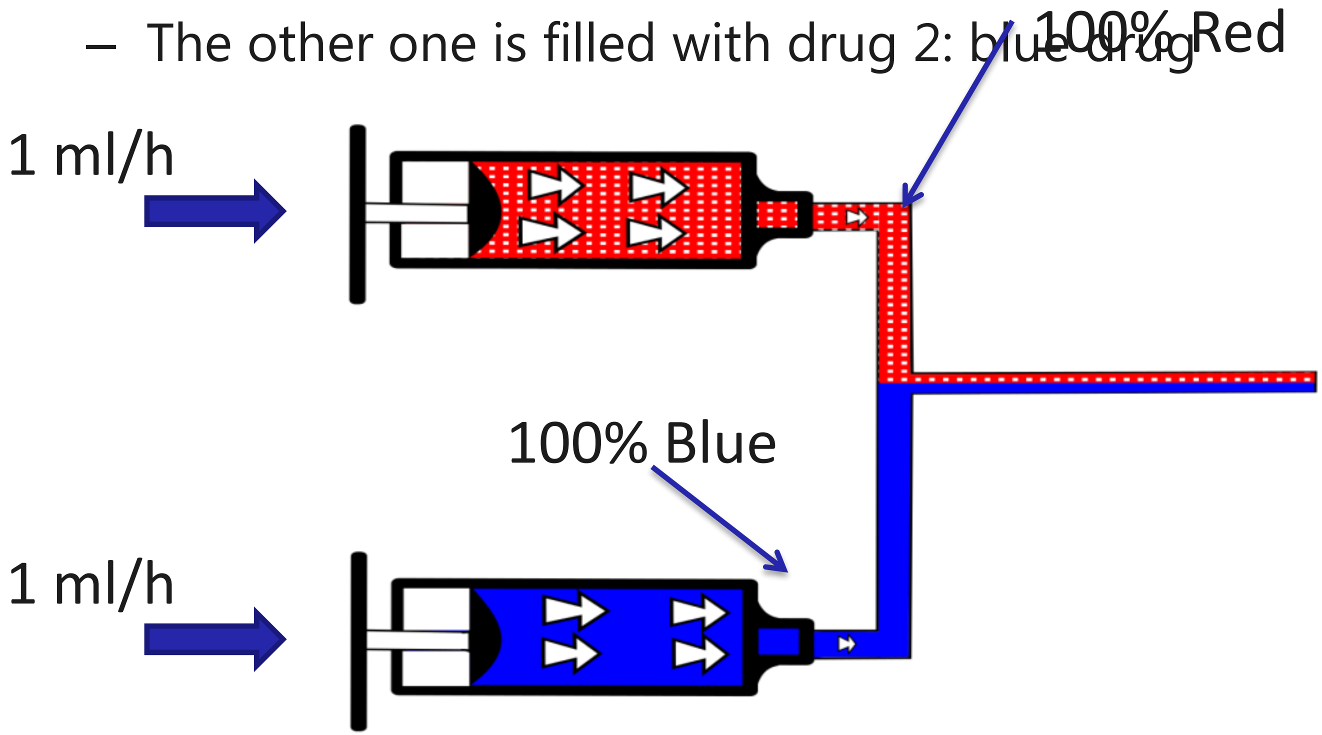
- The dead volume effect can also lead to dosing errors when pumps are already running



Dead Volume effect

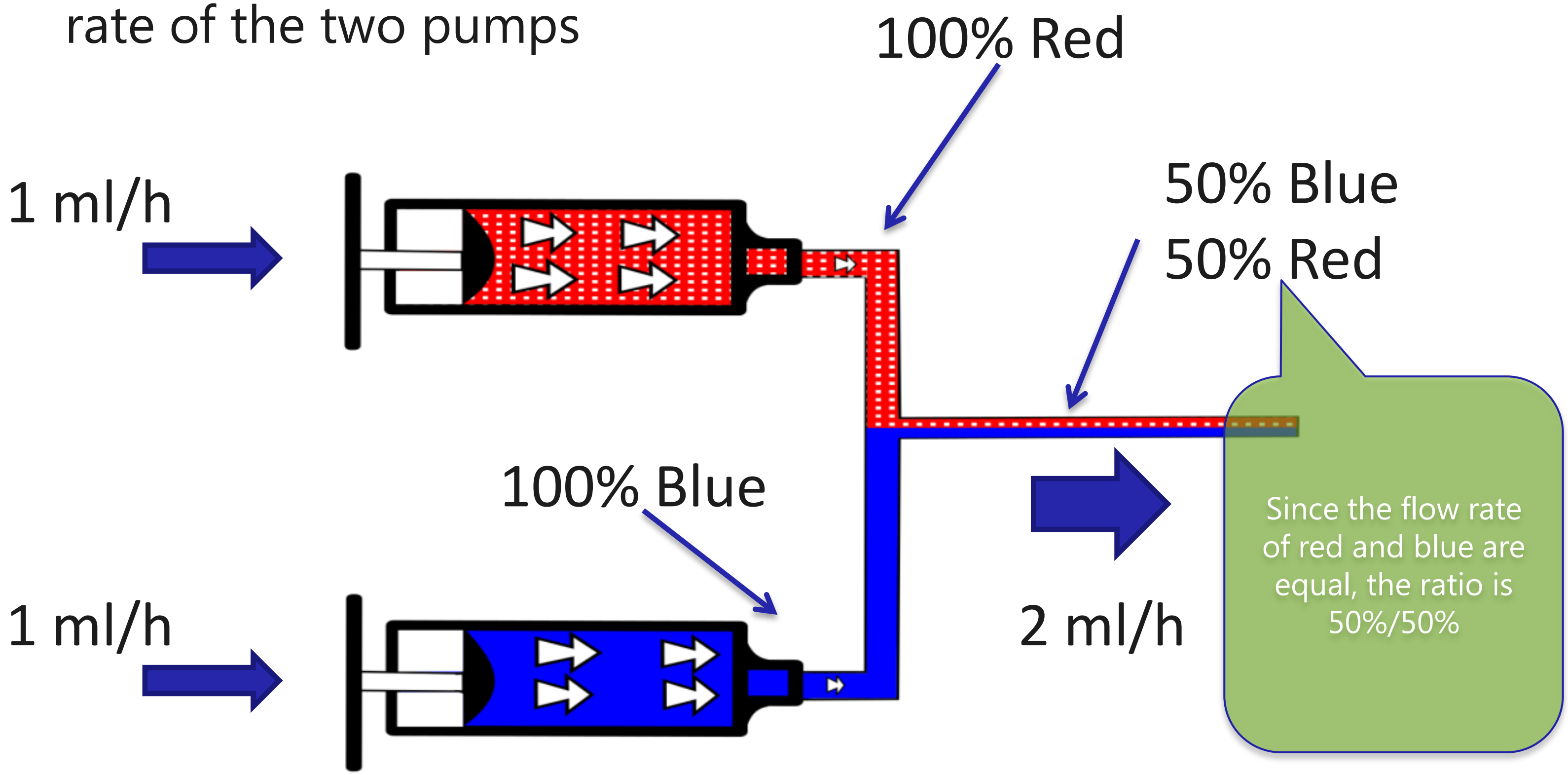
- Lets consider two syringe pumps
  - Both run at 1 ml/h
  - One is filled with drug 1: red drug
  - The other one is filled with drug 2: blue drug

- Up to the mixing point we have:
  - One line filled with only the red drug
  - One line filled with only the blue drug



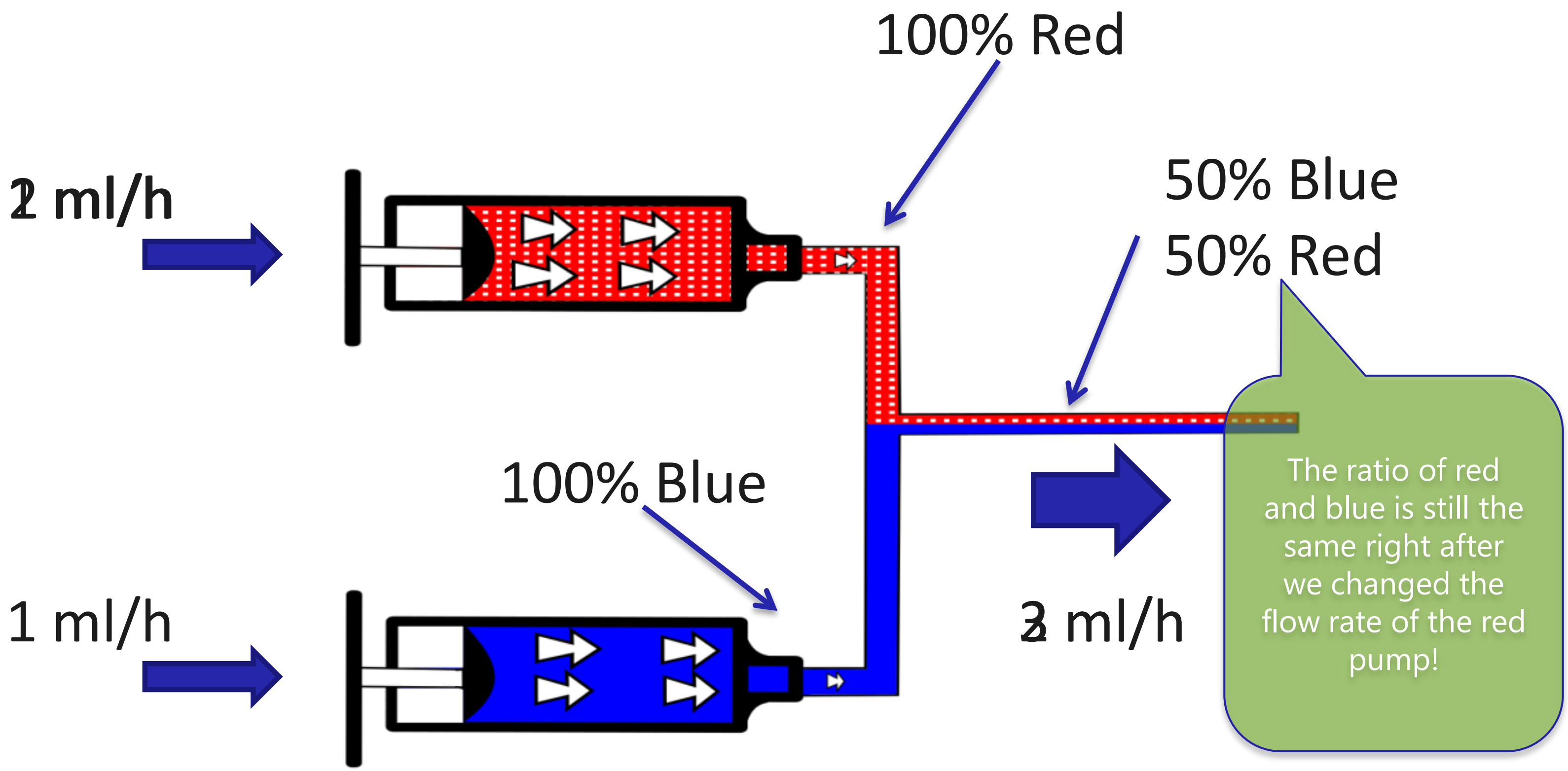
Dead Volume effect

- The dead volume contains both the red and blue drug:
- The flow rate in the dead volume is the combined flow rate of the two pumps



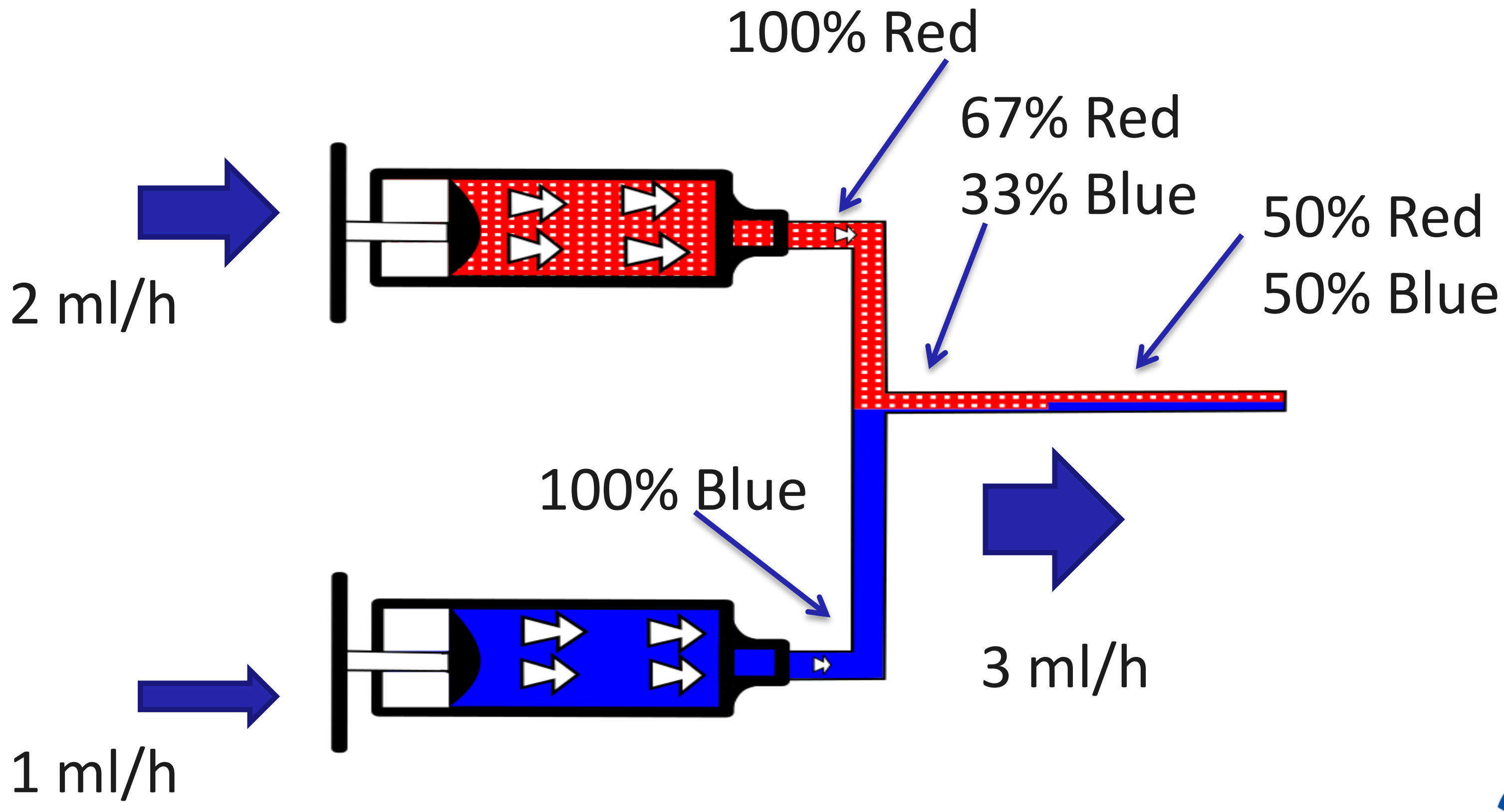
Dead Volume effect

- Now we increase the flow rate of our red drug to 2 ml/h
- The flow rate in the dead volume is now 3 ml/h



Dead volume effect

- After a while the dead volume is being filled with a new ratio of red and blue drug



Dead volume effect

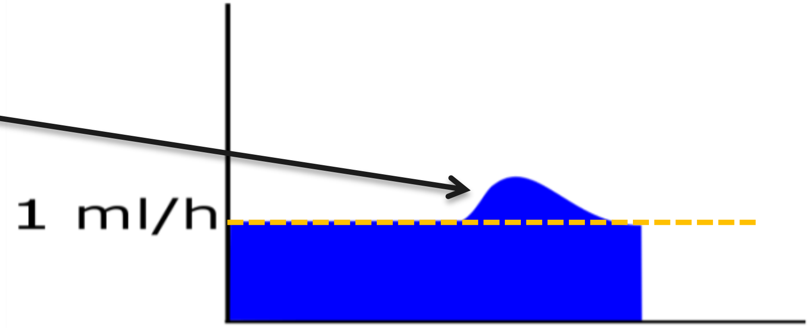
- After a while the dead volume is being filled with a new ratio of red and blue drug
- First old ratio of red and blue (50% 50%) needs to be pushed out of the dead volume
- We will flush at our new flow rate: 3 ml/h
- This means we adminster 50% red and 50% blue at 3 ml/h
- In other words we adminster:
  - 50% of 3 ml/h = 1.5 ml/h of the red drug
  - 50% of 3 ml/h = 1.5 ml/h of the blue drug

Not high enough: we wanted 2 ml/h!

Too high: we wanted 1 ml/h!

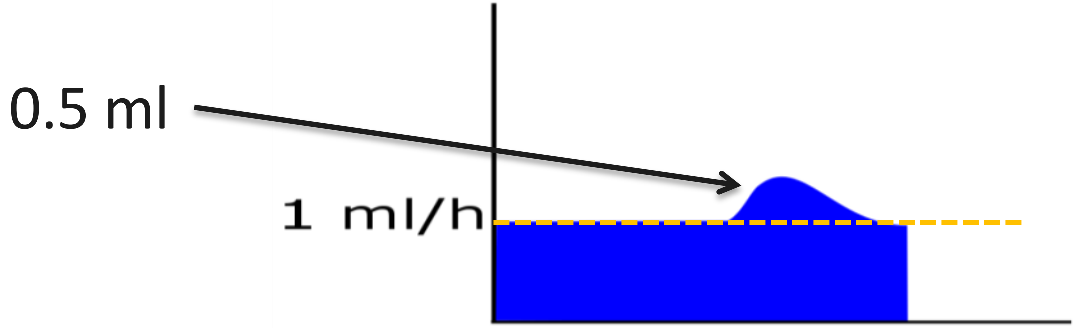
Dead Volume effect

- After a while the whole dead volume is filled with the new ratio of red and blue drug
- We now administer 66% of red drug and 33% of blue drug at 3 ml/h
  - 66% of 3 ml/h = 2 ml/h
  - 33% of 3 ml/h = 1 ml/h
- In our example the dead volume was 3 ml
  - The flushing of the dead volume will take 1 hour!
- During this time we administer:
  - Too much of the blue drug
  - Too little of the red drug



Dead volume effect

- During this time we administer:
  - Too much of the blue drug
    - For 1 hour the flow rate of the blue drug is at 1.5 ml/h
    - Intention: 1 ml/h
    - Error: 0.5 ml/h for 1 hour = 0.5 ml or 5 µg Noradrenaline
  - Too little of the red drug, for example 0.01 mg/ml Noradrenaline
    - For 1 hour the flow rate of the red drug is at 1.5 ml/h
    - Intention: 2ml/h
    - Error: 1 ml/h for 1 hour = 1 ml or 10 µg Noradrenaline: it can be noticed in the blood pressure



Dead volume effect

- At flow rate the **old** concentration ratio is administered at a **new** flow rate to the patient
- We can say that this effect acts in **same** direction as the flow rate change. This means:
  - If we increase the flow rate of one pump
    - The drug from the other pumps will be administered at a rate that is **too high**
    - The drug from the pump where the flow rate is increased will be administered at a rate that is **too low**
- If instead of increasing the flow rate, we decrease (or stop) one syringe pump, the same effect occurs, but in the other direction
- Clinically relevant dosing errors occur mostly at high (or large differences between) flow rates

- The drug from the pump that is lowered in flow rate will be administered at a rate that is **too high**
- The drug from the other pumps will be administered at a rate that is **too low**

Dosing errors

An animation showing the dead volume "push-out" effect can be found here:

http://drugmetrology.com/index.php/publications-logged-in-2

Dosing errors

- When do dosing errors occur?

- **Dosing error during a change in flow rate:**

- Whenever we change the flow rate of **any** pump in our infusion system, potentially a dosing error occurs.

- The severeness of dosing error depends on:
  - System components
  - The change in flow rates

We understand this now

We will consider this effect next

Dosing errors are caused by two effects:

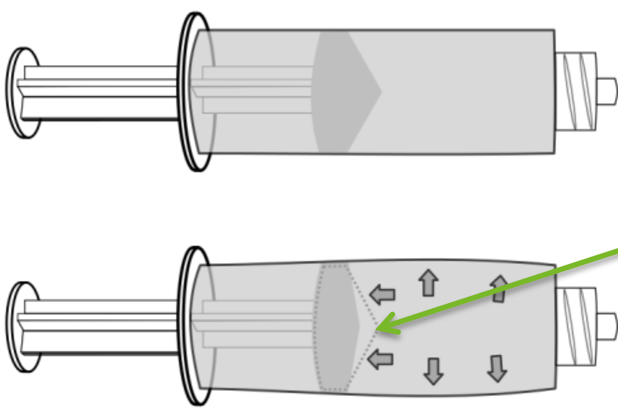
❖ Dead Volume effect

❖ Compliance effect

Compliance

- Compliance: deformation of components at pressure changes
- When we increase the flow rate of a syringe pump, the pressure in the syringe increases
- As a result some parts will deform
  - The plunge of a syringe will be compressed
  - Infusion lines can expand

This is the largest effect. You can see this yourself by pressing against a syringe.



Compliance

- Compliance: deformation of components at pressure changes
- When we increase the flow rate of a syringe pump, the pressure in the syringe increases
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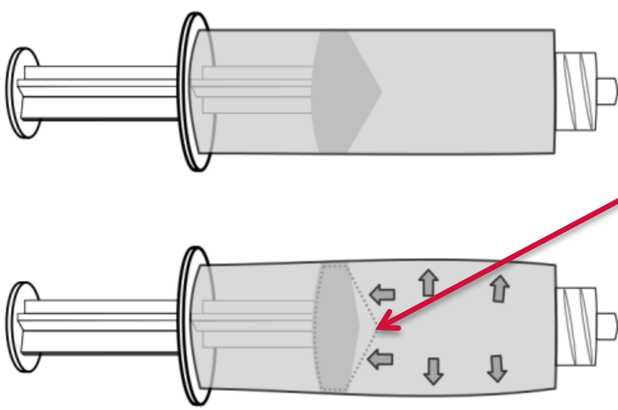
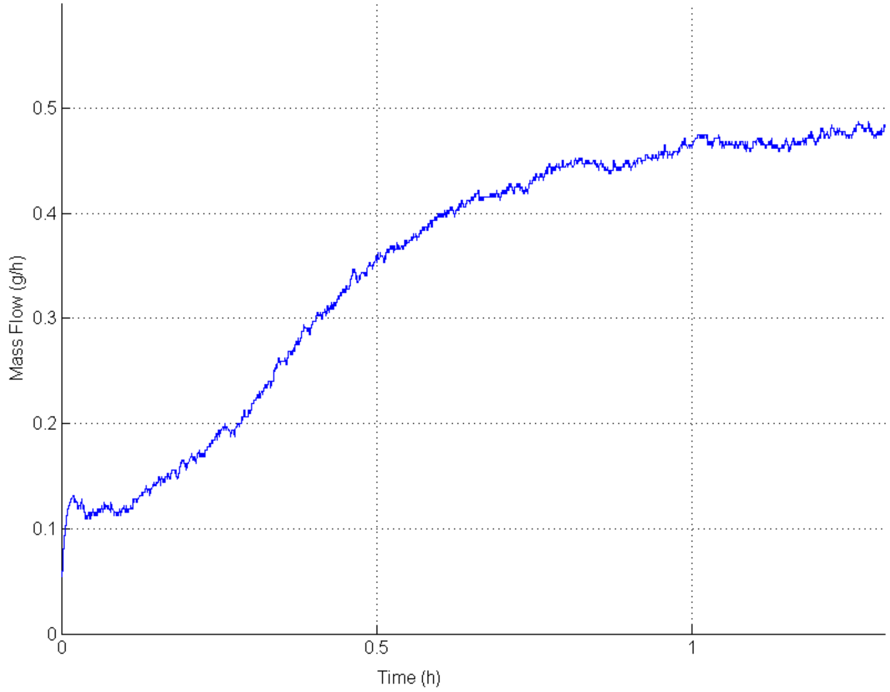
  - The plunge of a syringe will be compressed
  - Infusion lines can expand

Extra volume is created and will be filled with fluid.
This fluid was supposed to enter the patient!



Compliance

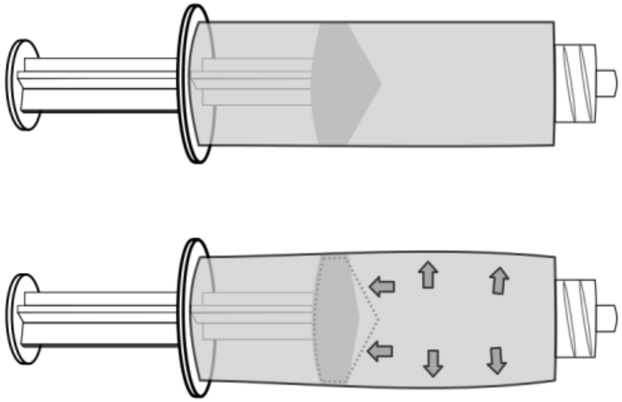
- Onset of flow rate may be delayed due to compliance
- In this clinical case an arterial line was simulated, using a syringe pump instead of a conventional pressure bag.
- It can be seen that the flow rate set point of 0.5 ml/h is reached after almost one hour.



Compliance

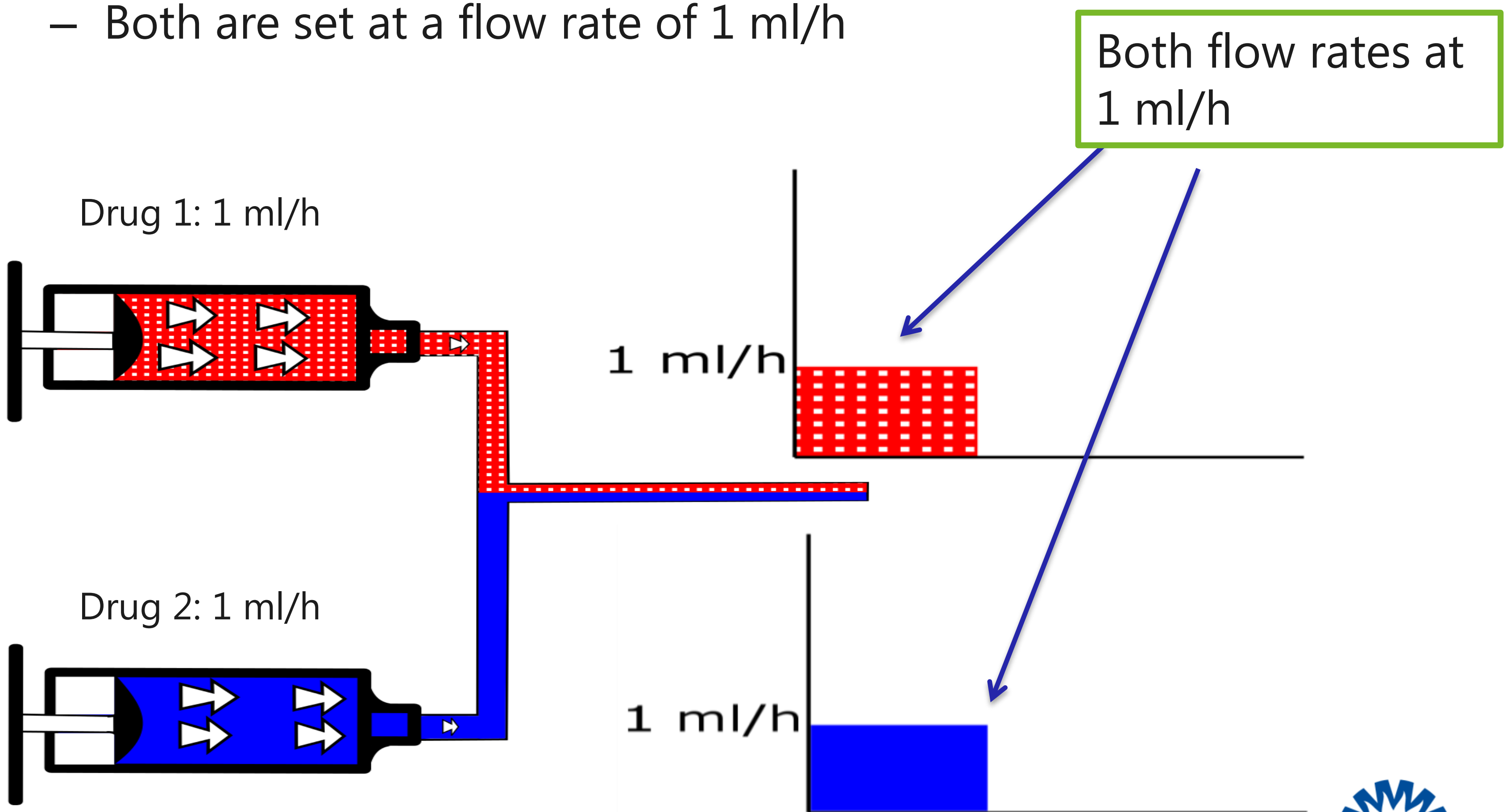
- Since some fluid does not reach the patient but is being used to fill the extra volume, our drug administration is delayed
- Besides delays, compliance can also lead other types of dosing errors
- Lets consider two syringes again
  - Blue drug pumping at 1 ml/h
  - Red drug pumping at 1 ml/h which we will increase to 2 ml/h

Dosing errors occur when we make a change in the flow rates of one of the pumps.



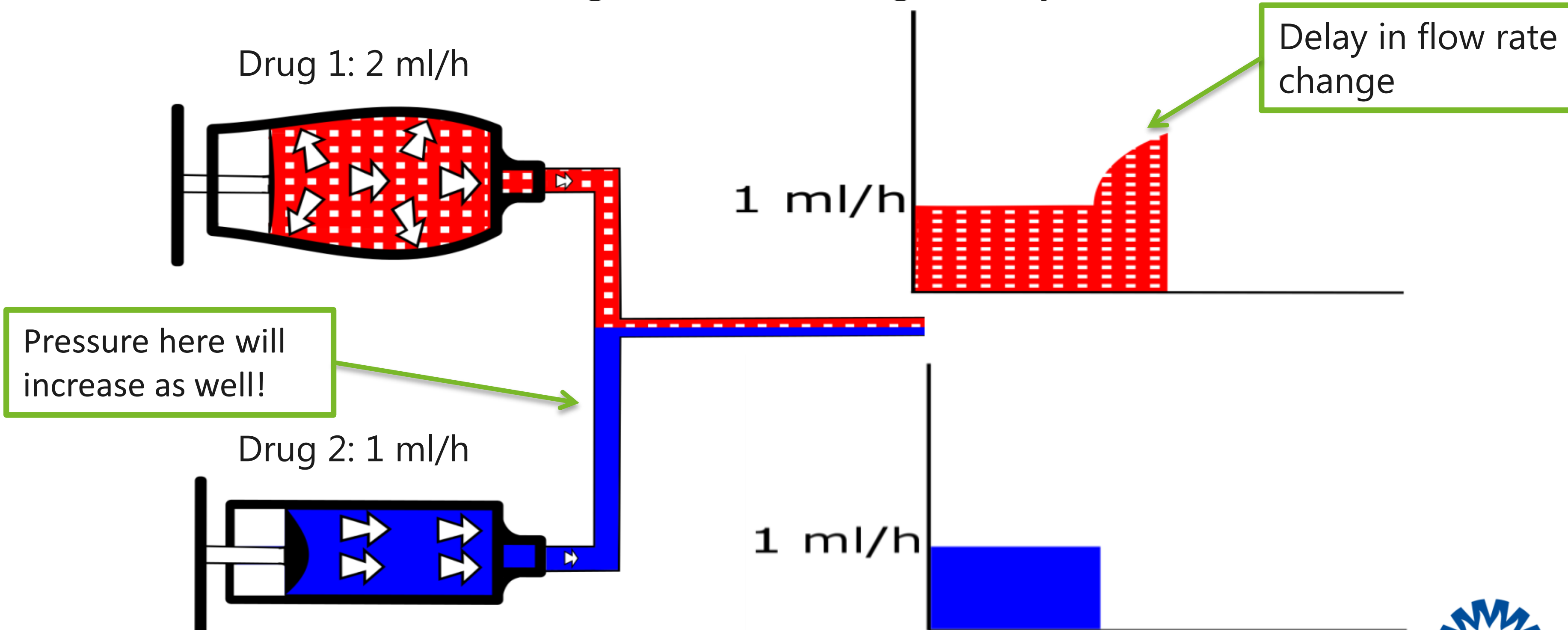
Compliance effect

- Again we have two pumps:
  - Both are set at a flow rate of 1 ml/h



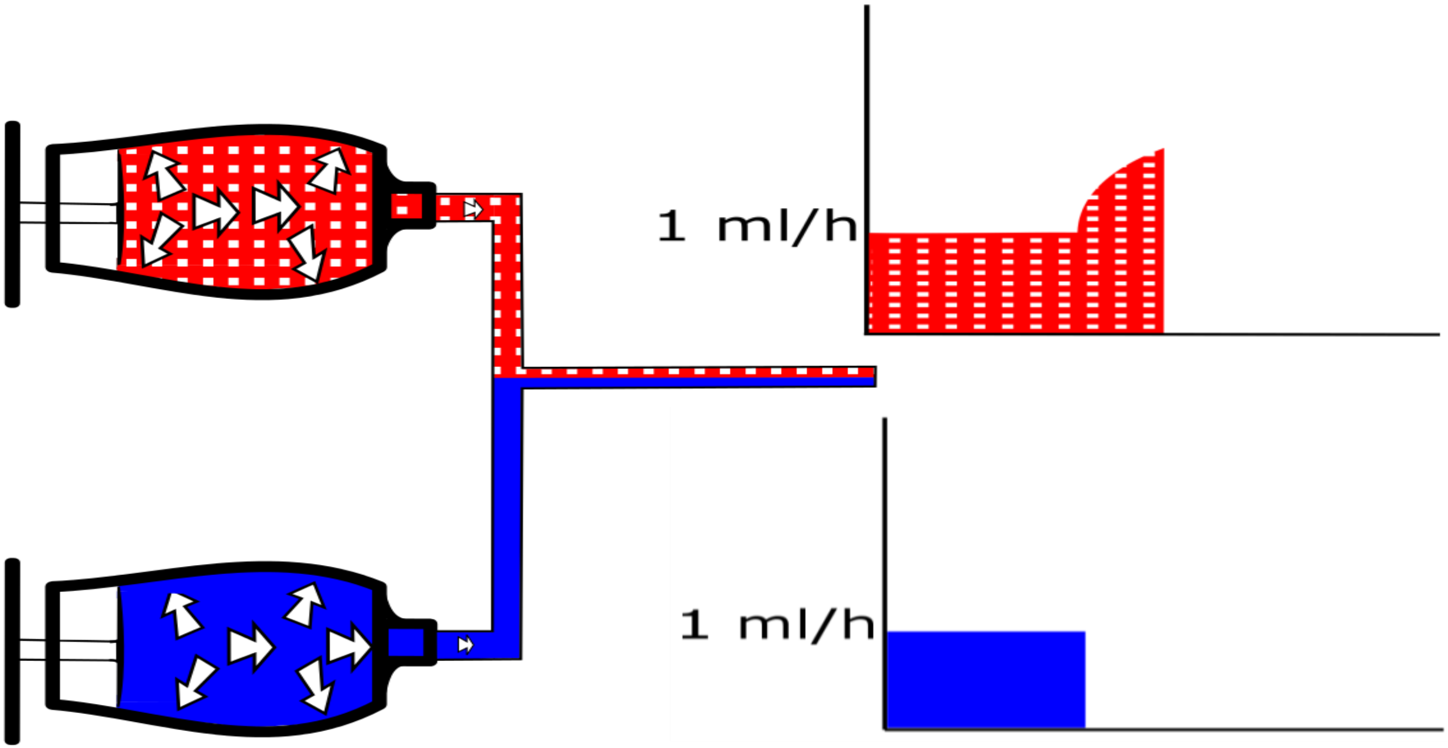
Compliance effect

- We increase the flow rate of the red pump to 2 ml/h
  - Some red fluid will be stored in the extra volume of the red syringe, because of the increased pressure
  - The flow rate change of the red drug is delayed



Compliance effect

- We increase the flow rate of the red pump to 2 ml/h
  - The pressure in the blue syringe will increase as well
  - The blue syringe will also be deformed



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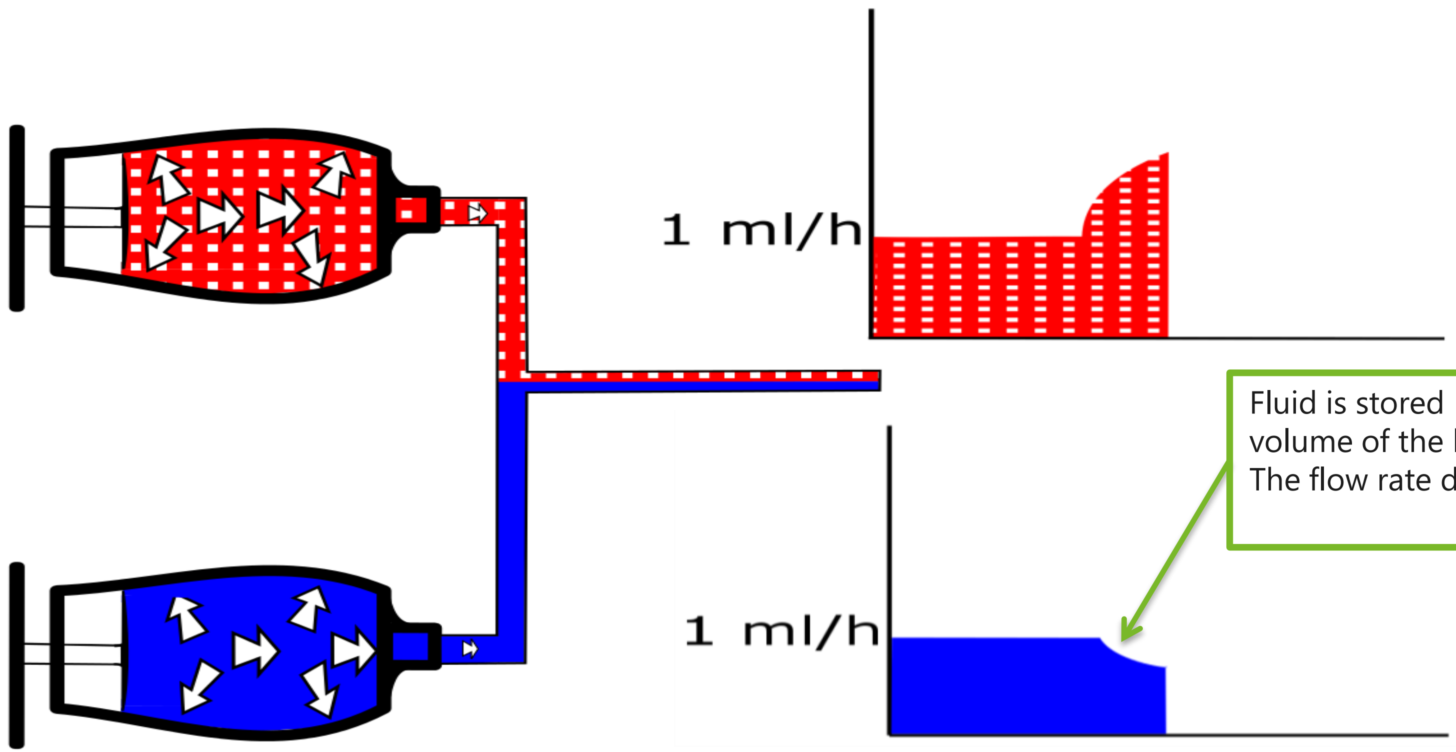
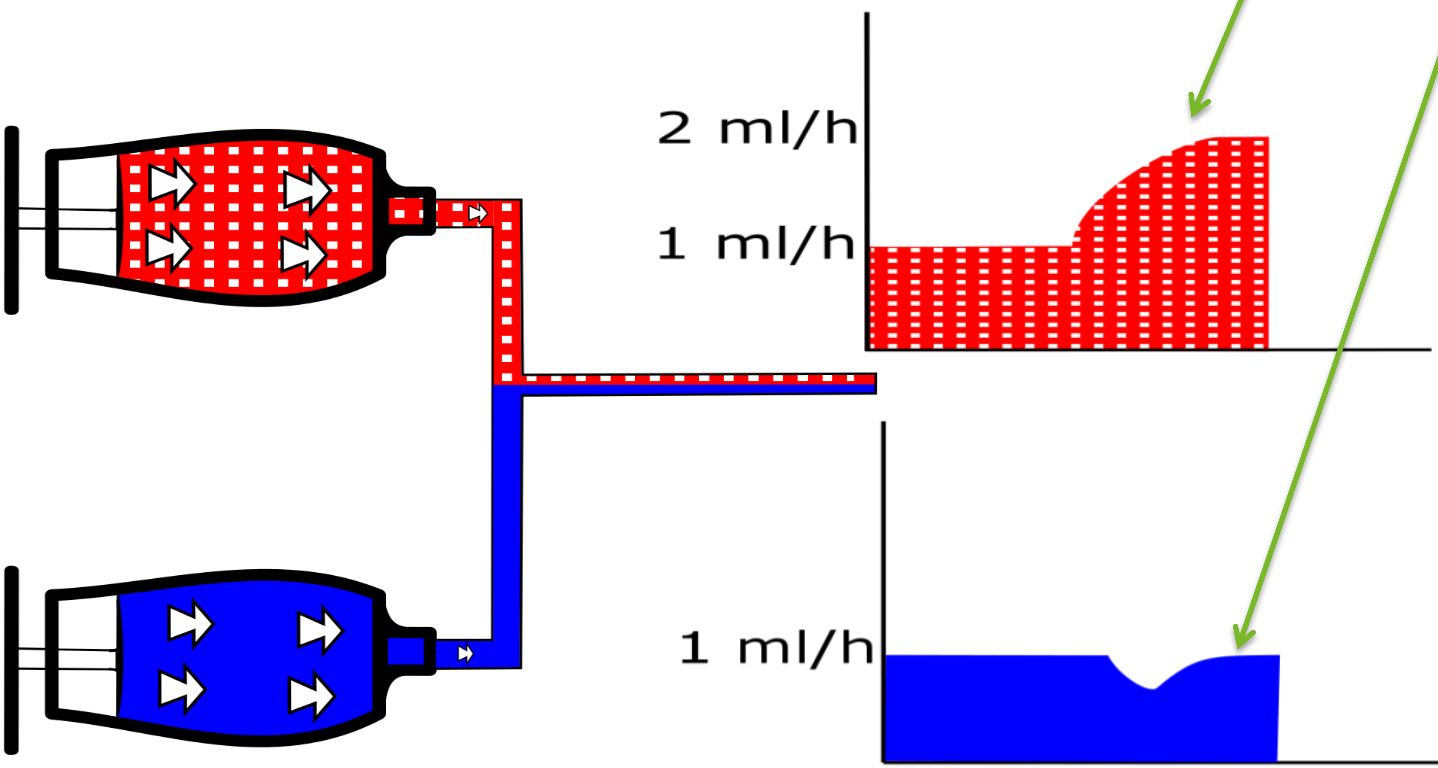


Fluid is stored in the extra volume of the blue syringe. The flow rate decreases.

Compliance effect

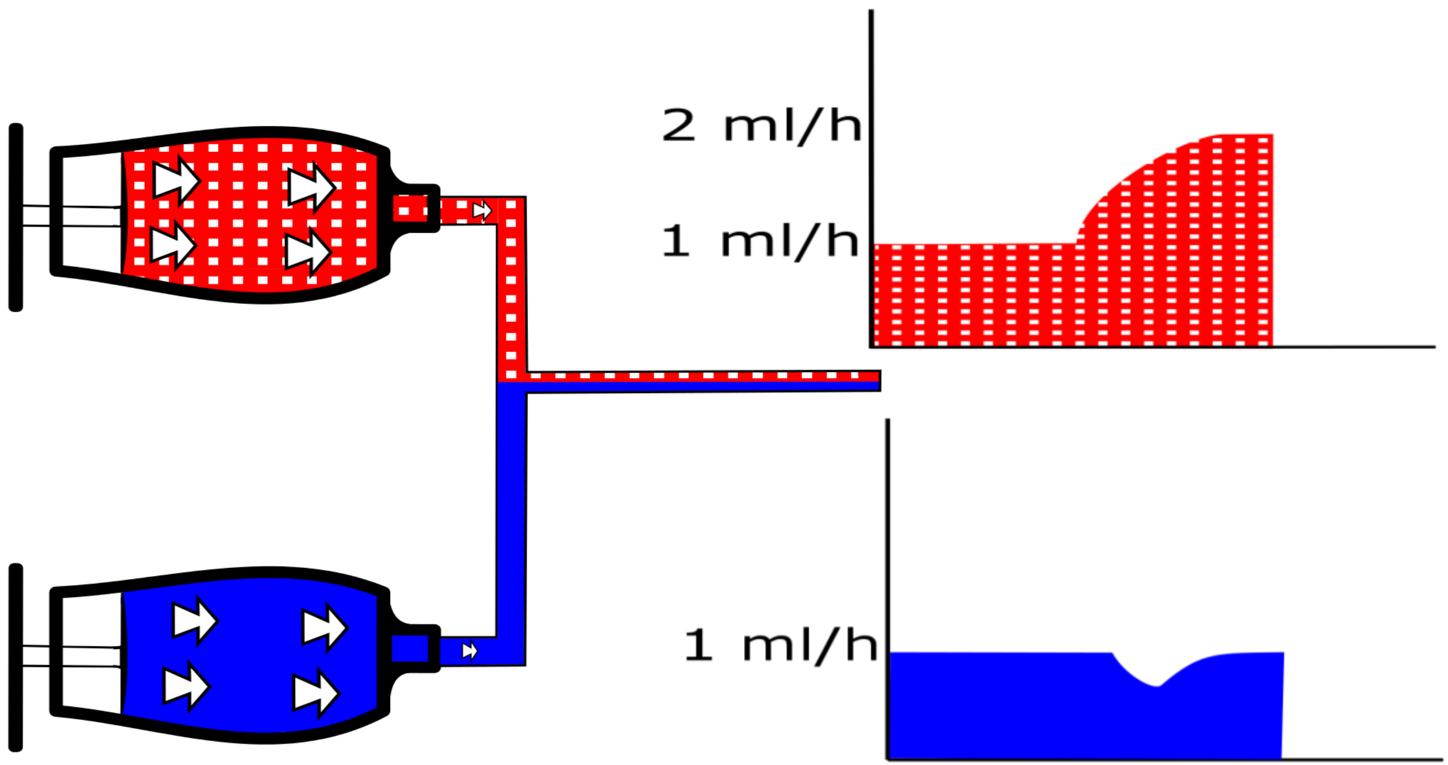
- We increase the flow rate of the red pump to 2 ml/h
  - After a while a new equilibrium is reached

Flow rates are now:
2 ml/h for red.
1 ml/h for blue



Compliance effect

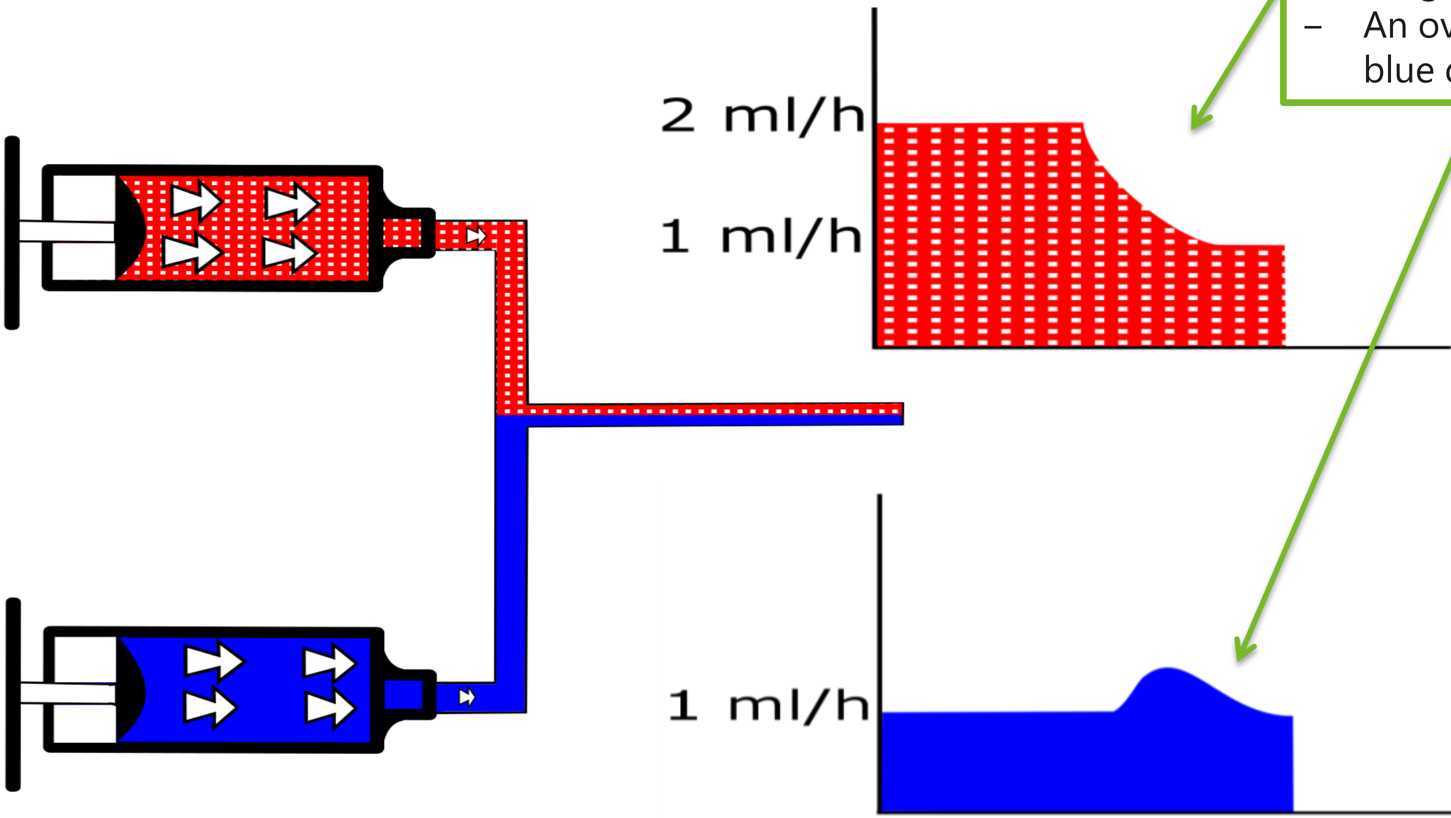
- What happens if we decrease the flow rate of a syringe pump?



Compliance effect

- The syringes will go back to their original volume
  - The drug that was stored in this volume will be administered to the patient

- A delay in decrease for red drug
- An overdose for blue drug



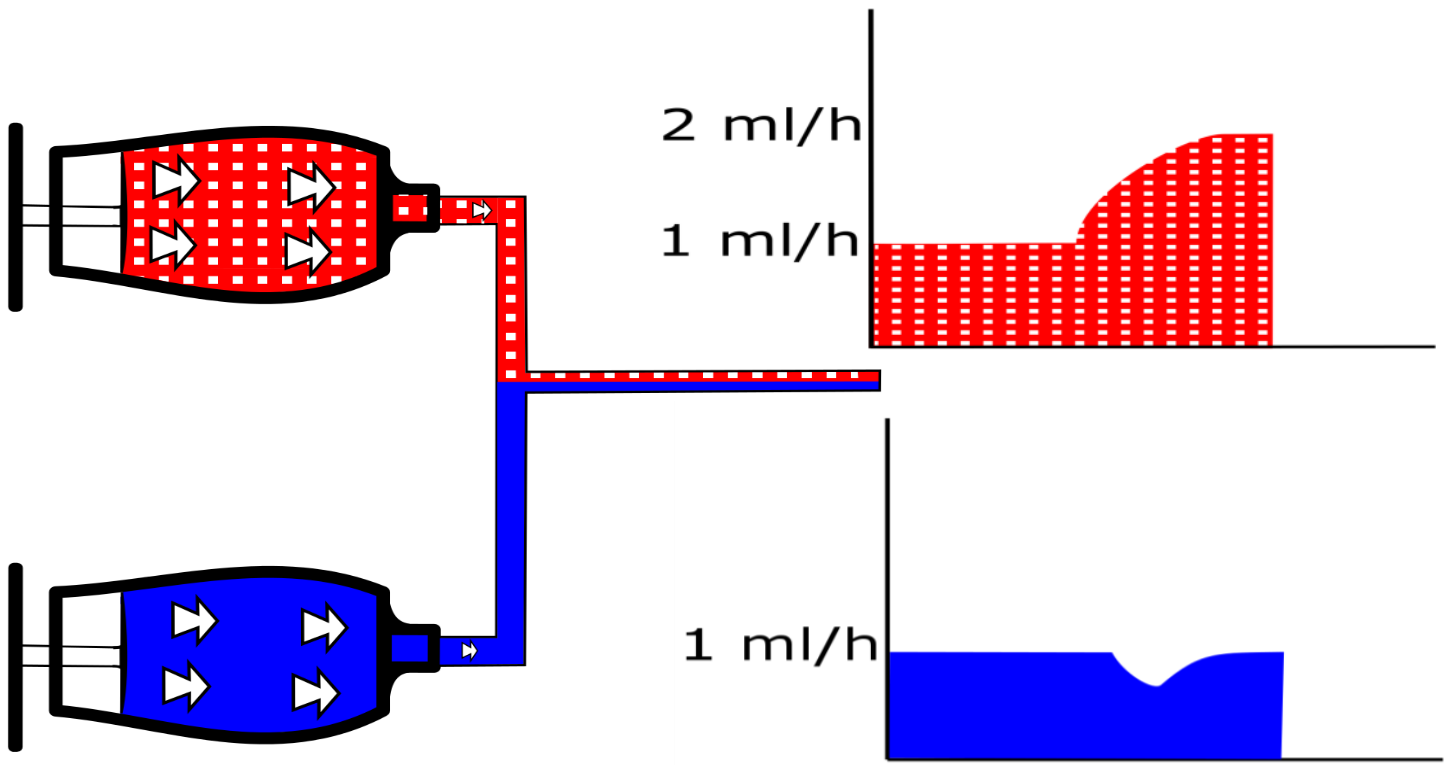
Compliance effect

- Compliance effect causes:
  - Delays in changes in flow rate
  - Dosing error in the pumps where the flow rate is not changed

- Acts in opposite direction as the flow rate change
  - If we increase the flow rate of one pump
    - The drug of the other pumps will be administered at a rate that is **too low**
    - The drug of the pump where the flow rate is increased will be administered at a rate that is **too high**

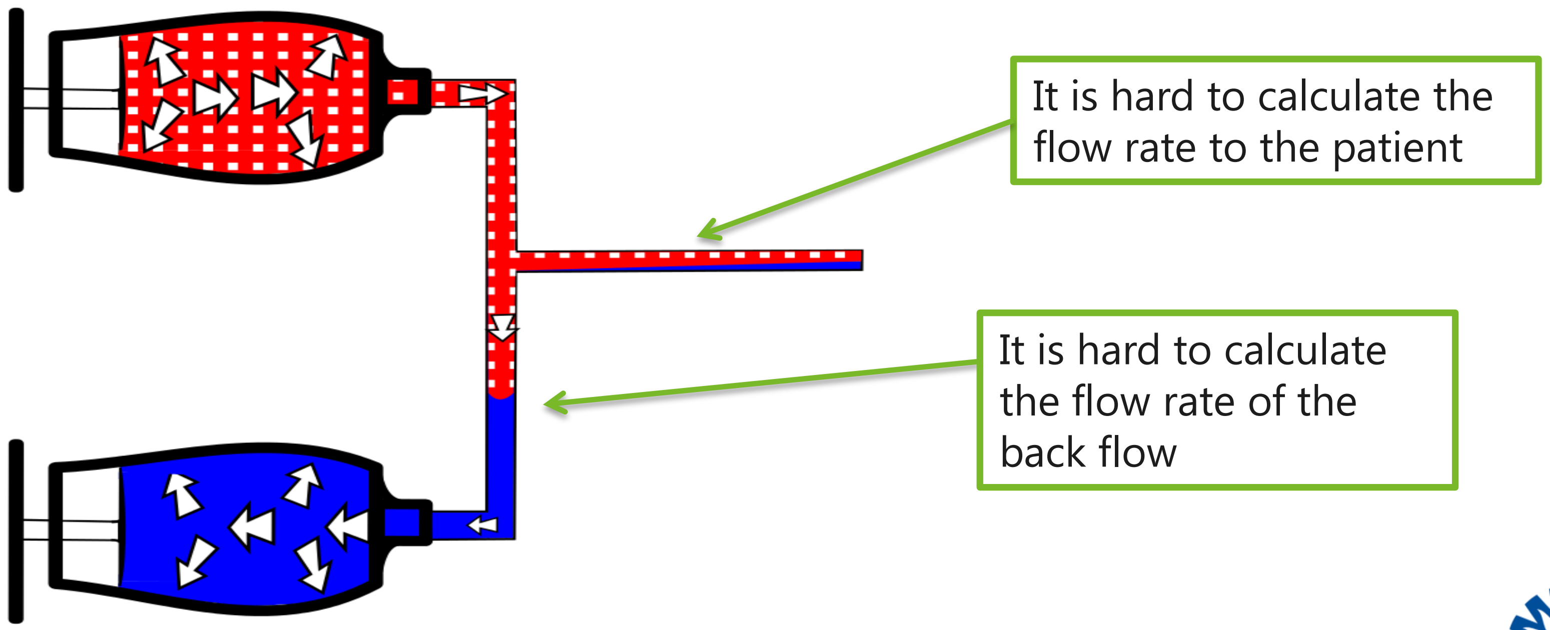
Compliance effect

- We can see a decrease in the output of the blue syringe pump
  - Can this output become negative for some situations?



Back flow

- Yes it can. This is called back flow
  - The drugs from the red syringe will flow into the blue syringe
  - This is possible because the blue syringe is deformed



Compliance effects

- Compliance effects are also visible when changing the height of a syringe pump and when infusion lines are occluded

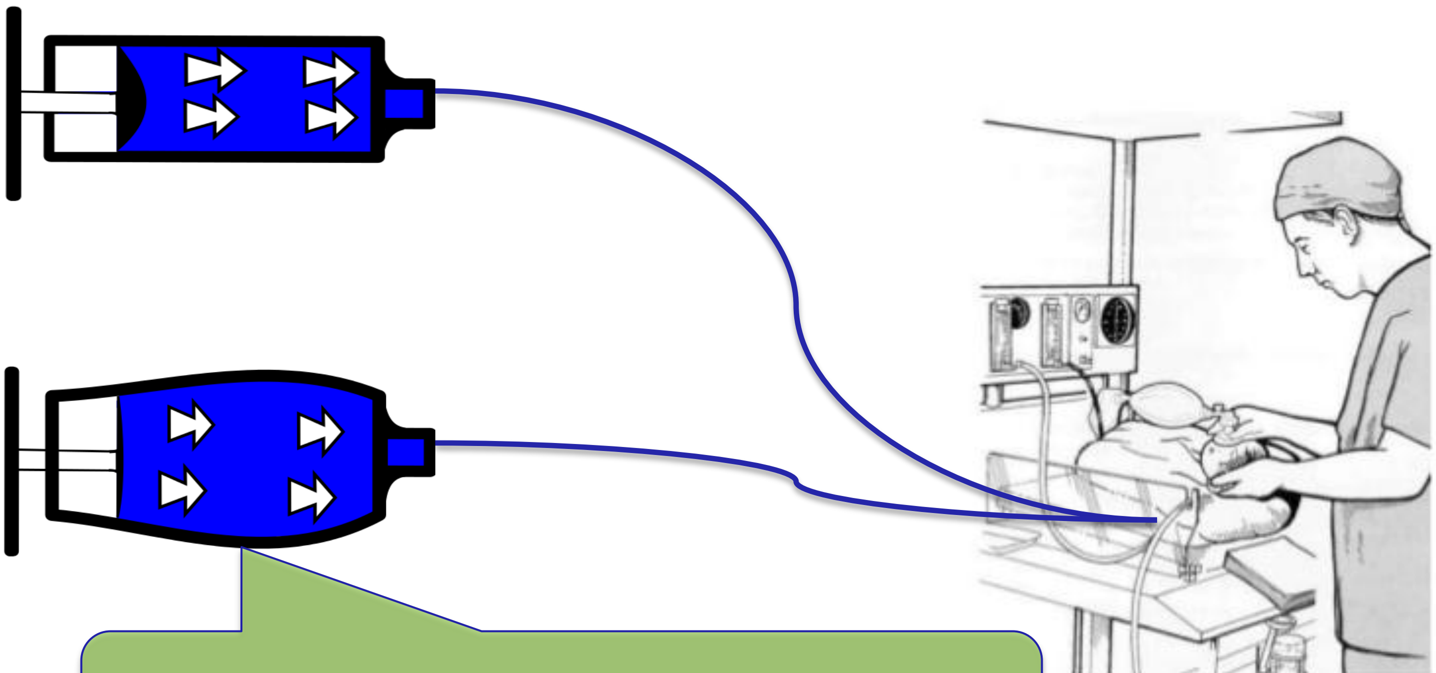
- Pumps are typically placed in different heights because users differ in height
- Lines are occluded when the flow is blocked

Height difference

- If we change the height of a syringe pump the pressure changes
- Pumps are typically placed in different heights because users differ in height

a)

b)



When the pressure increases the syringe deforms (compliance).

Height difference

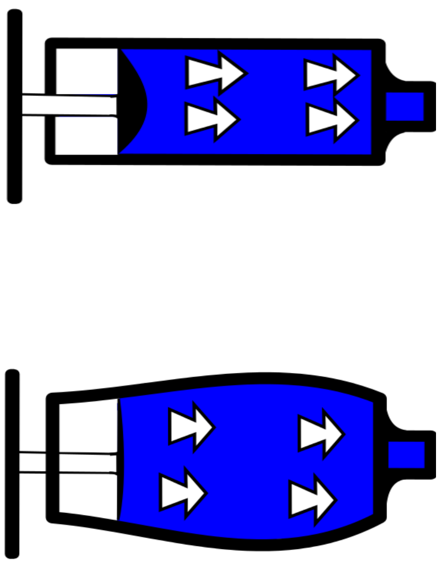
- Because of compliance:

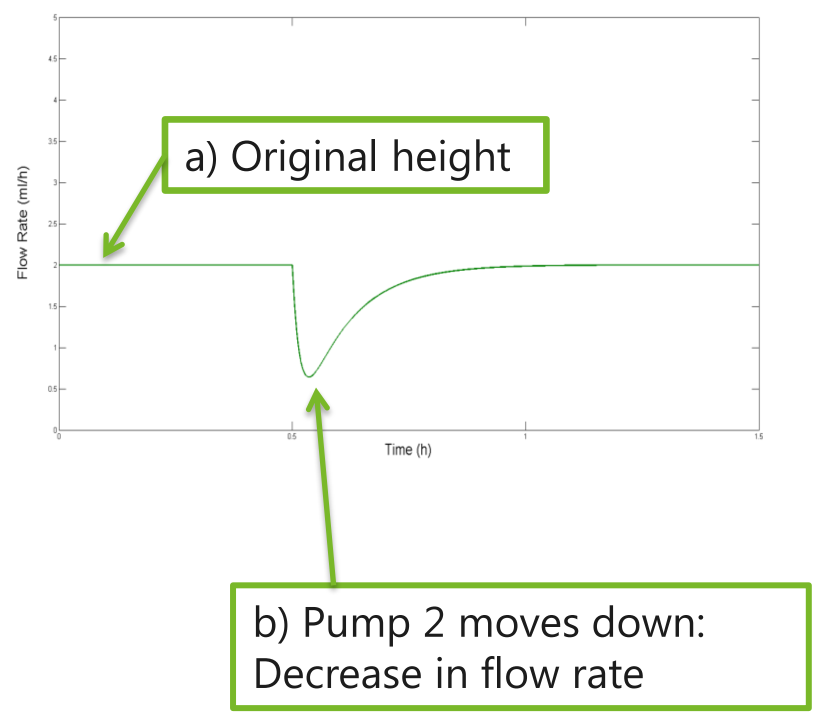
This is because the system has compliance

  - Extra volume is created in the syringe
  - The flow rate will be decreased

a)

b)

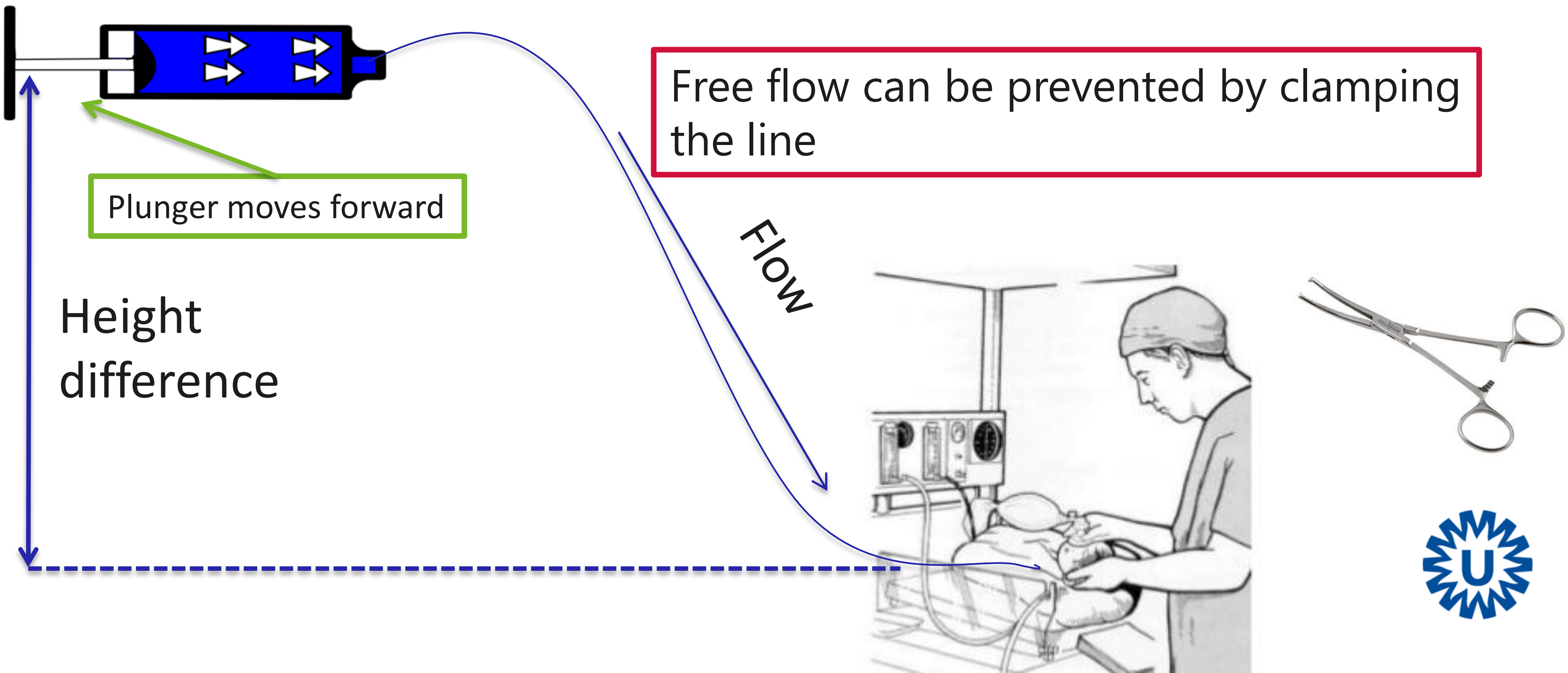




Free flow

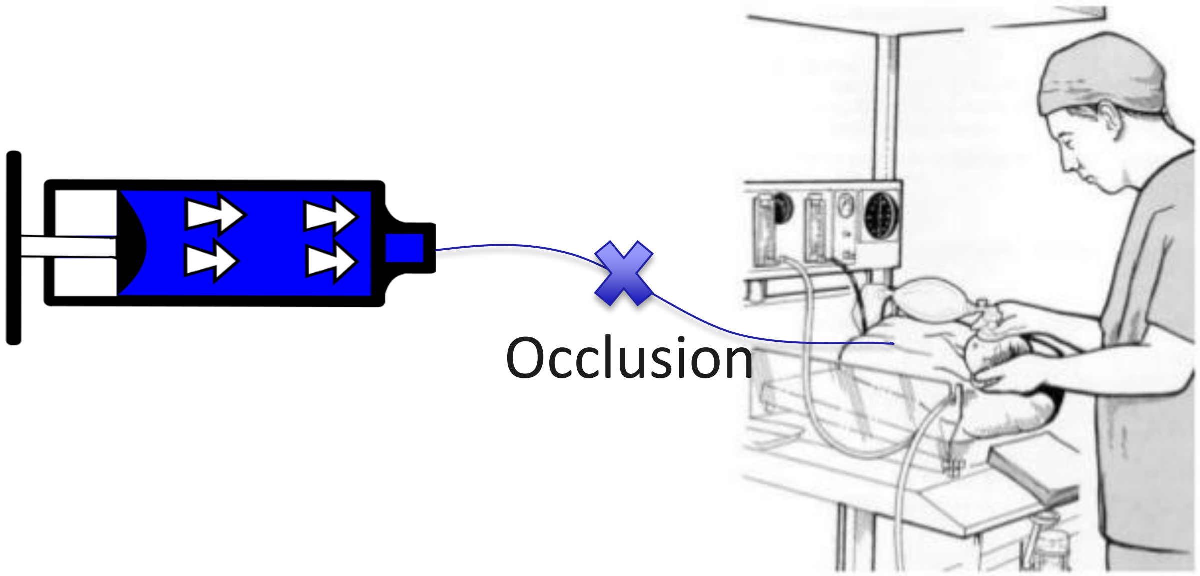
- Height difference between the syringe and the patient causes pressure difference
- When we replace a syringe, the plunger is loose
- Because of the pressure difference there is a flow: the plunger moves forward: Free Flow.

Free flow can be prevented by clamping the line



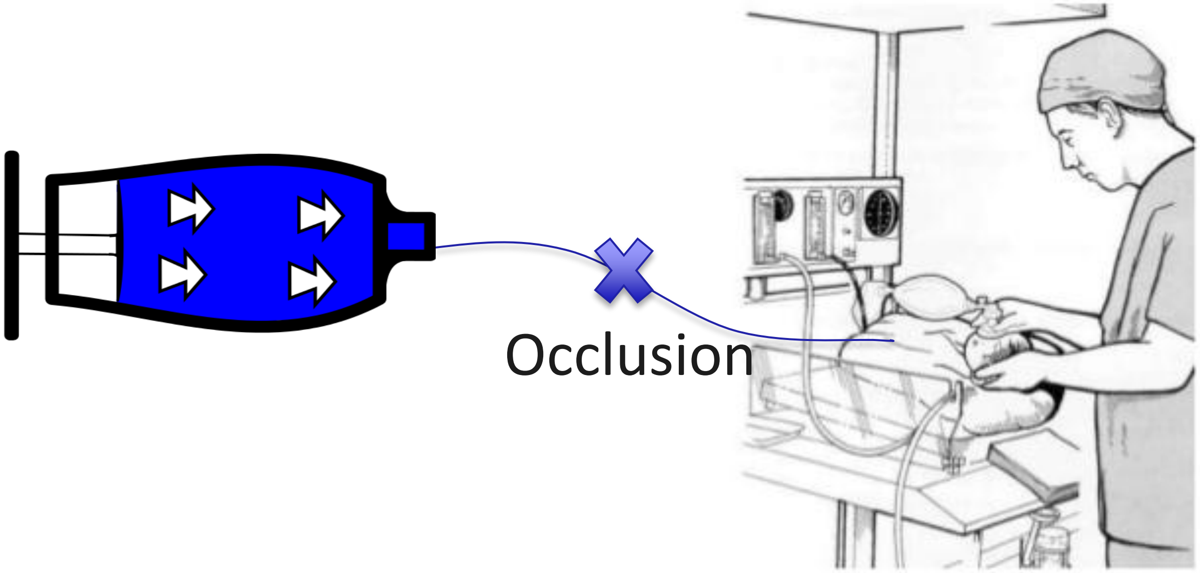
Occlusion

- If a line is blocked this is called occlusion. No drugs are administered.
- The pump is still pumping fluids and the pressure in the infusion lines increases
- Because the components are compliant they will deform.
- As a result the pressure increases only slowly



Occlusion

- As a result the pressure increases only slowly
- The occlusion alarm sounds if the occlusion pressure is reached
- Because the pressure increases only slowly, it can take a long time before the alarm is sound



Best Practices in multi-infusion

- Infusion systems can respond slowly. At every change, the user should take a waiting time into account, due to system compliance and push out effects of dead volume
- Use low compliant syringes in low flow rate applications
- Avoid combining high and low flow rate on one line
- Be extra careful when using potent drugs with low biological half time or small therapeutical range
- Always clamp/close your infusion lines when replacing a syringe
- Include disposables in calibration measurements of infusion pumps to acquire better performance information
- At low flow rates, the pumps not always meet the 2% accuracy