RESPIRATORY SYSTEM

PHYSIOLOGY

HANDOUT NO. 5

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Color code
slides
doctor
Important
Additional

***Continuation of lecture 4**

The minimal volume is the resting volume of the lung, used in **forensic medicine** to determine whether a baby was stillborn. If pieces of the lung are taken and they sink in water, it indicates the baby never took a breath. However, if the baby takes even a single breath, the minimal volume is established, and the lung pieces will float. This helps determine whether the baby was born alive or dead.

Compliance

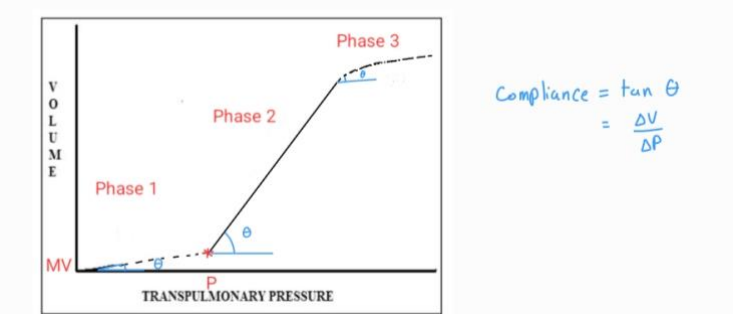
Compliance: Distensibility (stretchability): How easy the lungs can expand. How much force we need to expand the lung? If the force is small, then the lung is stretchable.

Compliance:It is the change in lung volume per unit change in transpulmonary pressure

$$\Delta V / \Delta P$$

Compliance pressure-volume curve:

1. **inflation curve**



Phase 1: When inflating the lung from minimal volume (MV=150 ml), especially outside the body, a significant amount of force is required to achieve even a small change in volume, **making the lung uncompliant or stiff**.

> For example: let's imagine two glass plates with a drop of water between them, they slide over each other but are difficult to separate. Similarly, at the end of expiration, the alveoli collapse, and reopening them is challenging.
>
> -- A comparable example is inflating a balloon, which requires considerable effort initially but becomes easier once the balloon starts to expand.

*** Important note** inflating a **totally deflated lung is inefficient** and requires significant pressure, which is related to the alveolar walls and the pressure-volume relationship.

Too much pressure is needed to inflate the lung → too much work

Work =ATP= $\Delta P \times \Delta V$

Pop opening pressure: At a **critical point,** the lungs become compliant.

Phase 2 : So, Once the alveoli open, the lung becomes **compliant** where small **increases in pressure result in significant volume changes**.

*** Important note** : It's **most efficient** to inflate a **partially inflated lung** because compliance is highest in this state. If we took the tan of the angle which represents compliance, we will observe that it's highest in phase 2.

Normally, **breathing occurs from the functional residual capacity (FRC =2.2 liters) in which the lung is partially inflated.** Adding 500 mL increases the volume to 2.7 liters.

Phase 3:the lung approaches **maximum volume**, further inflation becomes increasingly difficult.

> This diminishing return can be compared to studying: moving from a score of 90 to 95 might require less effort, but going from 95 to 99 demands significantly more time and energy.

*** Important note :**inflating already **maximally inflated alveoli** becomes nearly **inefficient**. This represents the upper limit of lung compliance and marks the endpoint of the pressure-volume relationship.

This is why breathing typically starts from the functional residual capacity (FRC), where the lung is partially inflated and compliance is optimal. **Do We Experience All 3 Phases?**

*Under normal physiological conditions:

- **Phase 2** is the primary phase of breathing because the lungs operate within the range of FRC to total lung capacity, where compliance is optimal.
- **Phase 1** and **Phase 3** are not typically experienced unless there is a pathological condition (e.g collapsed lungs in Phase 1) or extreme mechanical ventilation (Phase3).

2. **Deflation curve** (in blue)

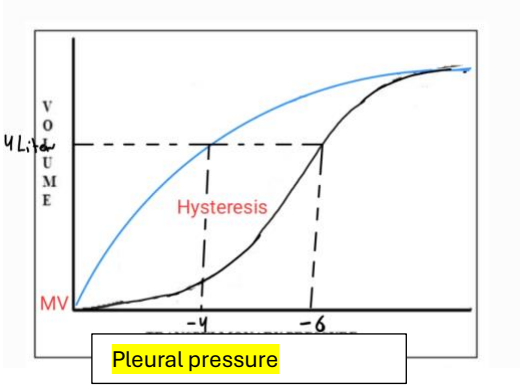


Figure 1

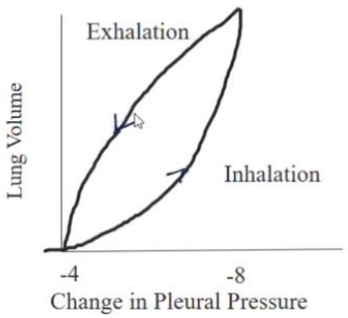
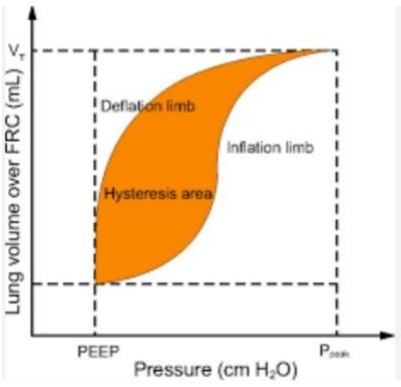


Figure 2: shows phase 2



Additional figure shows hysteresis area

*Notice that the x-axis indicates negative pressure values

(Figure 1) show when deflating the lung, the process involves gradual volume reduction it goes downward (e.g 100 mL →99 mL) until reaching zero. However, the deflation curve does not follow the same path as inflation. This phenomenon is called **hysteresis**, where the forward (inflation) is not the same as
backward (deflation) process. It's like saying simply that:

" it's difficult to open, easy to close"

During inflation, high pressure is needed to reopen collapsed alveoli, while deflation occurs more easily as alveoli close gradually.

For example, If a lung contains 4 liters of air, deflating it requires a pressure of "-4", while inflating it may require -6. This discrepancy seems illogical right?
as the tension in a system (such as holding an object at a fixed height) should not differ based on the direction of movement. In this case, something additional is at play, **but what is that?**

The primary cause of this phenomenon is **surface tension**

Surface tension

surface tension, refers to the cohesive forces at the air-liquid interface within the alveoli of the lungs. The surface tension in alveoli is primarily caused by intermolecular attractions, such as hydrogen bonds between H2O molecules. This tension tends to **collapse** the alveoli, making it harder for the lungs to expand during inhalation. To counteract this collapsing force, **an expanding force must be applied**, which requires pressure, but how much pressure we need?

This relationship is explained by the **Law of Laplace**, which tells that:

$$P = \frac{2T}{r}$$

- **P**:pressure required to inflate an alveolus.

  proportional to the surface tension (T)
  inversely proportional to the radius (R)

- **T**: Surface tension. The higher the surface tension, the greater the pressure required for inflation.
- **R**: Radius of the alveolus. Smaller alveoli (such as in baby) require significantly more pressure to overcome the collapsing force of surface tension -in simpler words, high pressure to keep alveoli open-

Thus, when the alveolar radius is small, such as at the end of expiration or in a collapsed state, a much higher pressure is needed to reopen the alveoli. This explains why inflating a collapsed lung requires greater effort compared to deflating it.

In infants, the small radius of their alveoli increases the pressure required to maintain it open, as a **smaller radius** demands higher pressure due to the **Law of Laplace**.

$P = \frac{2T}{r}$

This leads to increased work of breathing and higher ATP consumption. The problem becomes more significant if surface tension is high and the alveolar radius is small, needing excessive effort to keep the alveolus open.

If the alveolus is lined only with water from the inside, the surface tension would be high, requiring significant pressure (-23) to keep the alveolus open. If lined with interstitial fluid, the surface tension would be lower than with water (-13). However, surfactant plays a crucial role in reducing surface tension further, making it easier to maintain alveolar stability, requiring only -4 pressure

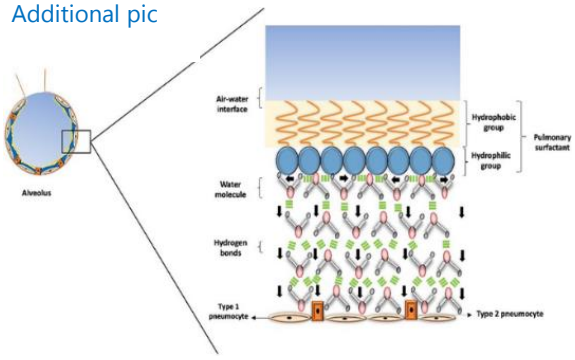
Lining Type	Surface Tension	Cause (This column is additional for ur better understanding)	Pressure Required
Water	High	Strong hydrogen bonding between water molecules at the air-water interface	**-23**
Interstitial Fluid	Lower than water	Presence of proteins and solutes reduces intermolecular attraction compared to water	**-13**
Surfactant	Minimal	Surfactant disrupts cohesive forces between water molecules, reducing surface tension	**-4**

Surfactant= surface-active-agent

Surfactant is a glycoprotein-lipoprotein molecule composed of:

- **2% carbohydrate**
- **90% lipid (mainly phospholipids)**
- **8% protein**
- **Calcium**

Additional pic

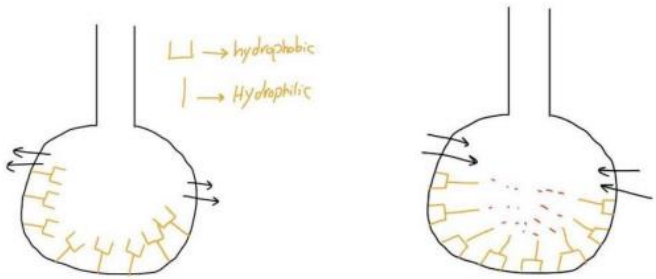


Phospholipids in surfactant have:

- **2 fatty acids** (nonpolar, hydrophobic)
- **1 glycerol head** (polar, hydrophilic)

This dual polarity enables surfactant molecules to orient themselves at the air-water interface within the alveoli. The **hydrophilic heads** face the water, while the **hydrophobic tails** face the air, reducing intermolecular attraction and, consequently, surface tension. This low

surface tension minimizes the collapsing force on the alveoli, significantly reducing the pressure required to inflate them.



✔On left: This orientation allows surfactant to reduce T effectively, as the hydrophilic heads stabilize the interaction with water, and the hydrophobic tails disrupt hydrogen bonding.

❌ On right: The hydrophilic heads must face the water lining

Function of Surfactant

1. **Reduces Surface Tension**: Both the <u>orientation and concentration</u> of surfactants play role in preventing alveolar collapse.
2. **Enhances Compliance**: Decreases the effort needed for lung inflation→ decreasing the work of breathing .

- **other** functions will be mentioned later

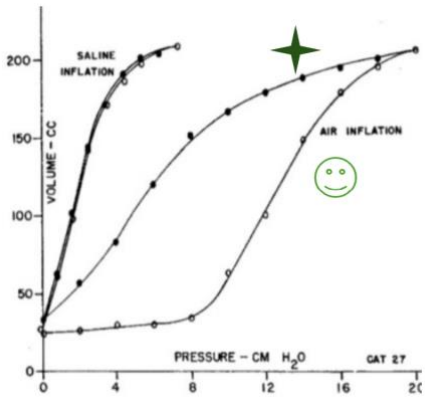
In the absence of surfactant or in cases of surfactant deficiency (i.e in preterm infants), the alveoli are at high risk of collapse, requiring external intervention, such as mechanical ventilation or surfactant replacement therapy. By reducing the surface tension, surfactant ensures that even a minimal pressure, such as (-4), is sufficient to maintain alveolar stability.

Surfactants are secreted by **type II alveolar cells**, which are cuboidal and not suitable for gas exchange. In contrast, **type I alveolar cells** are flat, thin, and long, facilitating efficient gas exchange.

Premature infants and babies born to diabetic mothers are at a high risk of **surfactant deficiency**, which leads to **respiratory distress syndrome "RDS"**. The production of surfactants by the fetus requires hormones such as **thyroxine**, **prolactin**, and **glucocorticoids**. For example, administering two doses of **dexamethasone**, which's a glucocorticoid 30 times more potent than cortisone, to a mother experiencing risk of preterm labor can significantly accelerate fetal lung maturity, each day delay can make a difference.

Without adequate surfactant, a premature baby's lungs face extreme difficulty maintaining proper function. Each exhalation would cause the alveoli to collapse, forcing the baby to work hard to reinflate them with every breath. This high effort leads to minimal volume and

significant energy expenditure, with up to 80% of the baby's energy consumed in supporting breathing, cuz baby needs now a pressure of -30 to inflate lung. If untreated, this can lead to death within hours. - with **surfactant it's a** thin loop , but without.. it's hard



represents person with surfactants, compliant lung, it starts from phase 2

Lungs without surfactant: The path is **longer and flatter**, requiring much more pressure in **Phase 1** and encountering more resistance in **Phase 3** due to high surface tension.

Why it starts at **Phase 1 not 2?** because it represents the initial stage of inflating a completely deflated lung, which is at or near **minimal volume (MV)**.

Remember what we said before few slides? our rule, "It's most efficient to inflate a partially inflated lung because compliance is highest"

Management for such cases includes **continuous positive airway pressure (CPAP)** or **PEEP** (Positive end-expiratory pressure) to maintain alveolar patency and support breathing. **IRDS** is strongly associated with minimal surfactant and premature lungs. To predict lung maturity and determine the risk of RDS, the **surfactant-to-albumin (S/A) ratio** in amniotic fluid is measured:

- **>55 mg**: Lungs are mature.
- **35–55 mg**: Intermediate maturity.
- **<35 mg**: Lungs are immature.

Delaying labor as much as possible and administering interventions to promote lung development can significantly improve outcomes in premature infants.

Filling lung with isotonic saline

Compliance of lungs is determined by **elastic forces**

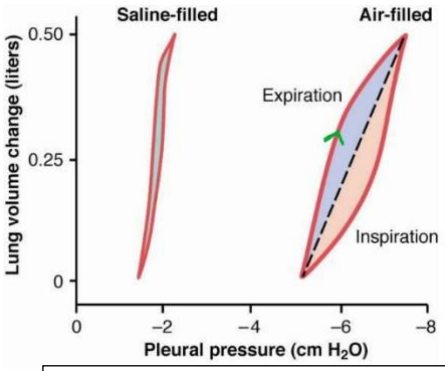
- Lung tissue.…One third

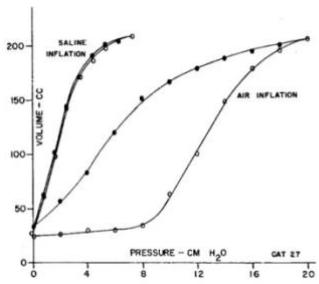
- Surface tension….two thirds

When **the lungs are filled with air,** two forces must be overcome for expansion: **surface tension** at the air-water interface within the alveoli and the **elastic fibers** of the lung tissue.

However, if the lungs are filled with a 0.9% isotonic **saline** solution instead of air, the surface tension is eliminated because the air-water interface no longer exists. This leaves **only the elastic fibers** of the lung tissue to resist expansion. Consequently, the pressure required to expand the lungs in this scenario is significantly **reduced** and is primarily attributed to the resistance of the elastic fibers in the lung tissue. This explains why **compliance is higher when the lung is filled with isotonic solution compared to air.**

check the figure , the focus is on the deflation curve because inflation is complicated by the process of **alveolar recruitment**—the sequential opening of alveoli— as it shows how much pressure is needed to open collapsed alveoli. In contrast, the deflation curve reflects how well the lungs keep those alveoli open (preventing collapse) as pressure decreases, which is key for maintaining proper lung function and avoiding atelectasis. By focusing on the deflation curve, the goal is to find the optimal pressure to keep the alveoli stable after recruitment.





Saline filled and air filled lung

But Why?

S**urface tension** happens at the boundary where water (or fluid) meets air. At this boundary:

- Water molecules at the surface experience unbalanced forces, pulling them inward and toward each other, creating a strong collapsing force.

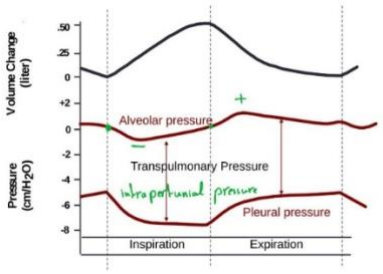
* If there's **no air**, and the lungs are filled entirely with fluid (like saline):

- The fluid molecules are surrounded on all sides by other fluid molecules.
- This eliminates the unbalanced forces at the surface, so **surface tension disappears**.

So, in general we have two components:

1. **Surface tension**: A major contributor when the lung is air-filled.
2. **Elastic fibers**: Present in both air-filled and liquid-filled conditions

Alveolar Pressure and Tidal Volume (الدكتور ما ركز عليه كثير دقيقة ٢٥:١٧)

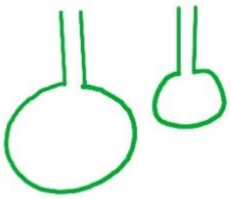


This section explores the changes in alveolar pressure in contrast to tidal volume during a typical respiratory cycle when 500 mL of air is inhaled.

Function of Surfactant

3. **Making surface tension volume-dependent**:
    - At smaller volumes, surface tension is reduced
4. **Promotes alveolar stability, meaning small alveoli coexist with large alveoli**

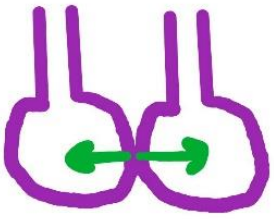
- When you have big and small alveoli, if we take the Law of Laplace:
  P=2T/r
  where **r** is small in the small alveoli, making it need great negative pressure, while in the bigger one, little negative pressure is needed. Intrapleural pressure (-4) will surround both, but for the small alveolus, -4 is not enough and it needs about -6, so it will collapse. This means that small alveoli can't coexist with large alveoli in the same area because they are both surrounded by the same magnitude of intrapleural pressure.



  However, this is not TRUE! In fact Small alveoli DO exist with large alveoli because:

  When you have a **small alveolus,** there will be more concentrated surface tension, which **increases surfactant production**. This leads to a decrease in surface tension, so a decrease in both **T** and **r** will keep **P** constant.

- When we talk about two alveoli, there is **alveolar traction** (alveolar interdependence) – the alveolar walls are attached to each other.
  Alveolar interdependence refers to the physical connection between alveoli, where the expansion or contraction of one alveolus influences neighboring ones, helping to maintain lung stability. Neighboring alveoli can affect each other, and if one collapses, others may collapse too, reducing lung function. Surfactant plays a key role by reducing surface tension, preventing alveolar collapse, and ensuring proper expansion. It allows alveoli to remain open, coordinating their inflation and preventing overexpansion or collapse, thus optimizing lung function



Pulmonary Capillary Fluid Dynamics

Let's discuss the four forces influencing fluid movement across the capillary membrane in the pulmonary capillary:

- **Capillary Hydrostatic Pressure (Pc):** 10 mmHg in the pulmonary capillary (compared to 30 mmHg in systemic circulation).
- **Capillary Oncotic Pressure (πc):** 28 mmHg.
- **Interstitial Hydrostatic Pressure (Pi):** -5 mmHg.
- **Interstitial Oncotic Pressure (πi):** 14 mmHg.

The net force totals +1 mmHg, favoring slight fluid movement outside the capillary. This small positive pressure is manageable by the lymphatic system, which returns the fluid to circulation. Even if the net pressure increases to +28 mmHg, the lymphatics can still handle it. This is known as the **lung edema safety factor**.

However, **in the absence of surfactant,** surface tension increases significantly, leading to a rise in the negative pleural pressure (e.g., from -4 to -14 mmHg). This exaggerated negative pressure around the capillaries pulls fluid out, causing **pulmonary edema**.

In conditions like **Infant Respiratory Distress Syndrome (IRDS)**, where surfactant is deficient, patients experience respiratory rates of 60 breaths per minute, acidosis, hypoxemia, and other severe symptoms.

Functions of surfactant (summary)

1) ↓ Surface tension forces which otherwise will pull inward and drive fluids into alveoli.

2) Makes surface tension volume dependent. Therefore surfactant prevents alveoli from being overstretched.

3) Promotes alveolar stability.

4) Prevent lung edema by decreasing T. Otherwise, high T will suck fluids from the wall of the capillaries.

5) Reduces work of breathing, reducing the muscular effort needed to expand the lungs.

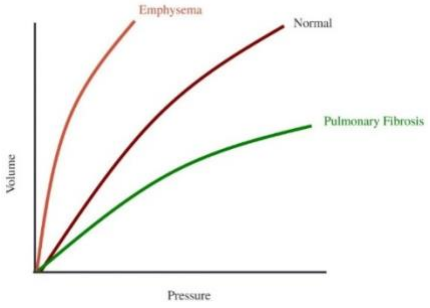
6) Lower elastic recoil at lower lung volume, preventing collapsing of alveoli at expiration. In RDS they collapse.

Alveolar stability: means small alveoli coexist with large alveoli because of:

1. Surfactant makes surface tension" volume dependent and thus at the same intra-alveolar pressure small alveoli and large one coexist. If we don't have surfactant, then the lungs contain hyperinflated alveoli and totally collapsed alveoli.

2. alveolar traction (alveolar interdependence) alveolar walls are attached to each other.

Compliance Curve



- **Emphysema:** Too much compliance, which is detrimental.
- **Pulmonary Fibrosis or IRDS:** Compliance decreases.
-

ARDS

There is also a condition called **Acute Respiratory Distress Syndrome (ARDS)**, which primarily affects adults and older children rather than infants.

Diagnosis of ARDS:

- The key diagnostic criterion for ARDS is when the **PaO2/FiO2 ratio is <200**.
    - FiO2 (Fraction of Inspired Oxygen)
    - PaO2 (Partial Pressure of Oxygen in Arterial Blood)
- Example:
    - In a healthy individual:

      FiO2 = 21%, PaO2 = 100 mmHg

      100/0.21 = 500

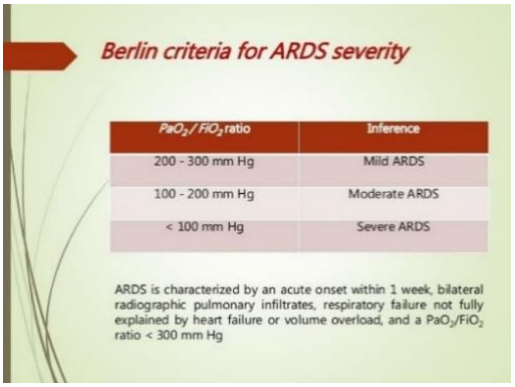
      while inhaling pure oxygen **(FiO2 = 100%), PaO2 = (500-600) mmHg very high**

      600/1 = 600
    - In ARDS patient,the ratio will NEVER exceed 200 (always < 200)

      Even When inhaling pure oxygen (FiO2 = 100%)

      For example: FiO2 = 100% ,PaO2 = 100 mmHg (100/1=100)

This low ratio is a hallmark of ARDS, which has a very high mortality rate. ARDS affects individuals with multiorgan failure, and this involvement often necessitates their admission to the ICU, making it a critical condition to manage. Check the figure for grading ARDS.

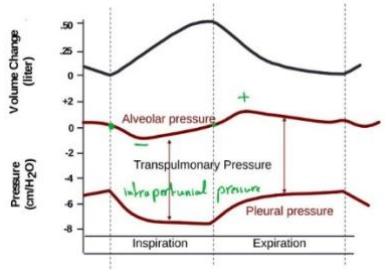


تم بحمد الله

Extra table (Helpful for exam purposes):

Intrapleural Pressure (Ppl) - This is the pressure within the pleural cavity, the space between the lung and the chest wall. It is always negative (subatmospheric) during normal breathing.

Intrapulmonary Pressure (Ppul) - This is the pressure within the lungs (or the alveoli). It is also known as alveolar pressure.



Respiratory Stage	Intrapleural Pressure (Ppl)	Intrapulmonary Pressure (Ppul)
During Inspiration	**More negative** (subatmospheric) as the chest expands	**Negative** (lower than atmospheric) to draw air in
At the End of Inspiration	**Most negative** (subatmospheric) due to full lung expansion	**Equal to atmospheric pressure** (no airflow)
During Expiration	**Less negative** (subatmospheric), or slightly positive during forced expiration	**Positive** (greater than atmospheric) to push air out
At the End of Expiration	**Less negative** (subatmospheric) or slightly positive during forced expiration	**Equal to atmospheric pressure** (no airflow)

Version 2:

- Page2: $\Delta V/\Delta P$ instead of $\Delta P/\Delta V$
- Page3: pleural pressure instead of transpulmonary pressure on the 1st graph x-axis
- Page10: 28 instead of -28
- Page12: adding an extra table