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INTEGRATED STUDY MASTER THESIS

**Any Possible Relation Between Primary Spontaneous Pneumothorax and
Pregnancy? Literature Review**

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Table of Contents

1	List of Abbreviations	4
2	Summary.....	4
3	Summary in Lithuanian	5
4	Key Words.....	7
5	Introduction	7
5.1	<i>Aim</i>	7
6	Methodology.....	8
7	Overview	8
7.1	<i>Anatomy of the Pulmonary System</i>	8
7.2	<i>Classification of Pneumothorax</i>	10
7.3	<i>Primary Spontaneous Pneumothorax: Pathophysiological background</i>	12
7.4	<i>Primary Spontaneous Pneumothorax: Clinical Features</i>	12
7.5	<i>Primary Spontaneous Pneumothorax: Evaluation</i>	13
7.6	<i>Primary Spontaneous Pneumothorax: Treatment and Prognosis</i>	17
7.7	<i>Primary Spontaneous Pneumothorax: Differential Diagnoses</i>	18
7.8	<i>Syndromes during Pregnancy</i>	19
7.9	<i>Pregnancy: Physiological Background and Changes in Ventilation</i>	21
8	Interrelation between Primary Spontaneous Pneumothorax and Pregnancy	24
8.1	<i>Hormonal Influence</i>	24
8.2	<i>Overview of Stress Factors</i>	25
8.3	<i>Clinical Signs</i>	26
8.4	<i>Diagnostics</i>	26
8.5	<i>Labor, Delivery and Primary Spontaneous Pneumothorax</i>	27
8.6	<i>Reported Cases and Epidemiological Insights</i>	27

8.7	<i>Fetal Outcome after Primary Spontaneous Pneumothorax</i>	30
8.8	<i>Overview of Case Reports</i>	31
9	<i>Management of Primary Spontaneous Pneumothorax in Pregnancy</i>	33
9.1	<i>Conservative vs. Surgical Treatment</i>	33
9.2	<i>Timing and Safety of Surgical Interventions</i>	34
9.3	<i>Obstetric Considerations and Delivery Planning</i>	35
10	<i>Discussion</i>	36
10.1	<i>Interpretation of Results</i>	36
10.2	<i>Clinical Implications</i>	38
10.3	<i>Gaps in Research and Future Recommendations</i>	39
11	<i>Conclusion</i>	41
11.1	<i>Key Findings</i>	41
11.2	<i>Concluding Thoughts</i>	41
12	<i>References</i>	43
12.1	<i>Citations</i>	43
12.2	<i>Figures and Tables</i>	46

1 List of Abbreviations

PSP	Primary Spontaneous Pneumothorax
SSP	Secondary Spontaneous Pneumothorax
COPD	Chronic Obstructive Pulmonary Disease
HIV	Human Immunodeficiency Virus
CP	Catamenial Pneumothorax
CT	Computer Tomography
VATS	Video-assisted Thoracic Surgery
FRC	Functional residual capacity
ERV	Expiratory reserve volume
RV	Residual Volume
VT	Tidal Volume
VE	Minute Ventilation
TLC	Total Lung Capacity
FEV1	Forced Expiratory Volume
FVC	Forced Vital Capacity
PCO2	Partial Pressure of Carbon Dioxide
PGF2 Alpha	Prostaglandin F2 Alpha
PGE1	Prostaglandin E1
PGE2	Prostaglandin E2
paCO2	Arterial Carbon Dioxide Partial Pressure
SVD	Spontaneous Vaginal Delivery
BHDS	Birt-Hogg-Dubé Syndrome
ICS	Intercostal Space
FLCN	Folliculin gene
LAM	Lymphangioleiomyomatosis
PTL	Placental Transmogrification

2 Summary

Primary spontaneous pneumothorax during pregnancy depicts a rare clinical entity among a generally broad spectrum of pneumological diseases. Occurring in absence of concomitant diseases primary spontaneous pneumothorax is most commonly provoked by apically presenting bullae and blebs. Consequent air accumulation within the pleural space leads to lung collapse and the development of primarily chest pain and dyspnea, the most common clinical signs presenting in pregnant patients.

These symptoms as well as diagnostic approaches are similar in non-pregnant patients, including imaging techniques such as chest radiography, ultrasound and CT scan. In contrast to non-pregnant patients, fetal exposure to radiation marks a crucial role during pregnancy and should always be minimized. Still, combined with sufficient abdominal shielding, it is mostly considered safe, as research indicates.

Treatment approaches of primary spontaneous pneumothorax during pregnancy depend on various factors including size of pneumothorax, severity of clinical signs and the general health condition of pregnant women. Reported cases about simultaneous presentation of pregnancy and primary spontaneous pneumothorax indicate the clinical relevance and offer various treatment approaches among different gestational ages individualized for each patient. Reaching from conservative approaches including supplemental oxygen and chest tube placement to more invasive measures up to Video-assisted Thoracic Surgery procedures. Depending on recurrent presentation as well as persistency of disease, surgical interventions are considered to be the safest during second trimester but should be evaluated among interdisciplinary doctors and specialists.

Overall, possible maternal and fetal compromise plays a crucial role in prompt recognition and management steps of primary spontaneous pneumothorax. The clinical picture therefore faces various obstetric, gynecological as well as thoracic surgical challenges. Concludingly, primary spontaneous pneumothorax marks a relevant clinical emergency requiring rapid recognition and orderly multidisciplinary handling.

Even though recent scientific data is still insufficient in order to either correlate or disconnect pregnancy with primary spontaneous pneumothorax exact pathophysiological development, physiological changes during pregnancy might possibly contribute to development of pulmonological conditions. Influence through hormones during pregnancy, as well as pressure and structural changes including tissue integrity are relevant adaptations being discussed and interrelated during the thesis. The master thesis outlines the relevance of the condition solely, describes physiological changes occurring in pregnant women and interconnects published cases of primary spontaneous pneumothorax in pregnancy with the ongoing question about a correlation among both: pregnancy and primary spontaneous pneumothorax. The literature search for the master thesis included medical databases such as PubMed, Science Direct combined with medical textbooks and case reports regarding primary spontaneous pneumothorax and pregnancy.

3 Summary in Lithuanian

Pirminis spontaninis pneumotoraksas nėštumo metu yra reta klinikinė situacija iš visų pulmonologinių ligų spektro. Pirminis spontaninis pneumotoraksas, atsiradęs nesant gretutinių ligų,

dažniausiai sukeliamas viršutinėje plaučių skiltyje susiformavusių bulų ir pūslelių. Pleuros ertmėje susikaupus orui plaučiai susitraukia ir sukelia krūtinės skausmą ir dusulį – dažniausius klinikinius simptomus nėščioms pacientėms. Šie simptomai bei diagnostikos metodai nėščiosioms yra panašūs į tuos, kurie taikomi įprastai spontaninio pneumotorakso atveju. Tai krūtinės ląstos rentgenografija, ultragarsinis tyrimas ir kompiuterinė tomografija. Skirtingai nei nėščiosioms pacientėms, vaisiaus apšvita nėštumo metu vaidina lemiamą vaidmenį ir visada turėtų būti kuo labiau sumažinta, todėl didelės apšvitos tyrimų, tokių kaip kompiuterinė tomografija, reikėtų vengti. Vis dėlto, kaip rodo tyrimai, kartu su pakankama pilvo apsauga, ji gali būti saugi.

Pirminio spontaninio pneumotorakso gydymo metodai nėštumo metu priklauso nuo įvairių veiksnių, įskaitant pneumotorakso dydį, klinikinių požymių sunkumą ir nėščiosios bendrą sveikatos būklę. Atveju, kai nėštumas sutampa su pirminiu spontaniniu pneumotoraksu, aprašymai rodo šio reiškinio klinikinę reikšmę ir siūlo įvairius gydymo metodus, pritaikytus kiekvienai pacientei atskirai, atsižvelgiant į skirtingą nėštumo laikotarpį. Jie varijuoja nuo konservatyvių metodų, įskaitant papildomą deguonį ir pleuros ertmės drenavimą, iki invazinių priemonių, tokių kaip torakoskopinė operacija. Priklausomai nuo pasikartojančių simptomų ir ligos užsitęsimo, chirurginės intervencijos laikomos saugiausiomis antrojo nėštumo trimestro metu, tačiau jas turėtų įvertinti tarpdisciplininė gydytojų ir specialistų komanda.

Apibendrinant galima teigti, kad yra svarbu greitai atpažinti pirminį spontanišką pneumotoraksą ir imtis atitinkamų gydymo veiksmų dėl galimo pavojaus motinos ir vaisiaus sveikatai. Todėl šis klinikinė situacija gali sukelti įvairių akušerinių, ginekologinių bei krūtinės chirurginių iššūkių. Pirminis spontaninis pneumotoraksas yra rimta klinikinė situacija, reikalaujanti greitos diagnostikos ir sistemingo daugiadisciplinio gydymo.

Nors naujausių mokslinių duomenų vis dar nepakanka, kad būtų galima nustatyti ryšį arba paneigti ryšį tarp nėštumo ir pirminio spontaniško pneumotorakso tikslios patofiziologinės raidos, fiziologiniai pokyčiai nėštumo metu galimai gali prisidėti prie pulmonologinių sutrikimų atsiradimo. Nėštumo metu hormonų daromas poveikis, taip pat slėgio ir struktūriniai pokyčiai, įskaitant audinių vientisumą, yra svarbūs prisitaikymo procesai, kurie aptariami ir nagrinėjami šiame magistro darbe. Magistro darbe apibūdinama šios klinikinės būklės reikšmė, aprašomi fiziologiniai pokyčiai, vykstantys nėščios moters organizme, ir paskelbtuose PSP nėštumo metu atvejuose ieškoma sąsajų tarp nėštumo ir pirminio spontaninio pneumotorakso. Literatūros paieška magistro darbui apėmė tokias medicinines duomenų bazes kaip PubMed, Science Direct, taip pat medicinines knygas ir atvejų aprašymus, susijusius su pirminiu spontanišku pneumotoraksu ir nėštumu.

4 Key Words

The following key words and their combinations were used: “Pneumothorax, Primary spontaneous pneumothorax, respiratory physiology in pregnancy, chest tube drainage, hormonal changes in pregnancy, video-assisted thoracoscopic surgery.”

5 Introduction

The clinical picture of primary spontaneous pneumothorax represents an infrequently occurring public health issue which mostly manifests in absence of an underlying pulmonological condition.

(1) Although the disease is rare in comparison to other thoracic and pulmonological pathologies it may lead to serious health issues in general addressing more men than women. (2)

Given that comparison of both genders it shows that women overall suffer less frequently from this health condition. (3) Pregnancy goes along with numerous physiological changes within the female body and might depict a contributing factor for ventilatory changes further possibly contributing to the occurrence of pulmonary diseases. (4) Even though cases of women during parturition and simultaneous presence of primary spontaneous pneumothorax are only scarcely published, the aim of this master thesis is to outline the relevance if the pulmonological condition is occurring during pregnancy.

This master thesis objectives will primarily focus on the incidence of the pulmonological condition during pregnancy, its pathophysiological background, further diagnostic approach and outcome for fetus and mother in case of pathology.

The written part will be completed by concluding and giving future implications about the pulmonary pathology and the physiological state of pregnancy.

The thesis will be mainly based on literature review of retrospective data analysis and published cases of medical experts in order to eventually draw a conclusion about a possible interconnection between pulmonary pathology and pregnancy.

5.1 Aim

The aim of the master thesis is to outline the relevance of primary spontaneous pneumothorax during pregnancy through providing an overview of the disease, its classification, clinical presentation as well as the inclusion of diagnostic and treatment approaches during pregnancy and eventually correlating pathology with the physiological state of pregnancy.

6 Methodology

The literature used as a base for this master thesis, was conducted including major electronic data bases such as PubMed and Science Direct. Digital platforms supported by publishers such as Thieme and Elsevier were used for literature research. Additionally, scientifically relevant articles, chapters of textbooks as well as case reports and original studies regarding primary spontaneous pneumothorax and pregnancy were included into literature research. The mentioned keywords supported broader research and enabled extensive coverage of the thesis topic.

Selected literature expresses relevant and contemporary information, including articles of past decades as well as foundational literature of earlier time, combining general principles with latest scientific findings. The time range of used articles reaches up to 2025 as well as publishing up to 2026. Studies used as base for the literature review included only human subjects and considered articles primarily in English language. Chosen articles and case reports dealt with epidemiology, clinical signs, diagnostic and therapeutic recommendations, maternal and fetal outcomes and prognostic values of primary spontaneous pneumothorax in pregnant women. Additionally, awareness of specifically physiological and anatomical changes during the pulmonary condition was created, using scientifically relevant literature. Articles consisting of original research, case series and comprehensive review were included. Research focusing solely on primary spontaneous pneumothorax as well as of primary spontaneous pneumothorax occurring during pregnancy was incorporated into the research.

Studies as well as articles addressing other pulmonary conditions, indicating irrelevant information were excluded for literature research and did not aid in comprehensive review of the topic

7 Overview

7.1 Anatomy of the Pulmonary System

The pulmonary system also known as respiratory system ensures the human body is capable of a functioning gas exchange including oxygen supply and carbon dioxide removal. (5)

Beside the major role of gas exchange the respiratory system takes over filtration, warming and moistening of the inhaled air. (6)

Generally, the pulmonary system is separated by two parts comprising various anatomical structures. The upper respiratory system includes nasal cavity, pharynx and larynx whereas the lower respiratory tract consists of trachea and lungs which further subdivide into bronchi, bronchioles, alveolar ducts and alveoli. (6)

Upper respiratory structures mainly exist to conduct and clean in- and exhaled air whilst lower pulmonary tract additionally functions as gas exchange instance, beginning with respiratory

bronchioles and eventually framed by the alveoli. (6) The pathology of primary spontaneous pneumothorax is a respiratory condition being limited to lower pulmonary structures, therefore this master thesis will primarily focus on lungs and pleural space.

The lungs as paired and spongy organs are located within human's thoracic cavity, cranially and dorsally limited by diaphragm. Sternum and ribcage protect the ventilated organ. They each contain apexes being located above the first rib and concave bases resting upon the diaphragm. The concave shape exists due to the dome shaped surface of the diaphragm itself, being located anatomically higher on the right than on the left side due to livers anatomical positioning.

Pulmonary surfaces can be described as mediastinal, diaphragmatic and costal whereas borders are termed anterior, posterior and inferior. (5)

Both lungs fulfil the same functions but are only similar in structure and architecture. The right lung is comprised of three lobes whereas the left lung consists of only two lobes, separated by fissures.

The pulmonary lobes are further divided into bronchopulmonary segments which are supplied by segmental bronchi. The right lung is formed by ten segments whereas the left lung is comprised of only eight or nine, depending on division of the individual lobes.

Another important structure is the pulmonary hilum allowing pulmonary vessels, nerves, lymphatic structures and bronchi to enter and exit the lungs. (5) The major protecting structure surrounding lung and further lining the thoracic cage is pleura. (7)

Pleura refers to as double-layered serous membrane composed of visceral and parietal coating. Visceral pleura covers all internal structures: lung, its tissue as well as relevant vessels. Parietal pleura in contrast covers chest wall, diaphragm and mediastinum directly from inside. Both membranes covering different pleural entities create a cavity which is called pleural space containing small amounts of pleural fluid ensuring lubrication and opposingly avoiding friction between pulmonary layers. (8) The described layers and pleural cavity are also depicted more accurately within Figure 1. Pulmonary cells additionally supporting facilitation of oxygen and carbon dioxide diffusion, secretion of pulmonary surfactant and progenitor cells as well as for elimination and phagocytosis are termed as Type 1 and 2 pneumocytes and alveolar macrophages. (5)

By facilitating these mechanisms, the mentioned cells ensure to support lubrication and the stability of the pulmonary interrelation.

Equilibrium in sufficient pressure and lubrication of the pulmonary layers ensure physiological gas exchange and maintain functioning of the respiratory circulation. Whenever this equilibrium is disrupted pathophysiological mechanisms may possibly occur and eventually result in the development of serious pulmonary health conditions, such as in primary spontaneous pneumothorax.

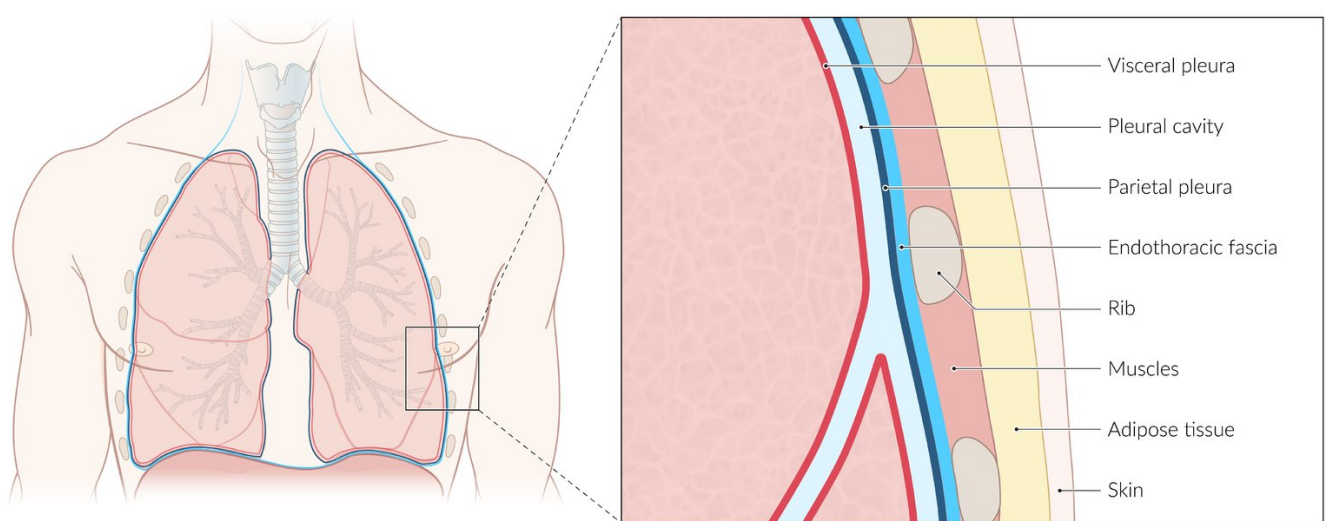


Fig. 1: Pneumothorax (1)

7.2 Classification of Pneumothorax

Pneumothorax represents a common disease, occurring worldwide with various underlying etiologies. Pneumothorax refers to as air accumulating within pleural space, the gap between visceral and parietal layer. During this pathophysiological condition the described air accumulation may lead to collapse of the lung and may elicit an even life-threatening scenario. (9) Its underlying developmental mechanisms may include infectious, inflammatory, malignant, hormonal and traumatic causes.

Localization, etiology and clinical presentation categorize pneumothorax into different categories which will be discussed broadly within the following chapter of the master thesis.

Based on anatomy and localization pneumothorax is primarily differentiated into open, closed and tension type. Closed type pneumothorax occurs through air accumulation within pleural space but in absence of an apparent external wound. This may impede prompt diagnosis and direct recognition of the condition. Open pneumothoraxes opposingly, occur through an open chest wound mechanism leading to rapid air accumulation within the pleural space. The larger the penetrating wound, most often symptoms are increasingly severe as well. (44) Another type of pneumothorax is tension pneumothorax. Tension pneumothorax marks a clinical emergency through its underlying pathophysiological mechanism. By creating a so-called one-way valve this subtype of pneumothorax allows air to enter pleural space but not exit. Therefore, increasing intrapleural pressure is reached, leading to mediastinal shifting and compression of intrathoracic structures. Hemodynamic instability may lead to an emergent clinical setting requiring prompt medical attention and treatment. (44)

Based on underlying etiologies another class of pneumothoraxes is distinguished. These types are spontaneous, traumatic and iatrogenic type of pneumothorax. Spontaneous pneumothoraxes are the most common pneumothoraxes occurring. They are further subdivided into primary spontaneous pneumothorax (PSP) and secondary spontaneous pneumothorax (SSP) as indicated in Figure 2 below. PSP appears without any underlying pulmonological precondition in otherwise healthy individuals. Risk factors such as smoking, male gender and often increased lung volumes increase the frequency of PSP to happen.

SSP opposingly occurs in patients with underlying conditions such as emphysema, pulmonary fibrosis or infectious diseases such as tuberculosis. The patients suffering from SSP are often more symptomatic than patients with PSP. (44)

Adversely to spontaneous pneumothoraxes another category of pneumothorax is termed as traumatic pneumothorax. As the name implies traumatic mechanisms are the base for this category of pneumothorax to occur. Trauma through dull or sharp injury may lead to damage of thoracic cage further enhancing air accumulation within pleural space. Despite of direct traumatic injury, rib fractures may enhance pneumothorax development.

The third category of etiologically classified pneumothoraxes is termed iatrogenic, occurring through medical induced drainages as well as surgical and anesthesiologic procedures.

Severity of pneumothoraxes may additionally be classified by its size. According to the British thoracic society a small pneumothorax is represented by an interpleural gap of less than 2 cm at the hilum. With measurements larger than 2cm a pneumothorax is already defined as large by definition.

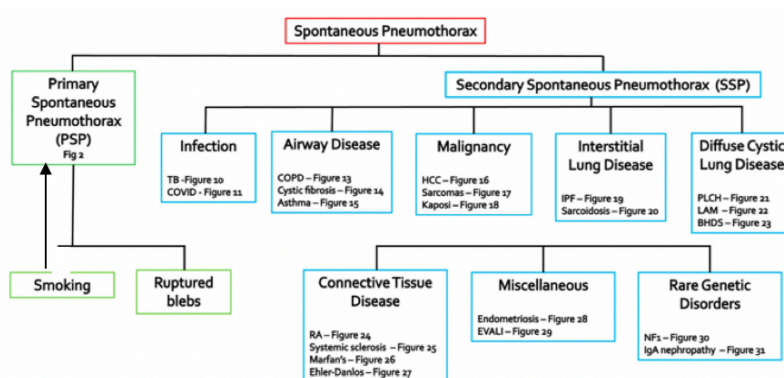


Figure 1. Etiological roadmap of spontaneous pneumothorax. Diagram illustrating the major categories and specific conditions leading to primary spontaneous pneumothorax (PSP) and secondary spontaneous pneumothorax (SSP). Key etiologies of SSP are grouped into infection, airway disease, malignancy, interstitial lung disease, diffuse cystic lung disease, connective tissue disease, miscellaneous causes, and rare genetic disorders, with corresponding illustrative figure numbers from the manuscript indicated for each condition.

Fig. 2: Etiological Roadmap of Spontaneous Pneumothorax (2)

7.3 Primary Spontaneous Pneumothorax: Pathophysiological background

Precise pathophysiological background of primary spontaneous pneumothorax still remains unknown and exact triggers for the pulmonary condition are not yet completely discovered. (2)

So far, scientists suspect the main cause of PSP to be subpleural emphysematous vesicles, known as blebs, as well as subpleural paraseptal emphysematous lesions, described as bullae, causing air leakage into the pleural space when rupturing. (10) Almost 90% of patients suffering from PSP are identified having emphysematous lesions, such as bullae or vesicles. (11)

Inflammatory diseases, genetic and familial history, anatomical differences of the bronchial tree, physiognomy related to increased negative intrapleural pressures as well as apical atypical ischemia, lower body weight and pathological connective tissue development might be provocative triggers for primary spontaneous pneumothorax to form. (2)

In general, young, thin males without prior medical diseases are most prone to develop PSP due to increased shear forces and greater negative pressure in apical lung parts. (12)

Primary risk factor for primary spontaneous pneumothorax to develop, is tobacco smoke due to increased inflammatory reactions occurring within smaller airway properties. (13) Beside tobacco smoke, cannabis might as well be increasingly associated with the occurrence of bullous diseases. (14) During the occurrence of primary spontaneous pneumothorax, pressure gradient changes appear to happen within the pulmonary circuit.

In physiological conditions pleural pressure, or “Ppl”, is approximately -3 to -5 cmH₂O at functional residual capacity. The negative pressure of pleural space compared to atmospheric pressure is necessary to ensure proper inflation of the lungs and prevention of the lungs to collapse. (15)

In case of primary spontaneous pneumothorax, the usual physiological negative pressure of pleural space tends to become more positive due to air accumulation further resulting in partial or complete lung collapse under their own elastic recoil. (15)

Regarding the area of the lung which is affected most during PSP, the apical pulmonary lobes are more prone to negative pressure and higher mechanical forces, leading to more frequent events of PSP in this location. (14)

7.4 Primary Spontaneous Pneumothorax: Clinical Features

As indicated above primary spontaneous pneumothorax by definition occurs in absence of an underlying pulmonary disease and without any reason. Therefore, patients suffering from PSP are often only mildly symptomatic, presenting with sudden ipsilateral chest pain and dyspnea. (9) The chest pain occurring during the condition is mostly described as sharp, pleuritic and often radiating

to the shoulder on the same side. Severity of clinical signs during the condition of primary spontaneous pneumothorax is mostly dependent on proportion and size of PSP. (14)

Beside the two main presenting symptoms - chest pain and dyspnea – tachypnea, discomfort during respiration, reduced tactile fremitus and auscultatory absent or diminished breathing sounds are sometimes present. (9) Another common finding might be reflex tachycardia often occurring in these patients as response to discomfort or respiratory compromise. (16)

Hemodynamic compromise is rather uncommon to be obtained during PSP diagnosis. Arterial blood gas analysis tends to be infrequently abnormal during PSP diagnostics: oxygen tension might decrease with enlarging pneumothorax but oxygen saturation mostly remains adequate. (14)

Summarizing, PSP is characterized by rather mild or even asymptomatic presentation. Whenever more severe clinical occurrence is obtained, tension pneumothorax as well as other pulmonary pathologies should be taken into consideration.

7.5 Primary Spontaneous Pneumothorax: Evaluation

For diagnostic approach of primary spontaneous pneumothorax various imaging techniques may be used in order to confirm the pulmonary pathology for further diagnostics. First of all, supine anterior-posterior chest radiography is often the primary diagnostic approach in emergent settings whereas computer tomography may provide even superior sensitivity in detecting abnormalities in lung parenchyma. (17) Nevertheless, various diagnostic modalities may be used which will be discussed broadly within this chapter.

Focusing on chest radiography first, it is important to mention the classic radiological findings in case of primary spontaneous pneumothorax: a pleural line with or without an air-fluid level may be significant, but sometimes not significant enough alone to diagnose a primary spontaneous pneumothorax. (16) Within Figure 3, a frontal anterior-posterior chest radiography indicates right sided pneumothorax, shown as an example. As already indicated in chapters above PSP tend to occur mostly within apical regions. (14)

Even though chest radiography in most clinical settings represents the primary diagnostic approach for PSP, small sized pneumothoraxes may be misinterpreted in chest X-rays. Therefore, additionally to radiography, various imaging modalities should be used for evaluation. (14)

Beside chest radiography, ultrasonography is used in clinical practice to confirm or diagnose pneumothoraxes. It is applied rapidly and prevents the patient being exposed to any kind of radiation. In trauma settings it shows accuracy and is of high diagnostic value. (14) One of the main ultrasound findings in case of primary spontaneous pneumothorax is when lung sliding appears to be absent. It usually represents the physiological sliding of visceral upon pleura and can be described as dynamic

sign indicating the horizontal movement across the pleural lining. (18) In case of PSP this phenomenon is diminished or even absent due to the collapse of the lung. The ultrasound machine, when used in M-Mode, creates a “barcode” or “stratosphere sign”, indicating that the pleural line does not show to-and front-motion anymore, supported by Figure 4 below.

M-Mode in physiological conditions detects motion of sliding over time and creates the so-called “seashore sign” in patients not having any pulmonary conditions. (18) Nevertheless, the absence of lung sliding is not only specific to PSP, as it may occur in other pulmonary condition such as ARDS, consolidations or pulmonary fibrosis. Consequently, the combination of various imaging modalities improves the accuracy of diagnosis and should be taken into consideration. (18)

Other ultrasound findings in case of PSP are absent comet-tail artifacts, also termed “B-lines”, which are usually produced by visceral pleura. Figure 5 illustrates these mentioned B-Lines further. They are not present during the pathology due to the accumulation of air, hindering the propagation of sound waves for the ultrasound machine to detect. Therefore, the presence of B-lines would rule out the pulmonary condition to be present due to the high negative predictive value. The presence of so-called “A-lines” in contrast, facilitate the diagnosis of PSP. They indicate the horizontal reverberation originating from the pleura. The distance between the lines equals the one between skin and parietal pleural layer. In physiological conditions B-lines mostly override A-lines, whereas in conditions such as PSP A-lines are visible on ultrasound and B-lines cannot be found. Together, A-lines and absent lung sliding, may indicate the presence of pneumothorax by above 90%. (18)

Another ultrasound sign of high diagnostic value is the “lung-point sign”. It resembles the contact point of occurring pneumothoraxes with the chest wall during inspiration. In M-mode of the ultrasound machine constant switching between “seashore-“and “barcode sign” is of high diagnostic importance for the diagnosis of PSP. It is 100% specific for pneumothorax’ occurrence and additionally may be used for the indication of PSP’s border. The location of “lung-point sign” may be a predictor for the size of pneumothorax: lateral and posterior locations indicate mostly increasing size of PSP. In contrast, medial and anterior location may resemble pneumothoraxes of smaller size. Still, “lung-point sign” is only relatively sensitive and does not even appear in M-mode in case of complete lung collapse. (18)

Therefore, CT findings should be consulted additionally for estimation of pneumothoraxes size as these diagnostic approaches may facilitate further treatment possibilities. (18)

Additionally, to radiography and ultrasound techniques, as above mentioned, CT scans may provide even more detailed and definite diagnosis of PSP. It may even detect underlying causes for PSP to occur. By using photon counting detector techniques the radiological technique might provide various beneficial aspects such as reduction in noise and reducing the radiation dose for patients, compared to regular CT scan. Further it provides improved visualization of subtle changes in lung parenchyma

as well as smaller airway and vascular structures which might be key in diagnosing underlying causes of pneumothoraxes. (17)

These might be bullae; pleural adhesions present during the condition or accumulating fluid within the pleural space. In case of primary spontaneous pneumothorax CT is able to detect pathological lung changes in case of 90%. (16) CT examination during suspicion of PSP should be performed on expanded lung in order to reveal the pathology.

Summarizing, various imaging modalities are used in order to confirm the pulmonary pathology. Depending on clinical situation, timing and individual patient information a broad spectrum of diagnostic measures is available. Combined, they facilitate the definite diagnosis of PSP.



Fig. 3: Frontal Anterior-posterior Chest Radiograph of Right-sided Pneumothorax (3)

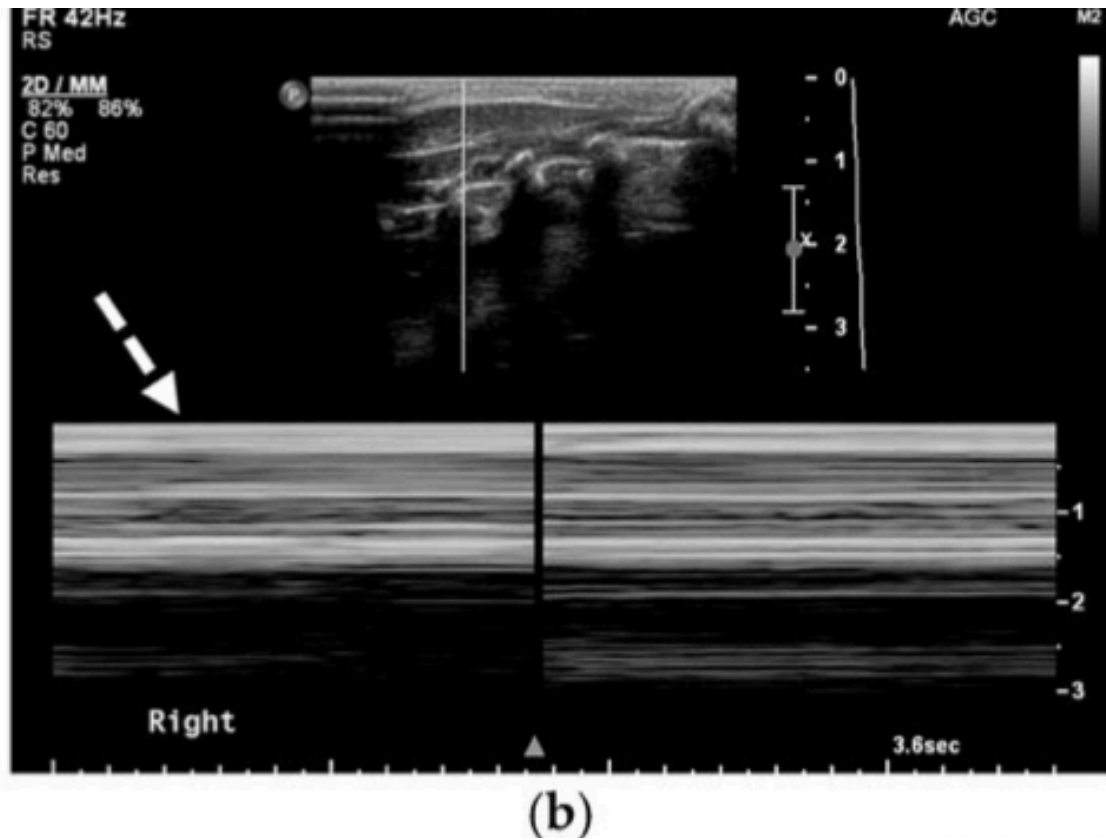


Fig. 4: Barcode Sign typical of Pneumothorax (4)

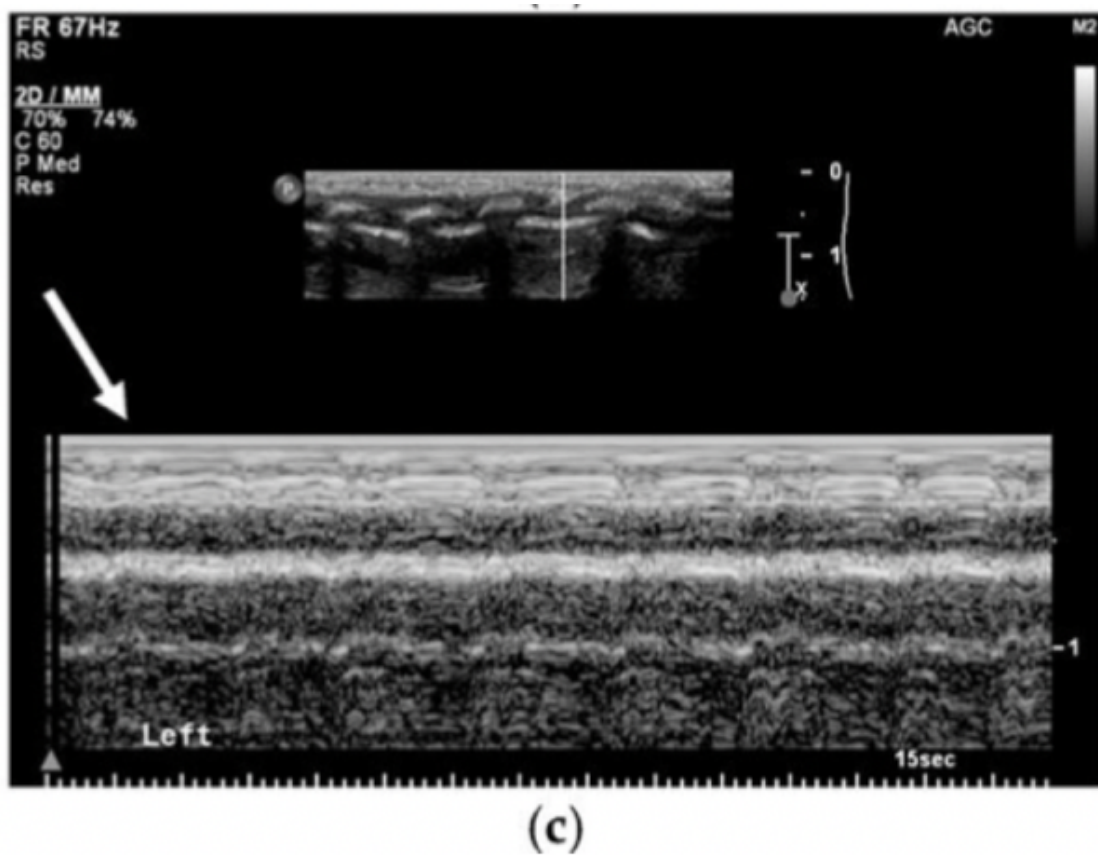


Fig. 5: Expected B-Lines and Presence of Seashore Sign (5)

7.6 Primary Spontaneous Pneumothorax: Treatment and Prognosis

Even though pneumothorax is a disease occurring worldwide, initial treatment approaches are still debated. (19) Primary spontaneous pneumothorax proposes three different disease characteristics representing the base for the main treatment approaches: first, respiratory malfunction, potentially having lethal risk as outcome, secondly ongoing air leakage and thirdly the possible recurrence risk. (19) Therefore, the aim of PSP's treatment should mainly be based on removal of air from pleural space, re-expansion of the affected lung as well as the reduction of recurrence. (20) Additionally, to these characteristics, management should be aligned to the patient's individual clinical situation.

Treatment of primary spontaneous pneumothorax ranges from conservative to more interventional techniques, depending on patient's symptom severity and the size of pneumothorax. Management spectrum includes measures from observation, needle aspiration techniques, supplemental oxygen therapy and chest tube drainage to more invasive pleurodesis, VATS and open surgical procedures. (14) Hemodynamic stability, PSP's size and air leakage as well as severity of clinical signs influence the management approach for affected patients.

Stability in hemodynamics and correction of the patient's vital signs points the primary landmark for physicians to interfere. Stable and asymptomatic patients are sufficiently treated with conservative measures such as supplemental oxygen therapy observation and analgesic support. Mostly, these patients suffer from only small pneumothoraxes by classification ($< 2\text{-}3\text{cm}$ and $< 15\%$ of hemithorax) and do not require hospital stays for surveillance. They perceive observation for about six hours and chest radiographic control in order to reevaluate the extent of PSP. (14)

Opposingly, unstable and symptomatic patients suffering from larger PSP ($> 2\text{-}3\text{cm}$ and $> 15\%$ of hemithorax) require immediate chest tube drainage or aspiration techniques. Aspiration is performed by using intravenous catheters and chest tubes regularly within the second ICS midclavicularly. These catheters promote lung re-expansion and can be removed after successful placement and lung re-filling. Control chest radiographs as well as pulmonary check-up after 4 weeks is sufficient enough for these performed conservative measures. (14)

Mentioned pleural catheters may also be permanent, which is termed thoracostomy. During this treatment approach chest tubes connected to valves are placed for several days in order to facilitate the evacuation of air leakages from the pleural space. (14)

Another option for continuous removal of air from pleural space is pleurodesis, either chemical or mechanical. Pleurodesis functions by initiating inflammation and fibrosis further inducing adhesion among visceral and parietal pleura. Chemical pleurodesis works by inducing agents such as talc to pleural space, further enhancing inflammatory reactions. Opposingly, mechanical pleurodesis describes a procedure, during which pleura is abraded mostly during surgeries. Mostly, pleurodesis is effective during recurrent pneumothoraxes. It is applied as of rapid improval of dyspnea and

reduction of further surgeries, but masks also several complications: fever, inflammatory reactions and infection might occur after. (41)

If these management approaches are not efficient enough, surgical procedures might be an alternative. Wider surgical approaches are termed video-assisted thoracoscopic surgery (VATS) and open thoracotomy. These interventions are used in case of recurrence or persistence of the pathology. Compared to conservative measures, surgery is often connected to longer hospital stays and patient discomfort due to its invasiveness. (14) Nevertheless, nowadays, VATS is performed frequently compared to open thoracotomy. Identification of blebs and bullae in CT imaging scans is often indicator for VATS initiation. Generally, less frequent reoccurrence, minimal invasiveness, high safety measures and effectiveness promote VATS to be the primary surgical option. (14) Compared to open thoracotomy it is characterized by less surgical trauma, bleeding risk and shorter post-surgical recovery. Mentioned open thoracotomy has been the long standing primary surgical technique due to allowance of extensive mechanical pleurodesis and bullae resection measures. Except of its higher invasiveness by resection of lung segments it has been sufficient enough to reduce recurrence rates of PSP. (14)

Generally, it should be reserved for more complex cases or patients in which VATS procedures have been insufficient.

Summarizing a great variety of treatment options for PSP is possible, but precise management approach should be individualized according to patients' clinical picture and symptom severity.

7.7 Primary Spontaneous Pneumothorax: Differential Diagnoses

As explained above broadly, the pathology of primary spontaneous pneumothorax is regularly occurring without an underlying pulmonary cause and in absence of any thoracic disease.

Still, concurrent clinical signs such as dyspnea and ipsilateral chest pain during the condition may resemble various other pulmonary, gastrointestinal, musculoskeletal, cardiovascular or psychiatric diseases. These differential diseases often impede immediate diagnostic recognition of primary spontaneous pneumothorax.

Concrete diagnosis and further management are facilitated by anamnesis and investigations but non-specific signs and symptoms initially may be shared with other systemic diseases which will be outlined in the following. (20)

Differential pulmonary conditions may mimic PSP by the occurrence of chest pain with acute and ipsilateral onset. These conditions might be either of bacterial or viral origin, such as pneumonia but may also be caused by chronic conditions such as asthma, bronchitis or tuberculosis.

Another pulmonary event resembling PSP by pleuritic chest pain and dyspnea might be pulmonary embolism. Less common but not less clinically significant differential pulmonary diseases of PSP might be lung abscesses.

The main initial clinical signs of PSP might not only resemble pulmonary conditions but may also be present in highly emergent cardiovascular conditions such as acute coronary syndrome or aortic dissection. Chest pain might be severe and possibly radiate to different body parts depending on the clinical situation. (20)

Inflammatory conditions such as pericarditis or myocarditis often also present with pleuritic chest pain similarly to primary spontaneous pneumothorax. In these cases, further diagnostic investigations are necessary for differentiation of the diseases.

Other differential diagnoses might be presented by gastrointestinal and musculoskeletal diseases especially when involving pleura or mediastinum. Conditions such as Boerhaave syndrome and Mallory Weiss syndrome may present with acute chest pain which might be misinterpreted as PSP on primary assessment. Esophageal spasm and gastroesophageal reflux disease might contribute to the initial suspicion of primary spontaneous pneumothorax by sometimes causing pleuritic chest pain. Additionally, musculoskeletal diseases such as costochondritis and diaphragmatic injuries may produce dyspnea and chest pain which should be differentiated from PSP by further diagnostic valuable strategies.

Further, psychiatric conditions such as anxiety and panic attacks may induce chest pain and the impression of dyspnea. The absence of other pulmonary clinical signs during these psychiatric condition aid in further diagnosing the diseases and differentiating it from PSP. (20)

Beside conditions emerging from different clinical origin, PSP additionally has to be differentiated from secondary and traumatic pneumothoraxes. Other than primary spontaneous pneumothorax, SSP occurs in presence of an underlying pulmonary disease. Traumatic pneumothorax appears due to prior or simultaneous injury to thorax and pleural layers. Both, traumatic and SSP should be clearly differentiated from PSP through investigations and examination. (20)

Being aware of differential diagnoses of primary spontaneous pneumothorax aids in understanding the disease deeply and in providing clear diagnosis which further improves clinical outcome.

7.8 Syndromes during Pregnancy

Pregnant women may experience signs and symptoms similar to pneumothorax in even otherwise physiological conditions. When associated to spontaneous pneumothorax these might also occur in several syndromes which will be described shortly within the following chapter.

First, Birt-Hogg-Dubé syndrome, a rare autosomal-dominant condition, in which FLCN gene mutations lead to predisposing lifelong presence of lung cysts and an increased risk for pneumothoraxes to occur. (27) Approximately 44-70% of diseases patients suffer from at least one collapsed lung, also occurring during reproductive years. (28) As predictors connecting pregnancy to BHDS are lacking, a study of Ludwig-Maximilian-Universität outpatient clinic has performed research on this topic. During 2005-2022 the study has involved 108 patients and their relatives. Summarizing, 46 pregnant patients suffering from Birt-Hogg-Dubé syndrome have experienced eight pneumothoraxes. The study compared the rate of pulmonary collapse in pregnant and non-pregnant as well as patients without prior collapse. Results showed there is no correlation between increased risk between pathology and pregnancy. Despite these findings, BHDS is still related to higher occurrence of PSP. (29) Therefore, concrete symptoms should be taken seriously and pregnant patients should be well informed about presenting dyspnea and chest pain. Awareness about the disease during pregnancy should be optimized for the best possible maternal and fetal clinical prognosis.

Secondly, lymphangioleiomyomatosis (LAM), which is a seldom cystic lung disease predisposing primarily women for pulmonological conditions to occur. Increased cyst formation and lung destruction is induced by pathological proliferation of smooth-muscle tissue. Hormones, such as estrogen, play a crucial role in exacerbation of the disease. This hormonal influence is particularly relevant during pregnancy. (42) Complications during pregnancy are pneumothorax, chylothorax or bleeding as consequence. Up to 70% of female patients suffer from pneumothorax during pregnancy. In some cases, LAM presents during pregnancy for the first time in their life. Recurrence of PSP is increased for these patients, by up to 1000 time higher than general, healthy female population. Therefore, preventive measures such as pleurodesis are often applied in LAM patients. Treatment of pneumothoraxes during LAM follows management schedule of secondary pneumothorax. Still, multidisciplinary recommendations are favored as of pregnancy and consequent maternal and fetal risks.

As of possible disease progression due to hormonal influence and exaggeration during pregnancy females suffering from LAM are often encouraged to avoid pregnancy. (42)

Lastly, another very rare clinical entity is represented by placental transmogrification of the lung (PTL). The disease is defined by formation of cysts and bullous lesions featuring placental villi even though they have no proper relation to placenta. Underlying pathophysiological mechanisms remain unsolved, but clinically several symptoms appear usually. These present as dyspnea, cough, increasing chest pain and sometimes even pneumothoraxes manifestation. (43)

Diagnoses of PTL are mainly based on histopathological explorations. For pneumothorax PTL remains a very rare differential diagnosis, but still should be taken into consideration as of similar

symptoms. Still, research indicates, there is no scientifically proven relation among pregnancy and PTL. (43)

Summarizing, these rare diseases might occur in correlation with primary spontaneous pneumothoraxes and should therefore be clinically remembered well for diagnostics, recognition and further management approaches. Overall, accurate exclusion of secondary causes and underlying diseases are essential in evaluation of primary spontaneous pneumothorax.

7.9 Pregnancy: Physiological Background and Changes in Ventilation

Physiological pregnancies are heavily influenced by hormonal, anatomical and physiological changes throughout all three trimesters. These changes alter pulmonary and ventilatory functions as well as gas exchange within the female body. Possible changes in respiration might also affect pulmonary diseases and the occurrence of pathological signs.

Mechanical changes are mostly characterized by the physiological expansion of the uterus and the diaphragmatic elevation whereas hormonal influence happens mostly through the changes in progesterone, estrogen, prostaglandins and relaxin. Hormonal changes and their exact influence will be discussed later in this thesis. (4)

For anatomical changes diaphragm elevation of up to 5cm appears to happen together with an increased subcostal angle. It usually increases from about 68.5° in the first trimesters to 103.5° at the last, indicated within Figure 6 below. (4) Additionally, the anteroposterior and transverse diameter of the thoracic cage largens by approximately 2cm. (21) These alterations occur early during gestation and tend to increase even more with later trimesters. By the occurring anatomical alterations, lung volumes change by decreasing functional residual capacity (FRC) and an increasing inspiratory capacity. (22)

FRC decreases up to 20-30% mainly due to the upward displacement of the diaphragm as a consequence of uterine enlargement. This mechanism reduces the resting lung volume at the end of normal expiration. Decrease in expiratory reserve volume (ERV) by 15-20% and residual volume (RV) by approximately 20-25% occur as the lungs are closer towards their minimal volume due to mentioned diaphragmatic elevation.

Tidal volume (VT) increases in pregnant women by about 30-50% due to the stimulating effect of progesterone upon the primary breathing center which further increases its CO₂ sensitivity.

Minute ventilation (VE) is defined as tidal volume multiplied by respiratory rate. As tidal volume is marked by an increase and respiratory rate does not change significantly, minute ventilation increases up to 30-50% in pregnant women. (22)

Inspiratory capacity tends to increase due to lower resting volume which leaves more space for deeper and larger inspiration. These changes are well illustrated within Figure 7 below. Additionally,

progesterone's effect is able to increase respiratory drive further and therefore increasing tidal volume in pregnant females.

Total lung capacity (TLC) remains unchanged during pregnancy as decreasing FRC is outbalanced by increased inspiratory capacity (5-10%) additionally to the ability of the rib cage to widen due to increasing subcostal angle. Forced expiratory volume in first second (FEV1) and forced vital capacity (FVC) often remain unchanged as well in pregnant women. This occurs as both parameters describe airflow and lung emptying which are not directly affected. Pregnancy has no effect on airway narrowing. Maximum volume being exhaled during each respiratory cycle remains within normal ranges. (22)

Consequently, lung compliance does not appear to be different in physiological pregnancies.

Beside the changes in respiratory parameters during pregnancy, basal metabolic rate, oxygen consumption as well as carbon dioxide production tend to increase throughout the trimesters in order to be sufficient enough to supply both: mother and fetus. Consumption of oxygen increases by about 15-20% whereas carbon dioxide production by approximately 30%. These changes occur mainly due to improved cholesterol and fat metabolism. (22)

Physiological pregnancies are characterized by respiratory alkalosis with an increased arterial oxygen and decreased arterial carbon dioxide. This reduction in arterial carbon dioxide promotes CO₂ transfer transplacentally by creating a diffusion gradient. Increased renal bicarbonate excretion compensates the physiologically created alkalosis for the mother. A right shift of the hemoglobin-dissociation curve created by the mentioned changes improves fetal O₂ delivery and enhances transplacental gas transfer. (22)

Occurring physiological changes have protective value but may also increase the risk for sleep-disordered breathing, reduce airway patency and may increase susceptibility to infections. Increased O₂ demand and anatomical changes of the chest wall may predispose to pulmonary diseases. (23)

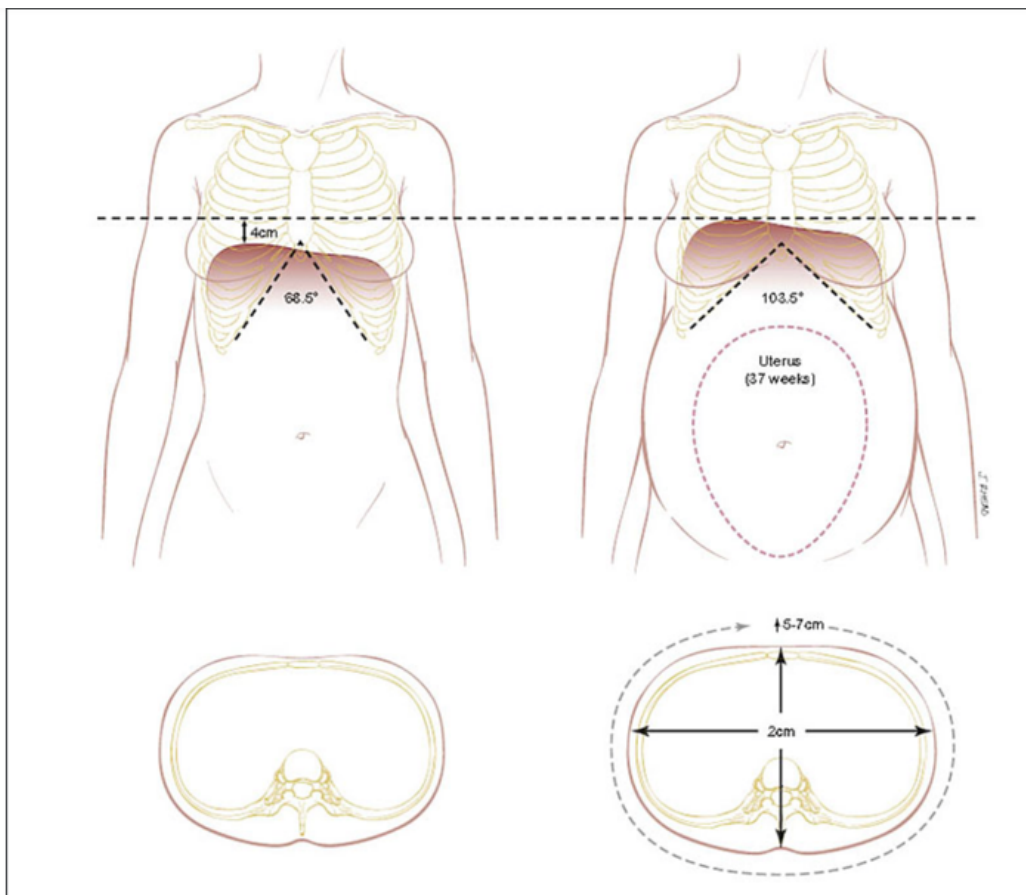


Fig. 6: Lung Volume Changes in Pregnancy (6)

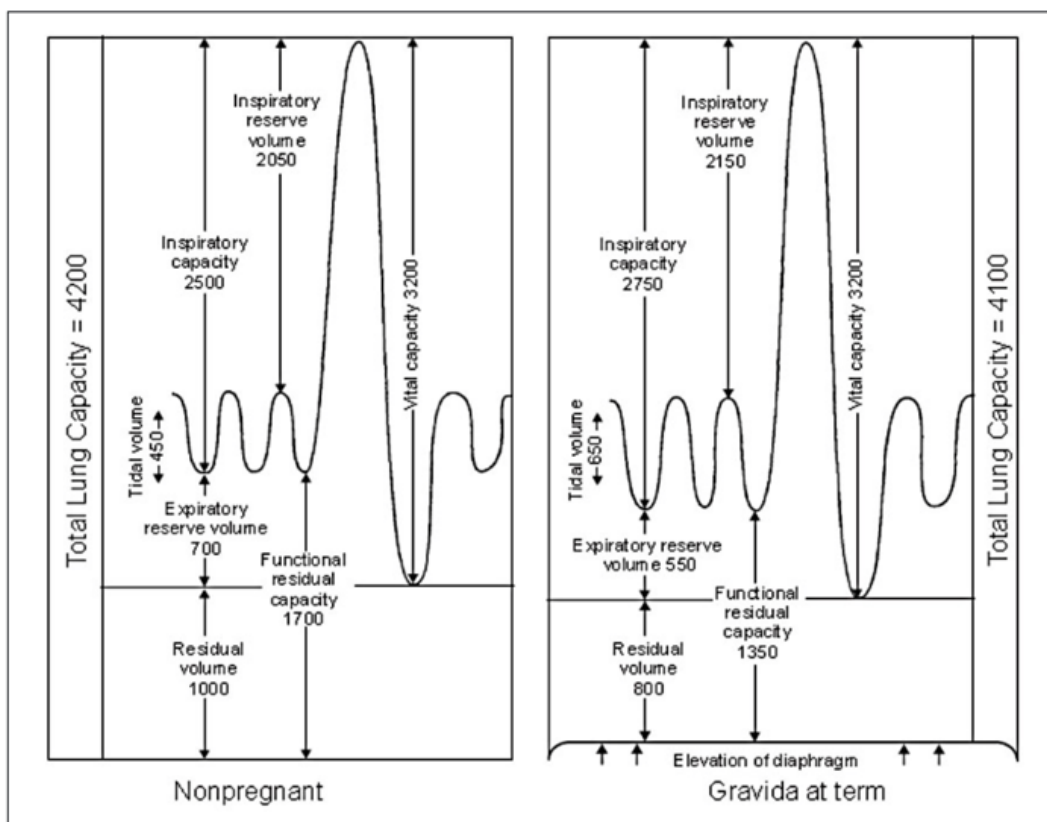


Fig. 7: Chest Wall Changes that occur during Pregnancy (7)

8 Interrelation between Primary Spontaneous Pneumothorax and Pregnancy

8.1 Hormonal Influence

Beside mechanical and anatomical factors, hormones play a crucial role regarding changes in ventilation throughout pregnancy, as described above already. The main hormones having an influence on respiratory system in pregnant women are progesterone, estrogen, prostaglandins as well as relaxin.

Progesterone's concentration during pregnancy increases slowly throughout the trimesters from 25 ngmL⁻¹ at 6 weeks to 150 ngmL⁻¹ at 37 weeks' gestation. (4)

Regarding upper respiratory tract, progesterone has influence on increased phagocytic activity, leakage of plasma into the stroma as well as on hyperactivity of the glands. These induced changes induce the mucosa to appear friable and thickened within the upper respiratory tract. (23)

By mediating hyperemia and mentioned edema of mucosal tissue progesterone may also lead to nasal congestion.

Progesterone appears to be a respiratory stimulant and functions as dilator of the bronchioles by relaxing the smooth muscles in the respiratory tract. Through these mechanisms it decreases the airway resistance which further enhances airflow and deeper breathing work.

Progesterone works as stimulator in respiration by lowering the threshold and increasing the sensitivity of the central chemoreflex response to carbon dioxide. (40) It not only affects central chemoreflex centers but also peripheral centers, such as carotid bodies, leading to increased sensitivity to hypoxic states.

As explained in another chapter, this hormonal influence may result in physiological hyperventilation and the sensation of dyspnea during pregnancy by increasing breathing depth but not rate. (24)

The additional increase in alveolar ventilation may cause alkalosis in pregnant women with PCO₂ being close to 30. Kidney's bicarbonate excretion is able to compensate partially by holding bicarbonate levels almost steady at 18-21 mEq/L. Therefore, respiratory alkalosis appears to be compensated during pregnancy. Nevertheless, alveolar or minute ventilation as well as respiratory alkalosis often continue to become worse during delivery. (22)

Estrogen as one of the other main hormonal mediators rises in concentration with ongoing pregnancy. Its concentration either increases prior or simultaneously with progesterone's concentration, first being secreted by corpus luteum and later by placenta. Estrogen is thought to increase the sensitivity for progesterone receptors within the primary neuronal respiratory related centers, namely hypothalamus and medulla oblongata, which enhances the amplification of progesterone's ventilatory effects. (4) It may lead to vascular mucosal repletion as well as it promotes capillary permeability within the upper respiratory tract further contributing to the occurrence of nasal congestion and alterations in airway resistance. (24)

Prostaglandins have a stimulating effect on uterine and bronchiolar smooth muscles while being present throughout all three trimesters of pregnancy. They function as promoters of bronchiolar smooth muscles by either constricting or dilating. PGF2 alpha acting as constrictor and PGE1 as well as PGE2 functioning as bronchodilators. They contribute to ventilatory changes through increasing tidal volume and decreasing paCO_2 . By influencing these ventilatory changes they additionally contribute to fetal development. (4)

Relaxin, initially secreted by corpus luteum and in later trimesters primarily by placenta, has important effects on preparing the female body for anatomical changes occurring throughout pregnancy. Its serum levels are the highest during mid-gestation. Relaxin has an expanding effect onto the maternal ribcage and subcostal angle by rising thoracic ligamentous laxity. The loosening effect onto the costal ligaments improves thoracic cages ability to widen and the diaphragm to stretch alongside rib margins. (24) Its hormonal influence balances out the continuous upward uterine pressure to the thoracic and diaphragmatic structures and maintaining lung volumes.

Despite respiratory adaptations relaxin has softening effects on female sacropelvic regions, such as pubic symphysis and joints being particularly important for giving birth. (24)

Concluding, these mentioned hormonal changes during physiological pregnancies lead to profound adjustments of pulmonary, anatomical and cardiovascular systems of pregnant women, preparing the female body for change and adaptation but may also predispose for pathological change when overriding physiological borders.

8.2 Overview of Stress Factors

During pregnancy a wide variety of factors may contribute to the lung's susceptibility for possible blebs rupture or pleural diseases to occur, even in otherwise physiological conditions.

In the following chapter aforementioned changes within the female body will be concluded. Summarizing mechanical factors, the increase in uterine size consequently induces a diaphragmatic elevation by approximately 4 cm, the minimal shifting of thoracic geometry and variation in thoracic pressures. The mechanical changes occurring physiologically during healthy pregnancies are important for fetus and maternal body in order to be in preparation for birth but can as well alter regional lung stress adaptation. (24)

This adaptation may occur within the lung apices as of higher negative pressure in pulmonary apex region, rising baseline alveolar distension and increased mechanical stress further promoting blebs creation. (25)

Regarding physiological respiratory changes, pregnancy is often marked by a state of ongoing hyperventilation due to increased tidal volume, induced by progesterone. (24)

Even though lung compliance in pregnant women is not affected by the induced changes, recurrent distension on alveolar basis may promote chest wall stress with already existing blebs.

Another factor for stress induction is marked by decreasing functional residual capacity during pregnancy and the reduction of pulmonary reserve. (24)

Concluding, pregnant women have altered pleural mechanics, decreased pulmonary reserves, changes in connective tissue, altered alveolar stretch and variations in pressure spikes. (4)

These changes throughout all trimesters might create an environment which possibly predisposes for pulmonary disease to occur without any preconditions.

The phenomenon of PSP still remains seldom in pregnant women but the overall awareness of concomitant stress factors is important in regard of diagnosis, evaluation of the disease and treatment either before, during or after delivery. (26)

8.3 Clinical Signs

Clinical signs occurring during primary spontaneous pneumothorax were already described in detail in chapter 3.4. The clinical picture of primary spontaneous pneumothorax in pregnant women presents with similar to almost equal symptoms as in healthy non-pregnant patients. These present as the abrupt onset of pleuritic chest pain which mostly appears to be ipsilateral as well as acute dyspnea and tachypnea. (26) Difficulty in recognition and diagnosis of these main symptoms may resemble physiological pregnancy signs occurring in approximately 75% of women which often interferes and impedes with prompt diagnosis of PSP in pregnancy. (26)

More difficult cases may show signs such as hyperresonance during percussion, decreased or even absent breathing sounds on the ipsilateral lung and decreased moving of the thoracic wall. (9)

The described signs and symptoms may occur at any time during pregnancy and require fast and correct management.

8.4 Diagnostics

Diagnostic evaluation tools for detection of primary spontaneous pneumothorax in pregnancy should not experience delay due to concern of radiation, possibly harming the fetus. As mentioned earlier, radiographic imaging of the chest is crucial for prompt diagnosis of the pulmonary condition and if combined with shielding of the abdomen it might expose the fetus to just approximately 2 mrad per examination, equaling 0.02 mGy. The declared radiation dose is considered secure for the developing infant. (35) Additionally, ultrasound, the diagnostic tool used without any radiation exposure, remains often the preferred option in trauma management of PSP. As well as in non-pregnant patients, it may be applied rapidly, having high diagnostic sensitivity.

Lastly, CT scan represents another possible imaging technique for PSP occurrence in pregnancy. By exposing the fetus by approximately a dose up to 0.66 mGy during one CT image, fetal harming is quite unusual.

Concluding, mentioned exposure doses are small and should not hinder from prompt diagnostic evaluation for occurrence of PSP during pregnancy. (35)

8.5 Labor, Delivery and Primary Spontaneous Pneumothorax

Ventilatory changes occurring during pregnancy might spike when undergoing labor and delivery. Labor is defined as an event of stress and hormonal spikes which might contribute to pathological mechanisms to occur. During labor and delivery, a high variability of VT and VE appears to occur. Tidal volume might range from 330 to 2250mL and minute ventilation between 7-90L/min. (23)

Hyperventilation is common during pregnancy as explained above, but might become even more intense during delivery as response to pain. (23)

Increasing oxygen demand and uterine anatomical expansion may consequently lead to fetal hypoxia. (30) Beside internal factors like respiratory fatigue, ventilatory insufficiency or above-mentioned hyperventilation also external triggers such as Valsalva maneuvers, positive pressure- or increased alveolar ventilation during or before delivery can induce sharp variations in intrathoracic pressures. (31) These pressure changes might be triggers for primary spontaneous pneumothorax to happen in pregnancy and postpartum period.

During labour, pregnant women with PSP mostly receive epidural anesthesia with long acting anesthetic such as ropivacaine for simultaneous pain relief as well as reduction of cardiovascular stress. (30) By combining epidural and instrumental delivery the second stage of birth is shortened in order to prevent even increasing thoracic and abdominal pressure spikes throughout the pushing stage of natural birth. (32) Generally, vaginal deliveries are the eligible delivery approach during PSP in pregnancy. Prognosis for both, mother and fetus, are usually of good value. (33)

Fetal and maternal monitoring, coordinated obstetrical and gynecological disciplinary approaches as well as anesthesiology and thoracic management increase fetal safety and improve the outcome.

8.6 Reported Cases and Epidemiological Insights

Primary spontaneous pneumothorax during pregnancy appears to be an extremely rare but possible life-threatening condition. The pulmonological disease itself occurs only seldomly and during pregnancy PSP is reported with less than 100 cases worldwide. (34) As research indicates, interrelation of the pulmonary disease during pregnancy still remains questionable.

Guidelines regarding treatment are still insufficient for optimal care and management of the condition. Recommendations are mostly guided by a risk benefit ration for both, maternal and fetal sites. (35) Due to this rarity in literature and systematic review, analysis of data is of high value and importance for fetus and pregnant women in order to achieve the best clinical results and medical care for both. In the following abstract several case reports will be evaluated among clinical presentation, stereotypic patient occurrence and epidemiological insights.

The selected case reports portray the variability in presentation, timing and clinical course of primary spontaneous pneumothorax among pregnant women.

Combined, they possibly support the assumption that PSP may occur in women without any pre-existing pulmonary disease, across a wide range of gestational ages.

The first case pictures a 30-year-old female patient, in her 5th week of pregnancy, presenting with acute chest pain and decreased breathing sounds on the right. Her laboratory results were in physiological ranges. In her anamnesis a smoking history is revealed. Additionally, the patient has already had primary spontaneous pneumothorax half a year ago, which was treated by thoracostomy. (26) During her presentation in the emergency room, ultrasound was performed, revealing right sided recurrent pneumothorax. While primary conservative oxygen therapy was inefficient for her and her clinical condition worsened, medical personnel recommended VATS to resolve PSP completely. The patient declined surgical intervention and instead tube thoracostomy was initiated. The tube was placed for five days, after which it could have been successfully removed. The patient had neither consequent symptoms of pneumothorax nor of chest tube placement and terminated her pregnancy on her own request. (26)

Another case depicts a 30-year old pregnant patient in her 28th week of gestation. The woman is suffering from sudden dyspnea as well as pleuritic chest pain located on the right side. Her clinical signs revealed during physical examination were of the following character: diminished breathing sounds as well as hyperresonance on percussion. (35) As personal risk factor long-term smoking was mentioned for the patient. The performed chest X-ray with an abdominal shield for protection during pregnancy showed a pneumothorax located on the right side. In this particular case, the woman was treated with conservative measures such as observation and oxygen therapy and recovery after 10 days was successfully reached. Her clinical improvement without catheter placement was gained. After performed control chest radiograph no more bullae and blebs were found. These were originally concluded as her source for PSP to occur. The consequent course of her pregnancy took place without further complications and she naturally delivered a healthy infant in her 39th week of gestation. (35)

The third case demonstrates the clinical picture of PSP in a 28-year-old woman in her 22nd week of gestation. The patient's main complaints are left-sided chest pain, decreased, left-sided breathing sounds with otherwise physiological oxygen saturation and vital signs. (26) In her case, abdominal ultrasound was performed which revealed PSP typical signs. In her anamnesis she revealed no risk factors for primary spontaneous pneumothorax and denied exposure to smoke. In her case thoracostomy with chest tube placement for 5 days was performed to resolve PSP as fast as possible. (26) Her clinical condition improved but the patient was diagnosed with recurrent pneumothorax about 7 days later. As of this fast progression the medical team recommended VATS surgery for pneumothorax. (26) After surgical treatment of PSP her pregnancy remained without further complications and the patient was able to deliver vaginally by 39 weeks of gestation under spinal anesthesia. This case depicts the clinical picture of PSP in pregnancy without the occurrence of prior risk factors but even surgical approach as a solution. (26)

The last chosen case deals with a 38-year-old, 32-week pregnant woman presenting with chest pain and dyspnea in the emergency department. During her clinical examination further, pulmonary signs were found: left hyperresonance of hemithorax and tachypnea. Her pulse oximetry as well as her arterial blood gases were in physiological range and she denies a history of prior smoking or pulmonary conditions predisposing her for the disease. (32) Her gynecological anamnesis reveals previous uterine fibroids, IVF treatment as well as pre-eclampsia. Infectious sources were excluded for her particular case. The performed chest X-ray indicates a left sided pneumothorax combined with total lung collapse. (32) The patient was treated with initial chest tube placement leading to resolution of PSP. Unfortunately, PSP reoccurred during her pregnancy and the patient required chest drain again. Her pre-eclampsia induced pre-term labour at 37 weeks and the patient delivered vaginally under epidural anesthesia.

As of good neonatal outcome and maternal postpartum conditions, the 38-year-old patient underwent VATS procedure with apical pleurectomy in order to resolve the condition of reoccurring PSP definitely. In her recovery she did not experience further pulmonary or gynecological symptoms.

Despite her uncomplicated recovery from both surgery and delivery, the patient experienced another reoccurrence of PSP several weeks after. She was treated by chest tube placement again. (32)

This case well demonstrates the occurrence of several primary spontaneous pneumothoraxes during pregnancy in even otherwise healthy patients. It as well indicates the presence of PSP in later pregnancy, conservative and surgical intervention pre- and post-partum, not requiring special fetal intervention.

Along the chosen cases, affected patients of primary spontaneous pneumothorax in pregnancy were young females of reproductive age. Most of them did not have any considerable medical

comorbidities. Common risk factors such as low body mass index or smoking history were either present or absent, stressing inconsistent risk stratification within the population.

The cases indicate that the pleural disease may present at any stage of pregnancy, reaching from early first trimester to late third trimester. PSP signs were often non-specific and comprised acute chest pain and dyspnea, sometimes overlapping with normal physiological and pregnancy-related complaints. (26) Recurrence of primary spontaneous pneumothorax was revealed in some cases, either during the same pregnancy or as subsequent to initial management.

Initial management strategies across the chosen cases ranged from ordinary observation and chest tube thoracostomy to escalation with surgical treatment when indicated. Despite differences in treatment, outcomes of the mothers were favorable, and most pregnancies proceeded to term with either successful vaginal or cesarean delivery.

No consistent pattern of adverse fetal outcomes was revealed when primary spontaneous pneumothorax was immediately recognized and treated appropriately.

Taking everything into consideration, these cases reflect wider epidemiological trends noted in the literature, including low reported incidence of primary spontaneous pneumothorax during pregnancy and the absence of large-scale observational data.

The dependency on published case reports limits the ability to calculate true incidence, recurrence rates and if pregnancy related risk factors even exist.

Consequently, current epidemiological understanding is mostly directed by reporting bias and underdiagnoses, emphasizing the need for pooled analyses or registry-based studies.

8.7 Fetal Outcome after Primary Spontaneous Pneumothorax

Even though PSP still remains a rare entity during pregnancy, reported cases indicate general favorable outcome for the fetus. If appropriate management of the pulmonary condition is acquired rapidly, fetal prognosis remains acceptable. Most patients with PSP in pregnancy achieve successful and uncomplicated natural birth. In most cases vaginal delivery remains standard (80%) and cesarean delivery is performed only due to further obstetrical reasons. (36)

Generally, fetal complications are not common and loss of newborns is reported by only 2% of published cases. (36) However, physiologically occurring respiratory changes during pregnancy may act as stressors upon female bodies and consequently affecting fetal growth. Hormonal influence by progesterone increases oxygen demand by up to one fifth as well as minute ventilation by approximately 30-50%. Increased tidal volume and anatomical adjustments may function as compensatory mechanisms but these changes lead to reduced respiratory reserves, predisposing the mother to hypoxia, consequently affecting fetal oxygenation and increasing the risk for preterm birth.

(32) In order to prevent this possible fetal compromise rapid and correct management induction is essential. (26) Typical symptoms of PSP may mimic physiologically occurring pregnancy signs, impeding rapid diagnosis. Additionally, limitations in radiological imaging as of concerns about fetal radiation exposure might delay management. Nevertheless, shielding during chest radiography and CT scan is considered safe for the fetus. In contrast, ultrasound is almost always considered as secure, valuable and radiation-free. Further management procedures during pregnancy are generally not different from these in non-pregnant patients. (36)

Summarizing, fetal outcome during PSP is favorable when prompt diagnosis is set and rapid management is initiated. Multidisciplinary approach should always be favored in order to oppose possible fetal risks including hypoxia and preterm birth. (36)

8.8 Overview of Case Reports

The following table provides a structured overview of a patient profile being affected of primary spontaneous pneumothorax in pregnancy. It demonstrates the main patient group being fertile women in reproductive age, typically suffering from the pulmonary condition in their second to third trimester. Some female patients have already experienced PSP prior in their life, but many of them suffer from the condition for the first time. Conservative measures such as chest tube insertion are noted to be the primary approach in selected stable cases, if otherwise not successful, definitive treatment through VATS and pleurectomy is initiated. The table shows a great variety of published results. Additionally, the scale supports the assumption of only minor complications for fetus and mother. When present, complications might include preterm birth or contractions or rarely worsening of pulmonary conditions.

As conclusion, the table indicates there is general favorable outcome for both: mother and fetus. If PSP occurs during pregnancy term delivery and resolution of the disease is not impossible with correct and prompt management. (35)

Table 1.: Case Reports of Spontaneous Pneumothorax in Pregnancy (8)

Table 1. Case Reports of Spontaneous Pneumothorax in Pregnancy

Study	Maternal age (years)	Gestational age (weeks)	History of prior pneumothorax	Success with initial chest tube placement	Success with VATS/pleurectomy	Complications	Management
Miyasita et al, 1991 [18]	37	13	No	No	Yes	No	
Levine et al, 1996 [14]	26	32	No	No	Yes	No	Recurrent thoracostomy with postpartum pleurectomy
Van Winter et al, 1996 [22]	26	23	No	No	Yes	Recurrent CT placements	Recurrent thoracostomy followed by antepartum thoracotomy with blebectomy and mechanical pleurodesis
Reid et al, 2000 [23]	29	32	No	No	Yes	Preterm contractions	
Gorospe et al, 2002 [24]	25	34	No	Yes	N/A	No	Antepartum thoracostomy
Wong et al, 2006 [25]	34	32	Yes	No	Yes	No	Recurrent thoracostomy followed by postpartum VATS
Sillis et al, 2006 [26]	21	5	Yes	No	Yes	Preterm birth (34 weeks)	Antepartum thoracostomy followed by thoracotomy with mechanical pleurodesis
Pinedo-Onofre et al, 2006 [20]	22	24	No	Yes	N/A	No	
Lal et al, 2007 [11]	22	11	No	No	Yes	No	
	27	15	Yes	No	Yes	Bilateral VATS	
Tanase et al, 2007 [17]	25	34	No	Yes	N/A	No	
Garg et al, 2008 [12]	30	28	No	No	N/A	No	Conservative management
Jain et al, 2009 [5]	38	32	No	No	Yes	No	Recurrent antepartum thoracostomy; postpartum VATS with pleurectomy
Sathiyathasan et al, 2009 [4]	37	40	Yes	Yes	N/A	Emergent C-section for respiratory distress	Postpartum thoracostomy
Avital et al, 2009 [13]	17	36	No	Yes	N/A	No	Antepartum thoracostomy
Mohammadi et al, 2011 [16]	27	38	No	Yes	N/A	Worsening pulmonary edema	
Annaiah et al, 2011 [2]	33	14	No	Yes	N/A	Preterm birth (36 weeks)	
Nwaejike et al, 2012 [3]	29	26	No	No	Yes	Preterm birth (36 weeks)	Recurrent thoracostomy followed by VATS
Akçay et al, 2013 [15]	19	15	No	No	Yes	No	
	22	25	No	Yes	N/A	No	
	20	19	Yes	Yes	N/A	No	
Onodera et al, 2013 [19]	31	9	Yes	No	Yes	No	
Kumar et al, 2014 [10]	30	36	No	No	Yes	No	Recurrent thoracostomy followed by postpartum pleurodesis
Yotsumoto et al, 2015 [21]	34	31	No	No	Yes	Recurrent CT placements	
Hamid et al, 2016 [27]	36	22	No	No	N/A	Recurrent CT placements, refused surgical intervention	Recurrent antepartum thoracostomy
Kavurmaci et al, 2018 [8]	30	5	No	Yes	N/A	TOP	Antepartum thoracostomy
	28	22	No	No	Yes	No	Recurrent thoracostomy followed by VATS
Lateef et al, 2018 [7]	34	34	Yes	No	N/A	Recurrent CT placements, refused surgical intervention	Recurrent antepartum thoracostomy
Yasuda et al, 2018 [6]	35	22	Yes	No	Yes	No	Thoracostomy followed by VATS with pleurodesis
La Verde et al, 2022 [9]	23	41	No	No	No	No	Expectant management

9 Management of Primary Spontaneous Pneumothorax in Pregnancy

9.1 Conservative vs. Surgical Treatment

The occurrence of primary spontaneous pneumothorax during pregnancy remains rare but still may be life-threatening to mother and child. As of this infrequency, formal and standardized treatment recommendations are lacking. Clinical implications and resolutions are mainly relying on published case reports as well as multidisciplinary decisions about risk benefit of mother and newborn. (35)

Still, the management of pregnant women with PSP should not be different from treatment in non-pregnant women. Adaptations should be taken into consideration as of possible fetal consequences and compromise, but no general differences are made. (32)

Generally, PSP management should be differentiated into conservative as well as surgical treatment approaches, depending on clinical severity of the pulmonary condition. (37) Recommendations for treating the pulmonary disease during pregnancy are initially conservative, especially with pneumothoraxes of smaller size and the patient being steady in hemodynamics and vital signs. Conservative measures are mostly primitive observation together with oxygen therapy, chest tube insertion, which is also termed thoracostomy or needle aspiration with the aim of reinflation of the collapsed lung. (37) Some published reports indicate that conservative treatment of PSP in pregnancy solely may be effective and a few pneumothoraxes can subside with only non-surgical observation and drainage procedures. Prior, guidelines existed, which indicate that basic aspiration together with patient observation is sufficient enough for PSP treatment in pregnant women. (38)

Even though conservative care is effective in some cases, there are pregnant patients suffering from persistent air leakages or blebs which are not solved by conservative care or drainage alone. These patients require further surgical intervention. (35)

A study has shown that approximately 40% of female pregnant patients suffering from persistent pneumothoraxes require surgery prior to delivery of the newborn after being treated conservatively first. (38) Surgery of PSP might be either performed prior or after delivery. Surgical procedures post birth might prolong hospital stays and interfere in mothers and child's bonding after birth. These surgically induced changes might be distressful and could be adapted through a planned pre-birth intervention. (38) Prior to surgical but generally invasive approaches, pregnant women before 36th weeks of gestation should receive tocolytic drugs in order to prevent them from pre-term birth and premature contractions. (37) Common surgical treatment options are video-assisted thoracoscopic surgery (VATS) combined with pleurodesis and blebectomy. In worse cases thoracotomy together with blebs resection is indicated. But generally, VATS procedure has largely replaced most alternative surgical interventions and has become standard of care for definitive treatment of PSP during pregnancy as well. (35) Additionally, VATS has proven to diminish pain post-surgery, to further reduce complication rates and shorten the stay in hospitals. (39) Some previous guidelines

evaluate VATS procedures post-delivery to be more efficient, but there is evidence of surgical thorascopies performed before giving birth to occur without adverse neonatal reactions.

Summarizing, conservative as well as surgical approaches require correct timing and indication in order to be efficient for these patients.

A study published an overview of surgical and non-surgical procedures taking their advantages and disadvantages into consideration. For surgical approaches thoracotomy and VATS procedure were compared in their features. Even though thoracotomy has been mainly outlined by VATS these days, the open surgery still has been a standardized technique that specialists are mostly able to perform and recurrence of PSP after thoracotomy is reduced. VATS in comparison reduces postoperative complications and pain as well as it is less invasive having higher cosmetic value especially in young female patients. Both surgical interventions definitely are risk factors for pregnant women as both techniques require general anesthesia. (39)

Conservative measures such as chest tube placement, secure pregnant patients from general anesthesia but opposingly might not guarantee definitive treatment of PSP, and further possibly increase patient discomfort during and after application. Implementation of the thoracic drain might increase the risk for blockade and reapplication as well as it often prolongs hospital stays. (39)

Reviewing these variabilities of results, different treatment approaches are valuable for PSP during pregnancy. Depending on symptom severity, recurrence and clinical situation a multidisciplinary team should be consulted to take timing, severity and risk/benefit ratio into consideration. Additionally, the patients themselves should receive education about the existing broad spectrum of therapeutic possibilities. This should also enable them to decide on treatment together with a team of specialists. Moreover, vaster research and studies are needed for strict diagnostic algorithms, correlational theories and management recommendations. (35)

9.2 Timing and Safety of Surgical Interventions

Shortage of literature regarding PSP during pregnancy creates a scarcity of guidelines for specifically surgical interventions for these patients. Still, surgical treatment emphasizes both: simultaneous stability of the mother's health condition as well as secure fetal protection.

Surgery as definitive treatment is recommended in cases of primary spontaneous pneumothorax when persistent bullae or recurring leakages are present in pregnant women. In these cases, conservative measures are not sufficient enough to cure the patient completely. (35)

Regarding the optimal time frame of surgical interventions for spontaneous pneumothoraxes during pregnancy, research has opted the second trimester of pregnancy to be most suitable. During 13th to 28th week organogenesis of the fetus is mostly terminated consequently lowering the risk for fetal

teratogenicity initiated through anesthetic procedures. Intervention during these gestational weeks might reduce the possibility of preterm labor other than in later stages of pregnancy. (38)

During the second trimester VATS combined with mechanical pleurodesis is considered as option of choice for pregnant women undergoing surgery due to the pleural condition. Within the third trimester surgical intervention might be increasingly risky due to proximity to term, and surgery might be postponed until post-delivery.

When comparing spontaneous vaginal delivery and caesarean section as birth options, SVD supported by regional anesthesia should be considered as primary approach for affected women while caesarean section is only indicated with further obstetric complications. (34) Research and published cases have confirmed that emergent surgical management of pregnant women with PSP may be executed at any pregnancy state if the pulmonological condition depicts lethal consequences for both: mother and fetus. Clinical maternal signs such as hypoxia might also danger fetal survival and growth. Other than emergent settings, elective surgeries of PSP during pregnancy up to the second trimester can be executed safely, as mentioned above, even though third trimester still constitutes a secure and possible time frame for surgeries as well. (38)

Summarizing, conservative treatment of primary spontaneous pneumothorax is still considered as initial approach during pregnancy. Nevertheless, surgical procedures such as VATS executed together with pleurodesis continue to be verified and secure treatment possibilities for pregnant women, especially for those with reoccurring and endangering pneumothoraxes.

Surgical timing should be individualized for each pregnant patient as well as taking severity of the condition and gestational age into consideration.

Discussion should take place within a multidisciplinary team, composed of obstetricians, surgeons, anesthesiologists as well as in incorporating family and the patient herself. (34)

9.3 Obstetric Considerations and Delivery Planning

Even though the condition of primary spontaneous pneumothorax during pregnancy remains a rare pulmonary event, obstetric consideration is of high importance as maternal pathological changes may directly alter fetal outcome. Especially the involvement of fetal oxygenation outlines the necessity of immediate obstetric management. (35)

Clinical signs such as dyspnea and chest complaints during PSP in pregnant women may resemble physiological pregnancy induced adjustments leading to delayed treatment and disease recognition. (4) Avoidance of delay in management may be crucial to improve both conditions, for mother and fetus. Obstetric management initially equals treatment and considerations of non-pregnant patients. For stable patients' conservative treatment such as chest tube placement are first line approaches for

PSP. (33) If conservative treatment fails or does not lead to rapid improvement of maternal condition surgical procedures are further initiated as discussed within chapters above. Surgical interventions have been executed successfully and enabled pregnant women to deliver mostly without occurrence of adverse fetal outcomes. (39)

Regarding delivery planning of pregnant patients suffering from primary spontaneous pneumothorax vaginal deliveries are possible to undergo after resolution of the condition as previous case reports have shown. (35) In order to prevent from PSP recurrence during labour, hyperventilation state as well as Valsalva maneuvers should be avoided as these events are risk factors for the pulmonary condition to occur. (31) During labor, oxygen consumption of the mother is increased by approximately 50%, indicating that states of less oxygenation are not well tolerated. (40)

To prevent an even increasing intrathoracic pressure during the second stage of labor, the pushing phase, patients with PSP are recommended to undergo epidural anesthesia combined with instrumental delivery when not having underwent definitive surgical treatment. (35) Cesarean section as delivery option should be primarily reserved for pregnant women with additional obstetric indications or pregnancy complications rather than primary spontaneous pneumothorax alone. (34)

Summarizing, published cases have shown that favorable outcome for both maternal and fetal sites can be achieved when delivery planning and obstetric management strategies are considered on time. Multidisciplinary approaches contribute to improving fetal and maternal states.

10 Discussion

10.1 Interpretation of Results

Primary spontaneous pneumothorax during pregnancy still remains a rare event, possibly connected with life threatening consequences, if untreated, delayed or misdiagnosed. Occurring without an underlying pathology PSP alone is characterized by a subtotal or total lung collapse due to air accumulation within pleural space, the layer between visceral and parietal lung layer. Concrete pathophysiological backgrounds are still in doubt, but scientists mostly believe bullae and blebs, defined as subpleural lesions and vesicles, to be the initial cause for PSP to occur. (33)

As of its seldom incidence, primary spontaneous pneumothorax during pregnancy still remains without concrete diagnostic, therapeutic and management requirements.

Additionally, physiological changes throughout pregnancy may as well create therapeutic confrontations for medical staff as well as for patients. Another peculiarity about PSP during pregnancy needs to be considered: handling of the mother consequently alters fetal well-being, making diagnosis, evaluation and treatment even more complex and fragile. (40)

The main symptom complex of pregnant women suffering from PSP contains sudden onset chest pain as well as difficulty in breathing. Additionally, pulmonary restrictions in auscultation and palpation may be found during clinical examination. (33) These disease-induced cardiopulmonary signs might resemble physiological pregnancy symptoms interfering with rapid diagnosis and management of actual PSP. (35) The physiological adaptations occurring throughout pregnancy include anatomical changes such as a constantly increasing uterine size, as well as hormonal and mechanical changes. These induce a decrease in functional residual capacity and simultaneous increase in tidal volume as well as in respiration. Through, increased oxygen consumption during the course of pregnancy and during labour by approximately 50% respiratory reserves from maternal side are additionally reduced making the mother more susceptible to hypoxemic states altering mothers and fetal oxygenation status during pregnancy and labour. (40)

However, if, in some cases PSP is not present even though the typical clinical signs are present, differential diagnostics should be taken into consideration. These include a broad spectrum of pulmonary diseases such as asthma and bronchitis resembling the clinical picture of PSP during the first impression. Furthermore, cardiological, gastrointestinal and general systemic pathologies might as well raise the assumption of primary spontaneous pneumothorax to be present. Differentiation should also happen between PSP and other pneumothorax types. These might require different interventions and management regimes. (20)

To exclude differentials, diagnostic measures are of high value to set the diagnosis of PSP in pregnancy. Ultrasound, chest radiographs and CT scan are the measures of choice. Imaging techniques with radiation are possible to use with shielding in pregnant women. Still, CT scans are rarely used as of higher radiation doses. (35)

If diagnosis of PSP during pregnancy is set, first management steps may be induced. Treatment is mostly based on pneumothorax size as well as the clinical situation of the individual patient. Generally, treatment might be either conservative or surgical and management in pregnant women with PSP is not different to the condition in non-pregnant individuals. (33) Conservative measures, such as oxygen therapy and basic observation are primary approaches in most pregnant patients. Needle aspiration and placement of a chest tube are used for further intervention, if pneumothoraxes are larger in size. About 75% of patients receive conservative chest tube insertion primarily. If pneumothoraxes of larger size occur, more invasive procedures could be taken into consideration, especially in case of recurrent events. Recurrence rates are up to 40%, especially during labour due to intrathoracic pressure spikes. If simple aspiration and drainage fail to succeed surgical techniques are used. (33) Here, VATS has become gold standard due to its lower invasiveness, shorter hospital stay and less postoperative pain. Surgery for pregnant women considers the second trimester to be

optimal for interventions as organogenesis is complete and fetal teratogenicity is less during that time frame. (38)

Regarding obstetric recommendations and modes of delivery, vaginal delivery should remain the goal, especially in patients with prior surgical treatment for PSP. Often epidural anesthesia is used during delivery for reduction of thoracic pressure and lowering maternal expulsion effort during pushing stage. Additionally, assisted delivery techniques, such as vacuum or forceps are useful. PSP solely should not be an indication for operative delivery, in the way of caesarean section, as it should be reserved for other obstetric cases. If delivery is performed through C-section, regional anesthesia over general anesthesia is favored, due to the avoidance of positive pressure ventilation, increasing the risk of PSP recurrence and coughing maneuvers while extubating. (40) In summary, if presentation of PSP during pregnancy arises, prognosis for fetus and mother is of good value, if involved specialists recognize the disease on time. Outcome has been proven to be good, as published case reports indicate, and surgical as well as non-surgical approaches are able to cure the condition with optimal outcome for both: mother and fetus.

Recapitulating, the disease presentation of primary spontaneous pneumothorax was broadly summarized, pregnancy related physiological changes were explained and published cases were depicted. Maternal and fetal handling in case of primary spontaneous pneumothorax in pregnancy was elucidated and scientifically published evidence through broader case presentation was connected to the topic. It became clear, that cases of primary spontaneous pneumothorax already exist, but it seems, literature does not exactly reveal if there is a clear correlation among the pulmonary disease and the physiological state of pregnancy. PSP rather coincidences during pregnancy, further risking maternal and fetal oxygenation state and leading to possibly fatal outcome. The question is still in doubt, if PSP appears more incidental during pregnancy or if pregnancy acts as causal factor. Still, it highlights the attention among the disease during pregnancy and that recognition of dyspnea and chest pain in pregnant women should always raise concerns for primary spontaneous pneumothorax, even though it is of only rare occurrence. (40)

10.2 Clinical Implications

Even though the clinical picture of primary spontaneous pneumothorax during pregnancy still remains a rather uncommon entity and direct correlation between pathology and physiological state of pregnancy is insufficiently evaluated in science, clinical implications should still be mentioned, as in case of PSP occurrence during pregnancy, it combines important physiological, pathological, obstetrical and surgical aspects.

First of all, awareness and prompt recognition of primary spontaneous pneumothorax in pregnant women is highly significant as the disease might lead to fatal consequences. During pregnancy, physiological changes in respiratory system occur, involving rising demand of oxygen as well as concomitant decrease of pulmonary reserves. Pathological developing air leakage during PSP might consequently lead to hypoxemia, further hazarding preterm labor and neonatal death. Due to this possibly fatal outcome, diagnosis, strict monitoring and prompt management of PSP in pregnant women should be induced immediately.

Additionally, awareness of necessary diagnostics should be known by specialists, dealing with the pulmonary disease in pregnant patients. Despite the state of pregnancy, the threshold to use diagnostic tools with radiation should be kept low, as prolonged diagnosis might increase risks for fetus and mother to have more severe signs or may even lead to fatal death. Therefore, if used with abdominal shielding most radiological imaging techniques are considered as secure for fetal and maternal body. Still, rapid diagnosis of the disease remains challenging even for specialists, as of rare occurrence during pregnancy and the possibility of overlap between physiological and pathophysiological signs. Often, scientists do not directly see correlation between pathology and pregnancy and diagnosis is delayed or remains unseen.

Furthermore, once diagnosis for PSP during pregnancy is set, treatment applications remain challenging. In general, treatment should not differ from that in non-pregnant patients, as research indicates, but still, fetal consequences should be questioned with initiating management steps. Conservative versus surgical approach should be outweighed, consequences well explained and active management for symptomatic patients initiated. Surgical treatment in second trimester might be performed safely. Knowing that, surgery might offer a possibly safe approach, especially in cases of recurrence. This further opposes surgical and non-surgical approaches, questioning indication, timing and approach creating a dilemma for involved specialists. Due to the lack of explicit guidelines for the disease during pregnancy a multidisciplinary team should be involved and discuss diagnostic, therapeutic and prognostic questions broadly. As PSP during pregnancy deals with implications regarding reproductive planning and has prognostic obstetric value, open communications should occur, involving the patients themselves about available interventional methods, risk of recurrence and correct handling with the condition.

10.3 Gaps in Research and Future Recommendations

Even though some published case reports but only few scientific data regarding primary spontaneous pneumothorax during pregnancy exist in literature, the current evidence is lacking, if, first of all, there is a correlation between pregnancy and the pulmonary disease, increasing the risk for misdiagnosis

or delayed interventions in pregnant women. Mentioning this, it becomes clear, research still owns several gaps regarding the topic. The following chapter will shortly provide an overview about the current scientific data, the created lacks and subsequently offer some recommendations for improvement in diagnosis and management.

First, mainly the mentioned lack of broader epidemiological data creates a gap for research to intervene early. The exact incidence and causative relation of PSP to pregnancy remains unknown, leading to an inability to calculate outcome for both, mother and newborn and additionally aggravating the assessment of risk factors and recurrence. Larger population-based scientific studies would be needed in order to fill these gaps properly and estimate prognostic values.

Randomized controlled trials are not possible to obtain as of small entity and very specific group description.

The lack of data consequently affects correct and chronological application of treatment in pregnant women. Although most sources state there is no difference in pregnant and non-pregnant PSP treatment application, the used management strategies are not explicitly designed for pregnant patients. This may result in unspecific treatment options being not very unique to the physiological state of pregnancy. A future recommendation would be exclusively pregnancy-specific guidelines easing proper management of PSP in pregnancy and providing clear diagnostic steps for involved doctors.

Another gap of PSP during pregnancy is the optimal timing of surgical interventions – if needed. Generally, the second trimester is considered safe for surgery, still this proposal is based on surgeon's experience, rather than on larger published scientific data. To generally improve surgical approaches and secure intervention, research on maternal and fetal outcome after surgery in comparison to conservative treatment would be of high importance.

Additionally, to correct timing of surgery, radiological and clinical predictors would be needed in order to evaluate an accurate rate of recurrence for pregnant patients with PSP. This would help improve whether definitive treatment is needed in specific cases or not and consequently promote accurate care of women.

Further, prognosis for mother and fetus is generally considered good after surgical treatment of PSP, but still, systematic review and scientific broader data for exact prognostic value including PSP recurrence, health outcome post-surgery as well as following pregnancies is lacking. Beside prognostics, so far, obstetrical outcome is insufficiently covered by published scientific data. Delivery and anesthesia during birth have great impact on fetal development. Vaginal delivery as well as epidural anesthesia are mentioned as most suitable for women with PSP during pregnancy. This is, what case reports and published data suggest, but still, comparative studies for various delivery modes comparing outcomes would be scientifically useful.

Beside diagnostics, treatment and prognostic value, another aspect, insufficient data are observed on patient's quality of life. For affected women, physiological pregnancy may be an intense period, including fetal distress and hormonal as well as mechanical changes within the body. If additionally, PSP occurs, anxiety and uncertainty might be present. The mentioned maternal perspective and impact of PSP has not been sufficiently considered in scientific data.

11 Conclusion

11.1 Key Findings

If primary spontaneous pneumothorax presents during pregnancy it marks a potentially serious health condition, even though being of rare frequency compared to other pulmonological diseases. Additionally, to its rarity of occurrence, causal relation between primary spontaneous pneumothorax and pregnancy still needs to be scientifically investigated in further depth. As of this uncertainty, physicians should be trained in recognizing clinical signs, being rather non-specific, typical for primary spontaneous pneumothorax presentation. Despite of non-specific appearance, dyspnea and chest pain during primary spontaneous pneumothorax might have lethal consequences, by inducing preterm birth and maternal hypoxemia, leading to fetal compromise. Management and diagnostics of primary spontaneous pneumothorax should be induced immediately, being not entirely different from non-pregnant patients. Surgical and non-surgical approaches are applied as both have advantages for different individual patient cases. Recurrence risk of primary spontaneous pneumothorax should be considered, mainly within labour stage, requiring professional obstetric and gynecological surveillance and planning. Vaginal delivery combined with epidural anesthesia is safely performed, as case reports indicate.

Concluding, fetal and maternal outcome is generally favorable if initiated on time and observed by specialized multidisciplinary teams. Nevertheless, more scientific data is required for primary spontaneous pneumothorax correlational pregnancy specific guidelines.

11.2 Concluding Thoughts

To conclude this master thesis, I would like to return to the proposing introduction. Even though primary spontaneous pneumothorax during pregnancy remains a scarce entity and its underlying pathophysiological correlation to the physiological state of pregnancy still remains incompletely discovered on scientific bases, it represents - if occurring - a clinical picture, requiring prompt need for action. Several cases of primary spontaneous pneumothorax in pregnancy are published, which have broadly been included as base of this master thesis.

The thesis provides a broad overview and brought details about clinical presentation, diagnosis, treatment and further recommendations of primary spontaneous pneumothorax, if occurring solely and additionally, in presence of pregnancy.

Still, pathophysiological background of primary spontaneous pneumothorax exclusively still remains scientifically doubtful and in correlation with pregnancy even more research is needed to interrelate both: pathology and pregnancy. Within published cases, the assumption of the occurrence of primary spontaneous pneumothorax during pregnancy is presupposed but questions of interrelation and causative occurrence is insufficiently discussed and therefore a lack around the introducing question is created. Concludingly, more research and clinical evidence is needed in order to provide clear information, if there is a scientific correlation and further, for strict diagnostic and management guidelines for the coincidental presence of pregnancy and primary spontaneous pneumothorax.

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