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# the **S Q U A R E**

Healthcare **bulletin**

- ▣ *Pneumonia in Children*
- ▣ *Postpartum Psychiatric Disorder*
- ▣ *Thyroid Disease & Female Infertility*
- ▣ *Immune Deficiency Disorders*



Test yourself

**39**

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# the SQUARE

healthcare bulletin

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### Editorial

Dear Doctor,

We welcome you to this addition of "the SQUARE" healthcare bulletin!

At the start of 2016 we take this opportunity to offer our best wishes from the editorial team of "the SQUARE"!

Happy New Year 2016!

This issue is enriched with a blend of topics those are very often encountered by the healthcare professionals. Firstly, we have focused on "Pneumonia in Children". Childhood pneumonia is an important cause of morbidity in the developed world, and morbidity and mortality in the developing world. We have emphasized on "Postpartum Psychiatric Disorder". During the postpartum period, about 85% of women experience some type of mood disturbance. We also have a detailed feature on "Thyroid Disease & Female Infertility". Abnormalities in thyroid function can have an adverse effect on reproductive health. Besides, we have included the facts on "Immune Deficiency Disorders", are associated with or predispose affected patients to various complications, including infections, autoimmune disorders, and lymphomas and other cancers. Our regular feature "Test Yourself" is here too!

We hope that you will find this newsletter both interesting and informative as well! The success of this healthcare bulletin depends on your comments, participation, contributions and ideas!

On behalf of the management of SQUARE we wish you all healthy, prosperous and peaceful lives!

Thank you!



*Omar Akramur Rab*

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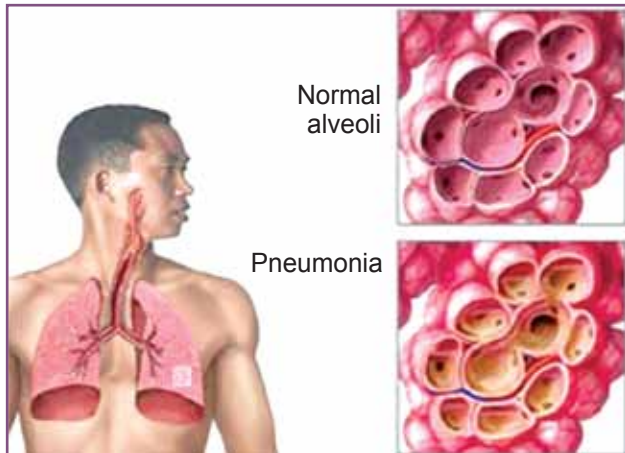
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**P**neumonia is an infection in one or both lungs. Pneumonia can be caused by bacteria, viruses, fungi, and parasites. Viruses are usually the cause of pneumonia in children. Children with viral pneumonia can also develop bacterial pneumonia. Often, pneumonia begins after an infection of the upper respiratory tract (nose and throat). This causes fluid to collect in the lungs, making it hard to breathe. Pneumonia can also occur if foreign material, such as food or stomach acid, is inhaled into the lungs.



Pneumonia and other lower respiratory tract infections are the leading causes of death worldwide. Because pneumonia is common and is associated with significant morbidity and mortality, properly diagnosing pneumonia, correctly recognizing any complications or underlying conditions, and appropriately treating patients are important. Although in developed countries the diagnosis is usually made on the basis of radiographic findings, the World Health Organization (WHO) has defined pneumonia solely on the basis of clinical findings obtained by visual inspection and on timing of the respiratory rate.

Pneumonia may originate in the lung or may be a focal complication of a contiguous or systemic inflammatory process. Abnormalities of airway patency as well as alveolar ventilation and perfusion occur frequently due to various mechanisms. These derangements often significantly alter gas exchange and dependent cellular metabolism in the many tissues and organs that determine survival and contribute to quality of life. Recognition, prevention, and treatment of these problems are major factors in the care of children with pneumonia.

### Risk Factors

While most healthy children can fight the infection with their natural defences, children whose immune systems are compromised are at higher risk of developing pneumonia. A child's immune system may be weakened by malnutrition or undernourishment, especially in infants who are not exclusively breastfed. Pre-existing illnesses, such as asthma, COPD, symptomatic HIV infections and measles, also increase a child's risk of contracting pneumonia.

The following are the risk factors related to the host and the environment that affect incidence of childhood clinical pneumonia in the community in developing countries -

#### Definite risk factors

- Malnutrition (weight-for-age z-score < -2)
- Low birth weight ( $\leq 2500$  g)
- Non-exclusive breastfeeding (during the first 4 months of life)
- Lack of measles immunization (within the first 12 months of life)
- Indoor air pollution
- Crowding

#### Likely risk factors

- Parental smoking
- Zinc deficiency
- Mother's experience as a caregiver
- Concomitant diseases (e.g. diarrhoea, heart disease, asthma)

#### Possible risk factors

- Mother's education
- Day-care attendance
- Rainfall (humidity)
- High altitude (cold air)
- Vitamin A deficiency
- Birth order
- Outdoor air pollution

### Epidemiology

In the United States, pneumonia accounts for 13% of all infectious illnesses in infants younger than 2 years. In a large community-based study shown that, the annual incidence rate of pneumonia was 4 cases per 100 children in the preschool-aged group, 2 cases per 100 children aged 5-9 years, and 1 case per 100 children aged 9-15 years. In school-aged children and adolescents, bronchopneumonia occurs

in 0.8-2% of all pertussis cases and 16-20% of hospitalized cases. *M pneumoniae* accounts for 14-35% of pneumonia hospitalizations in this age group and mycobacterial pneumonia has recently been noted with increasing frequency in some inner-city areas, particularly children in homeless shelters and group homes and those with household contacts.

**Table 1. Estimates of incidence and number of new cases per year of clinical pneumonia in children aged less than 5 years, by WHO region**

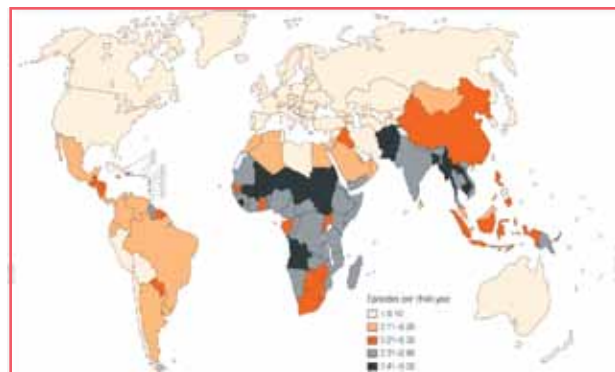
WHO region	Total population aged 0-4 years (millions)	Estimated incidence(e/cy) per year (millions)	Estimated no. of new cases
African	105.62	0.33	35.13
Americas	75.78	0.10	7.84
Eastern Mediterranean	69.77	0.28	19.67
European	51.96	0.06	3.03
South-East Asia	168.74	0.36	60.95
Western Pacific	133.05	0.22	29.07
Total (developing countries)	523.31	0.29	151.76
Total (developed countries)	81.61	0.05	4.08
Total	604.93	0.26	155.84

*e/cy, episodes per child-year. a Up to 10% of all new cases may progress to severe episodes and require hospitalization.*

Globally pneumonia and other lower respiratory tract infections are the leading cause of death worldwide. The WHO Child Health Epidemiology Reference Group estimated the median global incidence of clinical pneumonia to be 0.28 episodes per child-year. This equates to an annual incidence of 150.7 million new cases, of which 11-20 million (7-13%) are severe enough to require hospital admission. Ninety-five percent of all episodes of clinical pneumonia in young children worldwide occur in developing countries.

Approximately 150 million new cases of pneumonia occur annually among children younger than 5 years worldwide, accounting for approximately 10-20 million hospitalizations. A WHO Child Health Epidemiology Reference Group publication cited the incidence of community-acquired pneumonia among children younger than 5 years in developed countries as approximately 0.026 episodes per child-year and a study conducted in the United Kingdom showed

that 59% of deaths from pertussis are associated with pneumonia.



*Figure: Incidence of childhood clinical pneumonia at the country level*

**Table 2. The 15 countries with the highest estimated absolute number of new cases of clinical pneumonia**

Country	Predicted of new cases (millions)	Estimated incidence(e/cy)
India	43.0	0.37
China	21.1	0.22
Pakistan	9.8	0.41
Bangladesh	6.4	0.41
Nigeria	6.1	0.34
Indonesia	6.0	0.28
Ethiopia	3.9	0.35
Democratic Republic of the Congo	3.9	0.39
Viet Nam	2.9	0.35
Philippines	2.7	0.27
Sudan	2.0	0.48
Afghanistan	2.0	0.45
United Republic of Tanzania	1.9	0.33
Myanmar	1.8	0.43
Brazil	1.8	0.11

*e/cy, episodes per child-year.*

## Etiology

Pneumonia can be caused by a myriad of microorganisms. Clinical suspicion of a particular offending agent is derived from clues obtained during the history and physical examination. While virtually any microorganism can lead to pneumonia, specific bacterial, viral, fungal, and mycobacterial infections are most common in previously healthy children. The age of infection, exposure history, risk factors for unusual pathogens, and immunization history all provide clues to the infecting agent.

Specific etiologic agents vary based on age groups (ie, newborns, young infants, infants and toddlers, 5-year-olds, school-aged children and young adolescents, older adolescents).

## Newborns

In newborns (age 0-30 d), organisms responsible for infectious pneumonia typically mirror those responsible for early onset neonatal sepsis. This is not surprising in view of the role that maternal genitourinary and gastrointestinal tract flora play in both processes. Infections with group B *Streptococcus*, *Listeria monocytogenes*, or gram-negative rods (eg, *Escherichia coli*, *Klebsiella pneumoniae*) are common causes of bacterial pneumonia. These pathogens can be acquired in utero, via aspiration of organisms present in the birth canal, or by postnatal contact with other people or contaminated equipment.

Group B *Streptococcus* (GBS) was the most common bacterial isolate in most locales from the late 1960s to the late 1990s, when the impact of intrapartum chemoprophylaxis in reducing neonatal and maternal infection by this organism became evident. *E coli* has become the most common bacterial isolate among VLBW infants (1500 g or less) since that time. Other potential bacterial organisms include the following:

- ❑ Nontypeable *Haemophilus influenzae* (NTHi)
- ❑ Other gram-negative bacilli
- ❑ Enterococci
- ❑ *Staphylococcus aureus*

Some organisms acquired perinatally may not cause illness until later in infancy, including *Chlamydia trachomatis*, *U urealyticum*, *Mycoplasma hominis*, Cytomegalovirus (CMV) and *Pneumocystis carinii*. *C trachomatis* organisms are presumably transmitted at birth during passage through an infected birth canal, although most infants are asymptomatic during the first 24 hours and develop pneumonia only after the first 2 weeks of life.

Community-acquired viral infections occur in newborns, although less commonly than in older infants. The most commonly isolated virus is respiratory syncytial virus (RSV). Newborns may also be affected by the bacteria and viruses that

commonly cause infections in older infants and children. Risk factors for infection include older siblings, group daycare, and lack of immunization.



*Right lower lobe consolidation in a patient with bacterial pneumonia.*

## Young infants

In the young infant (aged 1-3 mo), continued concern about the perinatally acquired pathogens mentioned above remains. However, most bacterial pneumonia in this age group is community acquired and involves *S pneumoniae*, *S aureus*, and nontypeable *H influenzae*. *S pneumoniae* is by far the most common bacterial pathogen in this age group. Infection with any of these pyogenic bacteria may be complicated by lung abscess, parapneumonic effusions, and empyema, although *S aureus* is notorious for such complications.

At this age, infants are incompletely immunized and remain at higher risk for *H influenzae* type B and pneumococcal disease, although herd immunity gained from widespread immunization of the population has been broadly protective.

Most lower respiratory tract disease in young infants occurs during the respiratory virus season and is viral in origin, particularly in the patient with clinical bronchiolitis. The most common viral agents include RSV, parainfluenza viruses, influenza virus, adenovirus, and human metapneumovirus (hMPV).

*Bordetella pertussis* infection leads to pneumonia in as many as 20% of infected infants (as a complication of the whooping cough infection).

## Infants, toddlers, and preschool-aged children

Viruses remain the most common cause of pneumonia in this age group, accounting for approximately 90% of all lower respiratory tract infections. Other viruses that cause pneumonia less frequently in infants and young children include adenovirus, enterovirus, rhinovirus, and coronavirus. A recent addition to this list is hMPV, which causes an illness similar to RSV and may be responsible for one third to one half of non-RSV bronchiolitis. The herpesviruses (HSV, VZV and CMV) may rarely cause pneumonia, particularly in children with impaired immune systems.

Bacterial infections in this age group are seen on a regular basis. *S pneumoniae* is by far the most common bacterial cause of pneumonia. Among hospitalized children with bacterial pneumonia, *S pneumoniae* accounts for 21-44% of disease. Other agents to consider include *H influenzae* type B (HiB) (very uncommon in immunized children), *S pyogenes*, and *S aureus*.

Children younger than 5 years, children enrolled in daycare, or those with frequent ear infections are at increased risk for invasive pneumococcal disease and infection with resistant pneumococcal strains. Evidence suggests that breastfeeding has a protective effect against invasive pneumococcal infection.

## School-aged children and young adolescents

*M pneumoniae* is the most frequent cause of pneumonia among older children and adolescents. *Mycoplasma* accounts for 14-35% of pneumonia hospitalizations in this age group. Children in homeless shelters and group homes and those with household contacts are at particular risk. Similarly, the diagnosis must be considered in immunocompromised children. In this age group, pyogenic bacterial pneumonia remains a concern, usually caused by *S pneumoniae*. Other pyogenic bacterial pathogens to consider include *S aureus* and *S pyogenes*. *Chlamydomphila pneumoniae* also causes pneumonia. The related organism, *C psittaci*, is an unusual cause of pneumonia that occurs in people who work with and handle birds. In immunosuppressed individuals, opportunistic infections with organisms such

as *Aspergillus* species, *Pneumocystis jirovecii*, and CMV can occur.

Viral pneumonia remains common in this age group. Influenza pneumonia is a particular concern because ongoing infection with this virus predisposes to the development of bacterial superinfection, usually with *S pneumoniae* or *S aureus*.

## Older adolescents

*M pneumoniae* is the most common cause of community-acquired pneumonia during the teenage and young adult years. Atypical pneumonia caused by *C pneumoniae* can present with identical signs and symptoms. Bacterial pneumonia caused by *S pneumoniae* is also seen. Pulmonary infections caused by dimorphic fungi are also seen in this age group. *Histoplasma capsulatum*, which is found in nitrate-rich soil, is usually acquired as a result of inhalation of spores. Chicken coops and other bird roosts and decaying wood are often-cited sources. *Cryptococcus neoformans* is a common infection among pigeon breeders, but it is unusual in other immunocompetent individuals.

Viral pneumonias are common in this age group are usually mild and self-limited, but influenza pneumonia can be severe or protracted, particularly when a bacterial infection follows.

TB pneumonia in children warrants special mention. It can occur in any age group, and it is important to remember that children with TB usually do not present with symptoms until 1-6 months after primary infection. Any child with pneumonia who has a history of TB exposure, or who has traveled to a TB-endemic area of the world needs to be fully evaluated for the possibility of tuberculosis.

Not all pneumonia is caused by infectious agents. Children who have severe gastroesophageal reflux (GERD) may develop chemical pneumonitis secondary to recurrent aspiration. Inhalation of certain chemicals or smoke may cause pulmonary inflammation. Additionally, aspiration pneumonia is more common in children with neurologic impairment, swallowing abnormalities, gastrointestinal motility or a gastrostomy tube. Oral anaerobic flora, with or without aerobes, is the most common etiologic agent.

## Signs & Symptoms

The presenting features of viral and bacterial pneumonia are similar. However, the symptoms of viral pneumonia may be more numerous than the symptoms of bacterial pneumonia. In children under 5 years of age, who have cough and/or difficult breathing, with or without fever, pneumonia is diagnosed by the presence of either fast breathing or lower chest wall indrawing where their chest moves in or retracts during inhalation (in a healthy person, the chest expands during inhalation). Wheezing is more common in viral infections.

Newborns with pneumonia commonly present with poor feeding and irritability, as well as tachypnea, retractions, grunting, and hypoxemia. Very severely ill infants may be unable to feed or drink and may also experience unconsciousness, hypothermia and convulsions.

## Diagnosis

The signs and symptoms of pneumonia are often nonspecific and widely vary based on the patient's age and the infectious organisms involved.

Observing the child's respiratory effort during a physical exam is an important first step in diagnosing pneumonia. The World Health Organization (WHO) respiratory rate thresholds for identifying children with pneumonia are as follows:

- ❑ Children younger than 2 months: Greater than or equal to 60 breaths/min
- ❑ Children aged 2-11 months: Greater than or equal to 50 breaths/min
- ❑ Children aged 12-59 months: Greater than or equal to 40 breaths/min

Assessment of oxygen saturation by pulse oximetry should be performed early in the evaluation when respiratory symptoms are present. Cyanosis may be present in severe cases. Capnography may be useful in the evaluation of children with potential respiratory compromise.

## Other diagnostic tests may include the following:

- ❑ Auscultation
- ❑ Cultures
- ❑ Serology
- ❑ Complete blood cell count (CBC)

- ❑ Chest radiography
- ❑ Ultrasonography

## Management

Initial priorities in children with pneumonia include the identification and treatment of respiratory distress, hypoxemia and hypercarbia. Grunting, flaring, severe tachypnea, and retractions should prompt immediate respiratory support. Most cases of pneumonia require oral antibiotics. High-dose amoxicillin is used as a first-line agent for children with uncomplicated community-acquired pneumonia. Second- or third-generation cephalosporins and macrolide antibiotics such as azithromycin are acceptable alternatives. Combination therapy (ampicillin and either gentamicin or cefotaxime) is typically used in the initial treatment of newborns and young infants. Hospitalization is recommended only for severe cases of pneumonia, and for all cases of pneumonia in infants younger than 2 months of age.

## Prevention

Preventing pneumonia in children is an essential component of a strategy to reduce child mortality. Immunization against Hib, pneumococcus, measles and whooping cough (pertussis) is the most effective way to prevent pneumonia. Adequate nutrition is key to improving children's natural defences, starting with exclusive breastfeeding for the first 6 months of life. In addition to being effective in preventing pneumonia, it also helps to reduce the length of the illness if a child does become ill. Addressing environmental factors such as indoor air pollution (by providing affordable clean indoor stoves, for example) and encouraging good hygiene in crowded homes also reduces the number of children who fall ill with pneumonia. In children infected with HIV, the antibiotic cotrimoxazole is given daily to decrease the risk of contracting pneumonia.

## References :

- ❑ World Health Organization 2015
- ❑ World Health Organization Bulletin 2008
- ❑ Medscape
- ❑ Drugs.com

The postnatal period is well established as an increased time of risk for the development of serious mood disorders. The association between the postpartum period and mood disturbances has been noted since the time of Hippocrates. Women are at increased risk of developing severe psychiatric illness during the puerperium. Studies have shown that a woman has a greatly increased risk of being admitted to a psychiatric hospital within the first month postpartum than at any other time in her life. Up to 12.5% of all psychiatric hospital admissions of women occur during the postpartum period.

However recent evidence from epidemiological and clinical studies suggests that mood disturbances following childbirth are not significantly different from affective illnesses that occur in women at other times. Also, the clinical presentation of depression occurring in the puerperium is similar to major depression occurring at other times, with symptoms of depressed mood, anhedonia and low energy and suicidal ideation commonplace.

The three psychiatric disorders most common after the birth of a baby are postpartum blues, postpartum depression and postpartum psychosis. The prevalence, onset and duration of the three types of postpartum affective disorders are shown in the following Table (Adapted from Nonacs & Cohen, 1998).

Depression and psychosis present risks to both the mother and her infant, making early diagnosis and treatment important. Besides, there are also some other conditions which should be evaluated carefully.

## Postpartum Blue

Postpartum blues refers to a transient condition characterized by irritability, anxiety, decreased concentration, insomnia, tearfulness and mild, often rapid, mood swings from elation to sadness. A large number of postpartum women (30% to 75%) develop

these mood changes, generally within 2 to 3 days of delivery. Symptoms peak on the fifth day postpartum and usually resolve within 2 weeks. Typically, providing support and reassurance to the new mother and stressing the importance of adequate time for sleep and rest will be sufficient treatment for postpartum blues. The use of minor tranquilizers at low doses (e.g., lorazepam 0.5 mg) may be helpful for insomnia. Careful monitoring during this period is essential, since a small proportion of women with postpartum blues may develop postpartum depression.

## Baby pinks

Instead of suffering the baby blues, some women experience baby pinks when they are overly and illogically on top of the world (a mild to severe form of mania). These symptoms can sometimes be a trigger for a pending depressive imbalance, such as postpartum depression or postnatal psychosis.

## Postpartum depression

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) defines postpartum depression (PPD) as depression that occurs within 4 weeks of childbirth. However, most reports on PPD suggest that it can develop at any point during the first year postpartum, with a peak of incidence within the first 4 months postpartum. The prevalence of depression during the postpartum period has been systematically assessed; controlled studies show that between 10% and 28% of women experience a major depressive episode in the postpartum period, with the majority of studies favoring a 10% figure.

Several key risk factors have been identified as major contributors to the development of PPD, including:

- ❑ A history of postpartum depression.
- ❑ A history of depression before conception.
- ❑ A family history of depression, particularly PPD.

Disorder	Prevalence	Onset	Duration	Treatment
Blues	30 - 75%	Day 3 or 4	Hours to days	No treatment required other than reassurance
Postpartum Depression	10 - 15%	Within 12 months	Weeks - months	Treatment usually required
Puerperal Psychosis	0.1 - 0.2 %	Within 2 weeks	Weeks - months	Hospitalization usually required

Table: Three major postpartum psychiatric disorders: summary of onset, duration & treatment



In addition, several other factors may contribute to the development of PPD, including poor social support, the experience of adverse life events during the postpartum period, marital instability, young maternal age, and infants with health problems or perceived “difficult” temperaments.

Symptoms of PPD are similar to the symptoms of a major depressive episode (e.g. Depressed mood, loss of interest or pleasure, significant increases or decreases in appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or guilt, diminished concentration, recurrent thoughts of suicide or death etc.) experienced at any other time. There are, however, subtle differences, including:

- ❑ Difficulty sleeping when the baby sleeps.
- ❑ Lack of enjoyment in the maternal role.
- ❑ Feelings of guilt related to parenting ability.

A significant number of women also experience concomitant symptoms of anxiety, including panic attacks and obsessional fears or images of harm occurring to their babies. These can be very frightening for the mother.

Prior to making a psychiatric diagnosis in the postpartum period, it is important to rule out any underlying medical condition. Women suffering from early postpartum anemia may be at increased risk of developing postpartum depression. Likewise, we know that the postpartum period is associated in some women with pathological changes in thyroid function, especially thyroiditis. Testing for CBC and TSH should be part of a complete workup.

Despite the identified symptoms and risk factors associated with the illness, PPD is often missed at the primary care level. One explanation for this is that the care provider may be more focused on the health of the infant and may therefore miss any signs of maternal psychiatric illness. In addition, many women may try to conceal their illness because of shame or embarrassment about feeling depressed during what is supposed to be such a happy time. The consequences of misdiagnosing or not treating postpartum depression can be serious. For the mother, untreated depression can lead to the development of a chronic depressive illness and

poses a risk of suicide. Untreated PPD can also have many negative consequences for the infant; the negative interactive patterns formed during the critical early bonding period may affect the later development of the child. For example, conduct disorders, inappropriate aggression, and cognitive and attention deficits have been described in children exposed to maternal psychiatric illnesses and these disturbances have continued even after remission of the maternal depression.

Every new mother should be asked about her psychological functioning. Women with a history of major depression or a family history of psychiatric illness should be identified in pregnancy and followed closely in the postpartum period.

A very useful and easily administered screening tool for postpartum depression is the validated Edinburgh Postnatal Depression Scale (Figure 1 & 2). The patient can complete the questionnaire at her physician's office prior to her first postpartum follow-up appointment or when she brings her baby for immunization. For each question, the patient will choose one of four possible replies that reflect how she has been feeling over the past 7 days. Responses are scored as 0, 1, 2, or 3, for a maximum score of 30. A minimum score of 12 has been to identify most women with a diagnosis of postpartum depression.

### Postpartum psychosis

First-onset psychosis in the perinatal period is a rare condition. The prevalence of postpartum psychosis has consistently been reported as approximately 1 to 2 per 1000 live births. This condition has a rapid onset, usually manifesting itself within the first 2 weeks after childbirth or, at most, within 3 months postpartum, and should be considered a medical and obstetrical emergency. The presence of a psychotic disorder may interfere with a woman obtaining proper prenatal and postpartum care.

Several major risk factors have been identified in relation to postpartum psychosis:

- ❑ History of psychosis with previous pregnancies.
- ❑ History of bipolar disorder.
- ❑ Family history of psychotic illness (e.g., schizophrenia or bipolar disorder).

## Edinburgh Postnatal Depression Scale<sup>1</sup> (EPDS)

Name: \_\_\_\_\_ Address: \_\_\_\_\_

Your Date of Birth: \_\_\_\_\_

Baby's Date of Birth: \_\_\_\_\_ Phone: \_\_\_\_\_

As you are pregnant or have recently had a baby, we would like to know how you are feeling. Please check the answer that comes closest to how you have felt **IN THE PAST 7 DAYS**, not just how you feel today.

Here is an example, already completed.

I have felt happy:

- Yes, all the time
- Yes, most of the time      This would mean: "I have felt happy most of the time" during the past week.
- No, not very often      Please complete the other questions in the same way.
- No, not at all

In the past 7 days:

- |   |  |
|---|--|
| <p>1. I have been able to laugh and see the funny side of things</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> As much as I always could</li> <li><input type="checkbox"/> Not quite so much now</li> <li><input type="checkbox"/> Definitely not so much now</li> <li><input type="checkbox"/> Not at all</li> </ul> | <p>*6. Things have been getting on top of me</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes, most of the time I haven't been able to cope at all</li> <li><input type="checkbox"/> Yes, sometimes I haven't been coping as well as usual</li> <li><input type="checkbox"/> No, most of the time I have coped quite well</li> <li><input type="checkbox"/> No, I have been coping as well as ever</li> </ul> |
| <p>2. I have looked forward with enjoyment to things</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> As much as I ever did</li> <li><input type="checkbox"/> Rather less than I used to</li> <li><input type="checkbox"/> Definitely less than I used to</li> <li><input type="checkbox"/> Hardly at all</li> </ul>     | <p>*7. I have been so unhappy that I have had difficulty sleeping</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes, most of the time</li> <li><input type="checkbox"/> Yes, sometimes</li> <li><input type="checkbox"/> Not very often</li> <li><input type="checkbox"/> No, not at all</li> </ul>  |
| <p>*3. I have blamed myself unnecessarily when things went wrong</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes, most of the time</li> <li><input type="checkbox"/> Yes, some of the time</li> <li><input type="checkbox"/> Not very often</li> <li><input type="checkbox"/> No, never</li> </ul>                  | <p>*8. I have felt sad or miserable</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes, most of the time</li> <li><input type="checkbox"/> Yes, quite often</li> <li><input type="checkbox"/> Not very often</li> <li><input type="checkbox"/> No, not at all</li> </ul>  |
| <p>4. I have been anxious or worried for no good reason</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> No, not at all</li> <li><input type="checkbox"/> Hardly ever</li> <li><input type="checkbox"/> Yes, sometimes</li> <li><input type="checkbox"/> Yes, very often</li> </ul>                                      | <p>*9. I have been so unhappy that I have been crying</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes, most of the time</li> <li><input type="checkbox"/> Yes, quite often</li> <li><input type="checkbox"/> Only occasionally</li> <li><input type="checkbox"/> No, never</li> </ul>  |
| <p>5. I have felt scared or panicky for no very good reason</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes, quite a lot</li> <li><input type="checkbox"/> Yes, sometimes</li> <li><input type="checkbox"/> No, not much</li> <li><input type="checkbox"/> No, not at all</li> </ul>                                | <p>*10. The thought of harming myself has occurred to me</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Yes, quite often</li> <li><input type="checkbox"/> Sometimes</li> <li><input type="checkbox"/> Hardly ever</li> <li><input type="checkbox"/> Never</li> </ul>   |

Administered/Reviewed by \_\_\_\_\_ Date \_\_\_\_\_

<sup>1</sup>Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786 .

<sup>2</sup>Source: K. L. Wisner, B. L. Parry, C. M. Piontek, Postpartum Depression N Engl J Med vol. 347, No 3, July 18, 2002, 194-199

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Figure: 1

## Edinburgh Postnatal Depression Scale<sup>1</sup> (EPDS)

Postpartum depression is the most common complication of childbearing. The 10-question Edinburgh Postnatal Depression Scale (EPDS) is a valuable and efficient way of identifying patients at risk for “perinatal” depression. The EPDS is easy to administer and has proven to be an effective screening tool.

Mothers who score above 13 are likely to be suffering from a depressive illness of varying severity. The EPDS score should not override clinical judgment. A careful clinical assessment should be carried out to confirm the diagnosis. The scale indicates how the mother has felt during the previous week. In doubtful cases it may be useful to repeat the tool after 2 weeks. The scale will not detect mothers with anxiety neuroses, phobias or personality disorders.

Women with postpartum depression need not feel alone. They may find useful information on the web sites of the National Women’s Health Information Center <[www.4women.gov](http://www.4women.gov)> and from groups such as Postpartum Support International <[www.chss.iup.edu/postpartum](http://www.chss.iup.edu/postpartum)> and Depression after Delivery <[www.depressionafterdelivery.com](http://www.depressionafterdelivery.com)>.

### SCORING

**QUESTIONS 1, 2, & 4 (without an \*)**

Are scored 0, 1, 2 or 3 with top box scored as 0 and the bottom box scored as 3.

**QUESTIONS 3, 5, 10 (marked with an \*)**

Are reverse scored, with the top box scored as a 3 and the bottom box scored as 0.

Maximum score : 30

Possible Depression : 10 or greater

Always look at item 10 (suicidal thoughts)

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### Instructions for using the Edinburgh Postnatal Depression Scale:

1. The mother is asked to check the response that comes closest to how she has been feeling in the previous 7 days.
2. All the items must be completed.
3. Care should be taken to avoid the possibility of the mother discussing her answers with others. (Answers come from the mother or pregnant woman.)
4. The mother should complete the scale herself, unless she has limited English or has difficulty with reading.

<sup>1</sup>Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786.

<sup>2</sup>Source: K. L. Wisner, B. L. Parry, C. M. Piontek, Postpartum Depression N Engl J Med vol. 347, No 3, July 18, 2002, 194-199

Figure: 2

Patients may present with symptoms resembling an acute manic episode or a psychotic depression. They may present with delusions or hallucinations that are frightening to them. Many patients also have additional symptoms that resemble a delirium and involve distractibility, labile mood, and transient confusion.

Patients with postpartum psychosis have lost touch with reality and are at risk of harming themselves or their babies. Postpartum psychosis is an emergency that requires immediate medical attention. In most cases, it will be necessary for the mother to be hospitalized until she is stable.

Medications (including antidepressants, neuroleptics, and mood stabilizers) or electroconvulsive therapy may be needed to control the psychosis.

The absolute risk of neonaticide (death of the baby within 24 hours of birth) and of infanticide (death within the first year of life) committed by the mother are not known. Both are relatively rare but attract much media attention when they occur. It is imperative to ask all women suffering from a postpartum illness if they have any thoughts or plans of harming themselves or their children. Patients presenting with suicidal or infanticidal plans require emergency hospitalization.

## Others

### Disorders of the mother-infant relationship

Childbirth presents many challenges to the mother: trauma, sleep deprivation, breastfeeding, adjustments in conjugal and other relationships, and social isolation. However, the central and most important psychological process is development of the relationship with the infant. Disturbances in this process were recognised long ago, when hatred of children and child abuse were described. Various terms have been used for these disturbances. "Bonding" is a useful lay term, but neither "bonding" nor "attachment" describes the essential symptom, which is the mother's emotional response to the infant-aversion, hatred, or pathological anger. "Mother-infant interaction" reflects this response and has the advantage that it can be recorded and measured. But the concept of "postnatal depression with impaired mother-infant interaction" is inadequate to encompass such a profound emotional disorder, which can

occur without depression. The concept of mother-infant relationship disorder is controversial. It is not recognised in the tenth revision of the International Classification of Diseases (ICD-10) nor the Diagnostic and Statistical Manual IV (DSM-IV). One of the challenges for ICD-11 and DSMV is to find a place for these disorders, so that they can be recognised by practitioners and referred for expert treatment. This process will involve a difficult innovation, because "hatred" does not fit comfortably with the concept of disease or illness. But medicine has pragmatic rather than logical boundaries, and psychiatry often challenges the definition of disease.

Disorders of the mother-infant relationship are prominent in 10-25% of women referred to psychiatrists after childbirth. At the extreme of rejection of the infant, the mother may try to persuade a family member to take over care permanently or may demand that the baby be adopted. She may try to escape. The most poignant manifestation is the wish that the baby disappear-be stolen or succumb to cot death. Rejection is accompanied in many cases by pathological anger, with shouting, cursing or screaming at the infant, accompanied by impulses to strike, shake, or smother the child. These disorders are more common, intractable, and serious in their effects than puerperal psychosis. With treatment, they can resolve completely. Without it, there are high risks of child abuse and neglect, long-term impairment of the mother-child relationship, and psychiatric or learning disorders in the children. The effects have been studied indirectly through cohort studies of children born after refused termination of pregnancy.

For example, a Danish study followed up unwanted children in a cohort of 4269 male births. A combination of birth complications and early child rejection carried a risk of violent criminality four times higher than the reference category.

In management, depression should be treated, even when signs are negligible. The specific psychological treatment is play therapy in various forms, interaction coaching, or baby massage, which can be undertaken by nursing staff or psychologists. The aim is to help the mother to enjoy her interactions with the child.

**Post-traumatic stress disorder (PTSD)**

Long ordeals during labour led to secondary tocophobia, and the recurrence of tension, nightmares, and flashbacks towards the end of the next pregnancy. There are now about 40 publications on this disorder, which has been called the fourth postpartum mental disorder. The stressful experience is pain in most cases, but loss of control and fear of death can be the focus. There have been eight quantitative studies. Case reports suggest that depression, an impaired mother-infant relationship, and sexual dysfunction can result. In Stockholm, half of mothers with a very negative birth experience at their first delivery avoided any further pregnancy. These women should be referred for specific psychological treatment, such as massed practice, which might accelerate accommodation to the traumatic memory.

**Various morbid preoccupations**

Distress about the bodily changes resulting from pregnancy and childbirth are common. Such women complain of weight gain, stretch marks, or scars. They are reluctant to undress in front of their partners, avoid looking at themselves naked, and can even avoid being seen in public. In an unpublished prospective interview study of over 200 patients in the UK and New Zealand, this distress amounted to dysmorphophobia in 14% of clinic patients.

Conjugal jealousy is another disorder sometimes linked to pregnancy and childbirth. Preoccupying worries about the spouse's fidelity are an understandable reaction to pregnancy changes and the relative quiescence of sexual life.

Complaints about obstetric management can be preoccupying. They are relatively common after emergency caesarean section. Childbirth is a key experience, and a woman may feel bitter disappointment over delivery perceived as mismanaged. Such feelings can lead to litigation and in some cases preoccupy the woman for weeks or months and interfere with care of the infant.

These disorders are sometimes confused with PTSD, but the dominant emotion is ruminative anger not anxiety and the treatment is different—distraction

from the perceived injury and redirection of attention to positive activity.

**Anxiety disorders specific to the puerperium**

Several studies have reported the effect of pregnancy on panic disorder. A review of eight studies showed no overall effect: in 41% pregnancy brought an improvement, but in 44% there was an exacerbation in the postpartum period and in 10% new onset in the puerperium. Recent studies suggest that postpartum anxiety disorders are under-emphasised and are more common than depression. There could be a biological basis for some postpartum anxiety. A study found that the growth-hormone response to apomorphine (a test of dopamine D2 receptor sensitivity) in 14 puerperal women with a history of depression. The greatest increase in receptor sensitivity was found in three women who developed postpartum anxiety disorders.

ICD-10 and DSM-IV give criteria for anxiety disorders as a group, but the focus of anxiety is also important, because it can indicate specific psychological treatment. This issue is a challenge for the next generation of international classifications. De Armond described fear of the newborn infant based on the awesome responsibility of care. Most women are shielded from this fear by family support, but in isolated nuclear families it can be a severe problem. Support from family or nursing staff is all that is required. Fear of cot death can reach a pathological degree. Reproductive losses (eg, recurrent miscarriage) or infertility of long duration can be an antecedent factor. The main manifestation is nocturnal vigilance. The mother lies awake listening to the infant's breathing, and often checks that he or she is still alive. This fear can last for months and lead to exhausting sleep deprivation. It is not easy to treat. A baby monitor can be useful, as can nights of respite, when another trusted person looks after the infant and the mother sleeps under sedation. Involvement of a panel of mothers who have recovered from this disorder is useful, as in other postpartum disorders. Many mothers are excessively anxious about the health and safety of their children, described as maternity neurosis or maternal separation anxiety. There is some evidence that severe postpartum anxiety has adverse effects on the child, with a high proportion of insecure and disorganised attachments.

A woman with infant-focused anxiety may avoid the infant in a typical phobic reaction. Such women respond well to treatment by desensitisation in a mother and baby unit. Many cases of postpartum anxiety disorders require the skills of a clinical psychologist, using relaxation techniques and cognitive therapy.

## Obsessions of child harm

Obsessions of infanticide were one of the first postpartum disorders to be described, and several recent series have been published. The central symptom is of impulses to attack the child, but the setting is different from the pathological anger that precedes child abuse.

The mother is gentle and devoted. She experiences extravagant infanticidal impulses, together with fantasies of the family's horror and grief, causing intense distress and leading to reduced contact with the baby. The content can include child sexual abuse. Classic papers were written by Chapman and Button and Reivich, who found 42 cases among 1317 consecutive consultations. Buttolph and Holland reported that 27 of 39 female patients with obsessive compulsive disorder had onset or worsening in pregnancy or after childbirth. Jennings and colleagues interviewed 100 depressed mothers: 21 had repeated thoughts of harming their children and took precautions, and 24 were afraid to be alone with their children. An Italian group studied the triggers of obsessive compulsive disorder and found that childbirth was the only life event significantly associated with onset. The management involves specific psychological treatment as well as antidepressant therapy. Avoidance of the child should be discouraged and cuddling and play encouraged, strengthening positive maternal feelings.

## Drugs and breast feeding

The welfare of the child during treatment of the mother is always an important consideration and may dictate that bottle feeding be substituted for breast feeding. Psychotropic drugs, like most medications, are excreted in breast milk, the concentration depending on the solubility, protein-binding characteristics and pH of the drug. The pH of breast milk is 6.8 and that of plasma 7.4, so that acidic drugs concentrate less in breast milk than do alkaline

drugs. A general rule is that the concentration of drugs in breast milk is about 10% of the level in the mother's plasma, but there are wide variations.

The use of antidepressant medications in women who are breast feeding is controversial. A study stated that therapeutic levels of the tricyclic antidepressants are not excreted in breast milk in sufficient amounts to harm the baby; however, their effect on the infant's developing neurotransmitter system is not known, an uncertainty that warrants caution in their use for nursing mothers.

Benzodiazepines, which are sometimes administered to patients with puerperal neurotic depression, cause serious risk to the newborn, producing lethargy and impairing temperature regulation. They are not metabolized in the neonatal gut or liver from day 1 to 4, and they may cause jaundice, as the newborn is unable to conjugate them with glucuronic acid.

The major tranquillizers appear to concentrate less in breast milk than do the other medications; the breast milk level is one third of the level in maternal plasma and has not been associated with side effects in human newborns despite several large studies. However, some animal studies have shown serious side effects of haloperidol, and in our opinion caution is warranted in the use of such drugs.

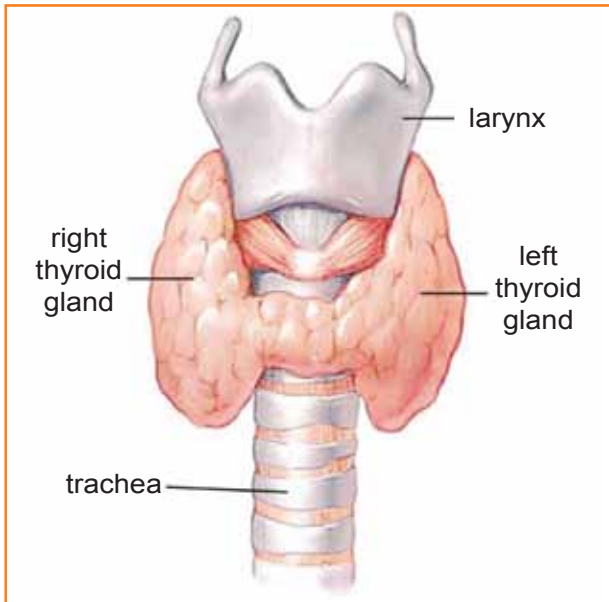
Although a study have asserted that nursing mothers can safely take lithium, other researchers have reported severe toxic effects in the infants.

The postpartum period can be a vulnerable time for women, particularly those with a history of psychiatric illness or a family history of psychiatric illness. Not treating a psychiatric disorder in the postpartum period can have both short and long-term consequences for both the infant and the mother. Administering a routine screening test, such as the Edinburgh Postnatal Depression Scale, can help identify those mothers who require treatment.

## Reference:

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- ❑ [www.thelancet.com](http://www.thelancet.com)
- ❑ CAN MED ASSOC J
- ❑ [www.who.int](http://www.who.int)

Thyroid disease is the most common endocrine condition affecting 1% of women of reproductive age due to the complex interplay between the hypothalamo-pituitary axis and the thyroid gland.



Thyroid hormones act systemically to control metabolism. It affects nearly every organ system in the body and appears to be a major regulator of metabolism. Thyroid Stimulating Hormone (TSH) controls the thyroid gland by inducing the transport of iodine into the gland, and then the subsequent

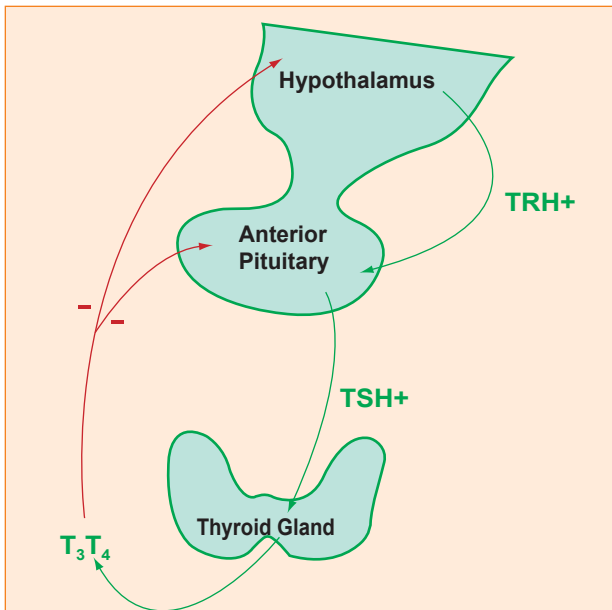


Figure: Regulation of thyroid hormone release. T<sub>3</sub> = triiodothyronine; T<sub>4</sub> = thyroxine; TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone

secretion of thyroxine (T<sub>4</sub>) and Triiodothyronine (T<sub>3</sub>) into circulation. Because function of the thyroid gland is under the control of the hypothalamo-pituitary axis, changes in thyroid function can impact greatly on reproductive function before, during and after conception. Abnormalities in thyroid function, including hyperthyroidism and hypothyroidism, can have an adverse effect on reproductive health and result in reduced rates of conception, increased early pregnancy loss and adverse pregnancy and neonatal outcomes. There is increasing evidence for the role of autoantibodies in subfertility and early pregnancy loss, even in euthyroid women.

### The thyroid gland and abnormalities of functions

The thyroid gland controls the rate of metabolic processes throughout the body via the production of two hormones triiodothyronine and thyroxine (T<sub>4</sub>). These hormones also have key roles in growth and development, particularly brain development. Thyroid hormone release is under the control of the hypothalamus and anterior pituitary gland.

Hypothyroidism	Hyperthyroidism
<b>Primary hypothyroidism</b> Autoimmune disease <input type="checkbox"/> Atrophic thyroiditis <input type="checkbox"/> Hashimoto's thyroiditis  <b>Iatrogenic</b> <input type="checkbox"/> Radioiodine therapy <input type="checkbox"/> Thyroidectomy <input type="checkbox"/> Antithyroid drugs  <b>Transient</b> <input type="checkbox"/> Subacute (de Quervain's) thyroiditis <input type="checkbox"/> Postpartum thyroiditis Iodine deficiency	Autoimmune <input type="checkbox"/> Grave's disease  Toxic nodular Goitre Toxic adenoma Subacute thyroiditis Iodine therapy Drugs (amiodarone, lithium)
<b>Secondary hypothyroidism</b> <input type="checkbox"/> Pituitary failure <input type="checkbox"/> Pituitary tumour	
<b>Tertiary hypothyroidism</b> <input type="checkbox"/> Hypothalamic failure	

Table : Causes of thyroid disease

Thyroid disease is classically divided into hyperthyroidism and hypothyroidism and the causes of thyroid disease are numerous. There is also a subset of patients who are euthyroid and have positive thyroid autoantibodies. The role of these antibodies in reproductive health has received increasing attention over recent years.

## Risk factors for thyroid dysfunction

- ❑ History of thyroid dysfunction/thyroid surgery
- ❑ Family history of thyroid disease
- ❑ Goitre
- ❑ Positive thyroid autoantibodies
- ❑ Clinical symptoms/signs of hypothyroidism
- ❑ Diabetes type I
- ❑ History of miscarriage/preterm delivery
- ❑ Other autoimmune disorders
- ❑ History of subfertility
- ❑ History of therapeutic head or neck irradiation
- ❑ Age  $\geq 30$  years
- ❑ Previous treatment with amiodarone
- ❑ Previous treatment with lithium
- ❑ Recent exposure to iodinated radiological contrast agents

## Hypothyroidism and infertility

Hypothyroidism is common in women of reproductive age and is defined as an abnormally elevated TSH concentration. This dysfunction has been shown to adversely affect fertility. The prevalence of hypothyroidism in women in the reproductive age (20-40 years) varies between 2% and 4%. Hypothyroidism is associated with a range of reproductive disorders, from abnormal sexual development to menstrual irregularities and infertility.

Severe hypothyroidism is commonly associated with failure of ovulation, but ovulation and conception can still occur in milder hypothyroidism. In adult women, more common ovulatory disorders associated with hypothyroidism include irregularities in the menstrual cycle, such as changes in cycle length and blood flow, as well as hirsutism. Menorrhagia is the most prevalent symptom and occurs in 60% of overt hypothyroid women. The impact of hypothyroidism on menstrual function and ovulation is related to numerous interactions of thyroid hormones with the female reproductive system.

Mild thyroid failure or subclinical hypothyroidism has a prevalence of approximately 2-4% and is characterized by raised serum thyroid-stimulating hormone (TSH) of more than 4.5 mU/l in combination with a normal T4 (9-25 pmol/l) and no clinical symptoms or

signs of hypothyroidism. Subclinical hypothyroidism is also associated with pregnancy loss and preterm delivery.

Hypothyroidism is known to affect pulsatile release of gonadotrophin-releasing hormone, which is required for cyclical release of follicle-stimulating hormone and luteinising hormone and subsequent ovulation. Additionally, thyroid hormone receptors are known to be expressed by ovarian granulosa cells, cumulus cells and oocytes themselves and may have a role in enabling activation of luteinising hormone receptors and progesterone production. Hypothyroidism may also alter feedback to the pituitary by changing estrogen metabolism and circulating levels of sex hormone-binding globulin.

## Hyperthyroidism and infertility

Hyperthyroidism (both clinical and subclinical) is thought to be found in approximately 2.3% of women presenting with subfertility, compared with an incidence of 1.5% of women in the general population. The link between hyperthyroidism and menstrual irregularity is well established and is most frequently associated with hypomenorrhoea and polymenorrhoea. The likely mechanism for these menstrual disturbances is an increased sensitivity to gonadotrophin-releasing hormone, resulting in a raised level of luteinising hormone and sex hormone-binding globulin, causing a rise in total estrogens. Hyperthyroxinemia increases the gonadotrophin response to GnRH and baseline gonadotrophin concentrations are also frequently elevated. The decrease in menstrual flow may also relate to effects on haemostatic factors, including the synthesis of factor VIII. Despite these metabolic changes, however, these thyroid-induced changes in the hypothalamo-pituitary-ovarian axis do not appear to be associated with anovulation and most women with hyperthyroidism remain ovulatory.

## Autoimmune Thyroid Disease (AITD) and infertility

Autoimmune thyroid disease (AITD) is the most common cause of hypothyroidism in women of reproductive age. The prevalence of AITD is 5-10 times higher in women than in men, which might be explained by genetic factors, the effects of oestrogens and perhaps chromosome X abnormalities.



There are two key aspects of thyroid autoimmunity. Firstly AITD is the most common autoimmune disorder in the female population, affecting 5-10% of women of childbearing age and secondly it is the most frequent cause of thyroid failure (sub-clinical and overt hyperthyroidism). Furthermore, AITD can be present without thyroid dysfunction and thus often goes undiagnosed.

Thyroid autoantibodies are present in almost all patients with Hashimoto's thyroiditis, two-thirds of those with postpartum thyroiditis and three-quarters of those with Graves' disease. The prevalence of thyroid autoimmunity has been found to be consistently increased in the subfertile population compared with fertile controls and is found to be high in those with endometriosis and polycystic ovary syndrome (PCOS). It is well established that a proportion of people with AITD have normal serum TSH. It has been suggested that thyroid autoantibodies are an early sign of lymphocytic infiltration and therefore a predictor of thyroid disease. Increased rates of subfertility are also seen in euthyroid women with AITD.

AITD has been consistently associated with poorer outcomes in the fertility setting in euthyroid women and specifically in those undergoing assisted conception, including lower fertilisation rates, poorer embryo quality and lower pregnancy rates.

### Management in clinical practice

Screening for thyroid function and autoimmunity should be performed as part of the work-up in women with infertility. Screening and treatment in women of infertile couples should be justified, based on the significant risks to offspring, the probable benefit of treatment and the probable low incidence of adverse outcomes from intervention. Given the potential implications of hypothyroidism on ovulatory function, screening is certainly recommended in the presence of OD (ovarian dysfunction). Screening and treating of thyroid disease in infertile women can be beneficial in the following ways:

- ❑ potential reversal of infertility
- ❑ avoidance of expensive ART procedures
- ❑ avoiding the evolution to overt thyroid dysfunction in pregnancy,

- ❑ avoiding the increased risk of miscarriage and postpartum thyroiditis and depression.

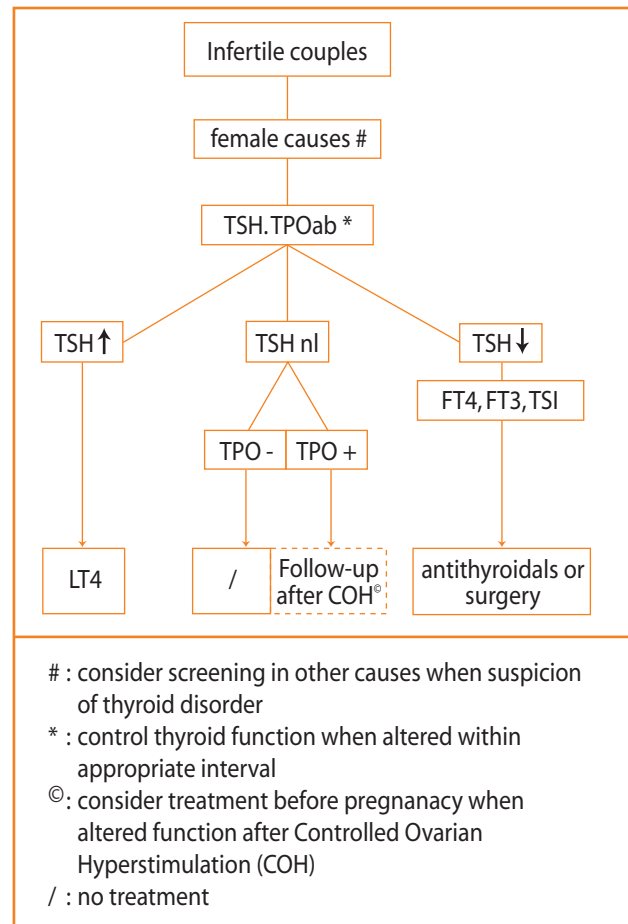


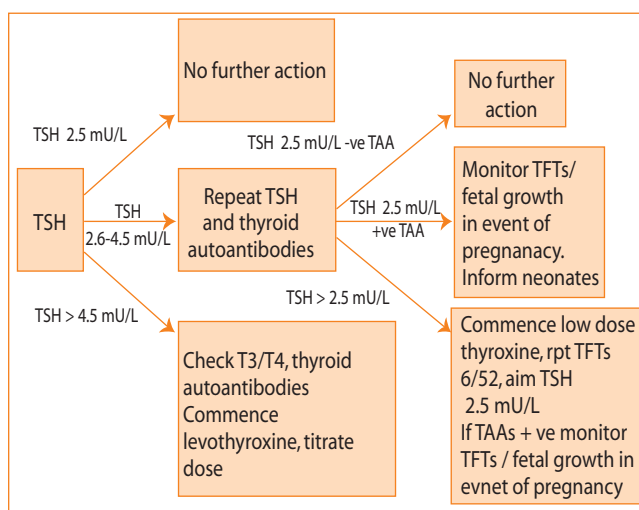
Figure: Algorithm for the screening of thyroid dysfunction and autoimmunity in infertile women.

Initially screening should include a serum TSH (normal range is approximately 0.5 to 5.5 mU/L) test, with the full panel of thyroid levels including Free Thyroxine (T4) (approximate normal range of free T4 is 0.8-2.0 mU/L) and thyroid antibodies. A first finding of subclinical hypothyroidism is high TSH (serum TSH of more than 2.5 mU/L with normal free T4) should prompt a repeat serum TSH level and for thyroid autoantibodies to be checked. Serum TSH levels should be maintained below 2.5 mU/L for those with both clinical and subclinical hypothyroidism.

If the serum TSH persists above 2.5 mU/L, Levo-Thyroxine (LT4) is a drug that can be used to treat it. The dose of LT4 should be titrated until the serum TSH is brought to 2.5 mU/L or less and during this period monitoring of T4 and TSH every six weeks is recommended.

Treatment with LT<sub>4</sub> is straightforward and has been shown to normalize PRL levels, to restore normal LH responses to its releasing hormone, to revert menstrual disturbances to normal levels and increase spontaneous fertility.

Women with suggestive of hyperthyroidism and infertility, should undergo a complete laboratory work-up and receive appropriate treatment. Although treatment of hyperthyroidism in infertile women is advisable for general health and to improve pregnancy outcomes. With pre-existing hyperthyroidism should continue on anti-thyroid medication and should closely monitor thyroid function.



**Figure:** Management of hypothyroidism in the fertility setting. T<sub>3</sub> = triiodothyronine; T<sub>4</sub> = thyroxine; TAA = thyroid antithyroglobulin antibody; TFT = thyroid function test; TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone

Women should be advised to achieve euthyroidism before planning a pregnancy. Importantly, as radioactive iodine is a commonly employed treatment for hyperthyroidism, particularly Graves' disease, radioactive iodine has not been associated with deterioration in gonadal function or adverse outcomes in offspring. However conception should be delayed for at least 6 months after radioactive iodine therapy. For those on medical therapy, propylthiouracil is the preferred agent, because of lower levels of teratogenicity. However, guidelines now suggest for carbimazole in the second trimester because of propylthiouracil-associated hepatotoxicity in offspring. Whichever agent is used, doses should be kept at the lowest possible level to achieve euthyroidism.

It is likely that euthyroid women with AITD have lymphocytic infiltration of the thyroid gland. It has been suggested that these women have a 5-10% risk of developing hypothyroidism in pregnancy, as a result of the increased requirement for T<sub>4</sub> in pregnancy. Studies have suggested that euthyroid women with AITD have a two to five-fold increased risk of an early miscarriage or preterm labour.

However, the risk during pregnancy for a woman with AITD and her unborn child can be reduced considerably with early administration of LT<sub>4</sub>. Though routine treatment of euthyroid women with AITD with LT<sub>4</sub> in pregnancy is not recommended.

## Conclusions

Thyroid hormones play an important role in normal reproductive function both through direct effects on the ovaries and indirectly by interacting with sex hormone binding proteins. Both hypo- and hyperthyroidism can disturb the normal menstrual pattern. Thyroid disease can lead to (reversible) menstrual irregularities and infertility and thereby effects on reproduction from conception to birth.

Women with infertility should be screened for thyroid dysfunction, particularly because endometriosis and the PCOS are more prone to be associated with AITD. Thyroid autoimmunity is significantly more common in infertile women and especially in women with endometriosis, compared with fertile women of reproductive age. However, with appropriate screening and prompt management, risks can be significantly reduced.

## References:

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**I**mmunodeficiency (or immune deficiency) is a state in which the immune system's ability to fight infectious disease is compromised or entirely absent. Immunodeficiency may also decrease cancer immunosurveillance. Most cases of immunodeficiency are acquired ("secondary") but some people are born with defects in their immune system, or primary immunodeficiency. Transplant patients take medications to suppress their immune system as an anti-rejection measure, as do some patients suffering from an over-active immune system. A person who has an immunodeficiency of any kind is said to be immunocompromised.

Distinctions between primary versus secondary immunodeficiencies are based on, respectively, whether the cause originates in the immune system itself or is, in turn, due to insufficiency of a supporting component of it or an external decreasing factor of it.

### Primary immunodeficiencies

A number of rare diseases feature a heightened susceptibility to infections from childhood onward. Primary Immunodeficiency is also known as congenital immunodeficiencies. Many of these disorders are hereditary and are autosomal recessive or X-linked. There are over 80 recognised primary immunodeficiency syndromes; they are generally grouped by the part of the immune system that is malfunctioning, such as lymphocytes or granulocytes.

The treatment of primary immunodeficiencies depends on the nature of the defect and may involve antibody infusions, long-term antibiotics and (in some cases) stem cell transplantation.

### Secondary immunodeficiencies

Secondary immunodeficiencies, also known as acquired immunodeficiencies, can result from various immunosuppressive agents, for example, malnutrition, aging and particular medications (e.g. chemotherapy, disease-modifying antirheumatic drugs, immunosuppressive drugs after organ transplants, glucocorticoids). For medications, the term immunosuppression generally refers to both beneficial and potential adverse effects of decreasing the function of the immune system, while the term immunode-

ficiency generally refers solely to the adverse effect of increased risk for infection.

Many specific diseases directly or indirectly cause immunosuppression. This includes many types of cancer, particularly those of the bone marrow and blood cells (leukemia, lymphoma, multiple myeloma), and certain chronic infections. Immunodeficiency is also the hallmark of acquired immunodeficiency syndrome (AIDS), caused by the human immunodeficiency virus (HIV). HIV directly infects a small number of T helper cells and also impairs other immune system responses indirectly.

### Primary Immunodeficiency

#### Definition

Primary immunodeficiency disorders - also called primary immune disorders or primary immunodeficiency - weaken the immune system, allowing infections and other health problems to occur more easily.

Many people with primary immunodeficiency are born missing some of the body's immune defenses, which leaves them more susceptible to germs that can cause infections.

Some forms of primary immunodeficiency are so mild they may go unnoticed for years. Other types are severe enough that they're discovered almost as soon as an affected baby is born.

Treatments can boost the immune system for many types of primary immunodeficiency disorders. Most people with the condition lead relatively normal, productive lives.

#### Symptoms

One of the most common signs of primary immunodeficiency is an increased susceptibility to infections. Someone may have infections that are more frequent, longer lasting or harder to treat than are the infections of one with a normal immune system. Someone may also get infections that a person with a healthy immune system likely wouldn't get (opportunistic infections).

Signs and symptoms differ depending on the type of primary immunodeficiency disorder, and they vary from person to person.

## Signs and symptoms of primary immunodeficiency can include:

- ❑ Frequent and recurrent pneumonia, bronchitis, sinus infections, ear infections, meningitis or skin infections
- ❑ Inflammation and infection of internal organs
- ❑ Blood disorders, such as low platelet counts or anemia
- ❑ Digestive problems, such as cramping, loss of appetite, nausea and diarrhea
- ❑ Delayed growth and development
- ❑ Autoimmune disorders, such as lupus, rheumatoid arthritis or type 1 diabetes

## Causes

Many primary immunodeficiency disorders are inherited - passed down from one or both parents. Problems in the DNA - the genetic code that acts as a blueprint for producing the cells that make up the human body - cause many of the immune system defects in primary immunodeficiency.

There are numerous types of primary immunodeficiency disorders. In fact, research has led to a dramatic increase in the number of recognized primary immunodeficiency disorders in recent years, so they are not as rare as once thought. They can be broadly classified into six groups based on the part of the immune system that is affected:

- ❑ B cell (antibody) deficiencies
- ❑ T cell deficiencies
- ❑ Combination B and T cell deficiencies
- ❑ Defective phagocytes
- ❑ Complement deficiencies
- ❑ Unknown (idiopathic)

## Risk factors

The only known risk factor is having a family history of a primary immune deficiency disorder.

## Complications

Complications caused by primary immunodeficiency disorders vary, depending on what type a person has. They can include:

- ❑ Recurrent infections

- ❑ Autoimmune disorders
- ❑ Damage to heart, lungs, nervous system or digestive tract
- ❑ Slowed growth
- ❑ Increased risk of cancer
- ❑ Death from serious infection

which increases the risk of having the condition.

## Tests and diagnosis

To help decide whether recurrent infections could be due to primary immunodeficiency, doctor will ask about the history of illnesses and whether any close relatives have an inherited immune system disorder.

A physical examination is usually performed. Tests used to diagnose an immune disorder include:

- ❑ **Blood tests.** Blood tests can determine if someone has normal levels of infection-fighting proteins (immunoglobulin) in your blood and measure the levels of blood cells and immune system cells. Abnormal numbers of certain cells can indicate an immune system defect.

Blood tests also can determine if your immune system is responding properly and producing antibodies - proteins that identify and kill foreign invaders such as bacteria or viruses.

- ❑ **Prenatal testing.** Parents who've had a child with a primary immunodeficiency disorder may want to be tested for certain immunodeficiency disorders during future pregnancies. Samples of the amniotic fluid, blood or cells from the tissue that will become the placenta (chorion) are tested for abnormalities.

In some cases, DNA testing is done to test for a genetic defect. Test results make it possible to prepare for treatment soon after birth, if necessary.

## Treatments and drugs

Treatments for primary immunodeficiency involve preventing and treating infections, boosting the immune system, and treating the underlying cause of the immune problem. In some cases, primary immune disorders are linked to a serious illness, such as an autoimmune disorder or cancer, which also needs to be treated.

## Managing infections

- ❑ **Treating infections.** Infections require rapid and aggressive treatment with antibiotics. Infections that don't respond may require hospitalization and intravenous (IV) antibiotics.
- ❑ **Preventing infections.** Some people need long-term antibiotics to prevent respiratory infections and associated permanent damage to the lungs and ears. Children with primary immunodeficiency may not be able to have vaccines containing live viruses, such as oral polio and measles-mumps-rubella.
- ❑ **Treating symptoms.** Medications such as ibuprofen for pain and fever, decongestants for sinus congestion, and expectorants to thin mucus in the airways may help relieve symptoms caused by infections.

Postural drainage - using gravity and light blows to the chest to clear the lungs - may help relieve the discomfort of repeated (chronic) respiratory infections.

## Treatment to boost the immune system

- ❑ **Immunoglobulin therapy.** Immunoglobulin consists of antibody proteins needed for the immune system to fight infections. It can either be injected into a vein through an IV line or inserted underneath the skin (subcutaneous infusion). IV treatment is needed every few weeks and subcutaneous infusion is needed once or twice a week.
- ❑ **Gamma interferon therapy.** Interferons are naturally occurring substances that fight viruses and stimulate immune system cells. Gamma interferon is a manufactured (synthetic) substance given as an injection in the thigh or arm three times a week. It's used to treat chronic granulomatous disease, one form of primary immunodeficiency.
- ❑ **Growth factors.** When immune deficiency is caused by a lack of certain white blood cells, growth factor therapy can help increase the levels of immune-strengthening white blood cells.

## Stem cell transplantation

Stem cell transplantation offers a permanent cure for

several forms of life-threatening immunodeficiency. Normal stem cells are transferred to the person with immunodeficiency, giving him or her a normally functioning immune system. Stem cells can be harvested through bone marrow, or they can be obtained from the placenta at birth (cord blood banking).

The stem cell donor - usually a parent or other close relative - must have body tissues that are a close biological match to those of the person with primary immunodeficiency. Even with a good match, however, stem cell transplants do not always work.

The treatment often requires that functioning immune cells be destroyed using chemotherapy or radiation before the transplants, leaving the transplant recipient temporarily even more vulnerable to infection.

## Coping and support

Most people with primary immunodeficiency can go to school and work like everyone else. Still, one may feel as if no one understands what it's like to live with the constant threat of infections. Talking to someone who faces similar challenges may help.

Patients may ask doctor if there are support groups in the area for people with primary immunodeficiency or for parents of children with the disease.

## Prevention

Because primary immune disorders are caused by genetic defects, there's no way to prevent them. But when someone has a weakened immune system, he/she can take steps to prevent infections:

- ❑ Practise good hygiene
- ❑ Take care of teeth
- ❑ Eat healthy, balanced diet
- ❑ Be physically active
- ❑ Get enough & regular sleep
- ❑ Manage stress
- ❑ Avoid exposure from people with colds or other infections and avoid crowds

## References:

- ❑ [www.wikipedia.org](http://www.wikipedia.org)
- ❑ [www.mayoclinic.org](http://www.mayoclinic.org)

## Test Yourself - 38

Correct Answers :

1. c   2. b   3. c   4. a   5. b   6. c

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## Test Yourself - 39

1. The followings are true for "Thyroid Disease & Female Infertility" except :

- Thyroid hormones affect nearly every organ system in the body.
- Changes in thyroid function can impact greatly before, during and after conception
- Hypothyroidism only can disturb the normal menstrual pattern.
- Women should be advised to achieve euthyroidism before planning a pregnancy.

2. All the followings are correct for "Postpartum Psychiatric Disorder" except :

- Postpartum depression can develop at any point during the first year postpartum.
- Postpartum depression is often missed at the primary care level.
- Edinburgh Postnatal Depression Scale is a very useful and easily administered scoring tool for postpartum depression.
- Postpartum psychosis has a delayed onset and within 01 year postpartum.

3. All the below are true for "Pneumonia in Children" except :

- Children with viral pneumonia cannot develop bacterial pneumonia.
- Malnutrition, low birth weight is among the definite risk factors of pneumonia.
- About 150 million new cases occur annually among children younger than five years worldwide.
- The specific etiologic agents vary based on aged groups.

4. All the followings are correct for "Immune Deficiency Disorders" except :

- Most cases of immunodeficiency are acquired.
- Many specific diseases directly or indirectly cause immunosuppression.
- Primary immunodeficiency disorders can be broadly classified into six groups based on the part of the immune system affected.
- Stem cell transplantation does not provide any permanent cure for immunodeficiency.

5. The followings are right for "Postpartum Psychiatric Disorder" except :

- Women are at increased risk of developing severe psychiatric illness during the puerperium.
- Postpartum blues, postpartum depression and postpartum psychosis are most common after birth of a baby.
- Depression and psychosis present risks to the mother only.
- Symptoms of postpartum depression are similar to symptoms of a major depressive episode experienced at any other time.

6. All the followings are correct for "Pneumonia in Children" except :

- Observing the child's respiratory effort during physical examination is an important step in diagnosing pneumonia.
- Assessment of oxygen saturation should be performed infrequently in the evaluation when respiratory symptoms present.
- Identification and treatment of respiratory distress, hypoxemias are among the initial priorities in children with pneumonia.
- Hospitalization is recommended only for severe cases and infants younger than two month of age.

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