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the SQUARE Healthcare bulletin

- Safe Blood Transfusion
- Melioidosis
- Pregnancy and Diabetes
- Viral Pneumonia

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the SQUARE
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Contents

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Editorial

Dear Doctor,

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

At the start of 2014 we take this opportunity to offer our best wishes from the editorial team of "the SQUARE" !

In this issue we have presented a blend of topics. Firstly, we focused on "Safe Blood Transfusion". Blood safety encompasses actions aimed at ensuring that everyone has access to blood and blood products that are as safe as possible, available at reasonable cost, adequate to meet the needs of patients, transfused only when necessary. We have emphasized on "Melioidosis", a disease of public health importance in Southeast Asia and northern Australia that is associated with high case-fatality rates in humans and animals. True global prevalence of melioidosis is challenged by the fact that clinical symptoms associated with *B. pseudomallei* infection are extremely varied and may be confused with diverse conditions such as lung cancer, tuberculosis, or *Staphyloccocus aureus* infection. Here, we have also included a topic on "Pregnancy and Diabetes". Diabetes is often diagnosed in women during their childbearing years and can affect the health of both the mother and her unborn child. Poor control of diabetes during pregnancy increases the chances for birth defects and other problems for the baby. It can cause serious complications for the women, also. Besides, in this issue we have presented a feature on "Viral Pneumonia". Depending on the virulence of the organism, as well as the age and co morbidities of the patient, viral pneumonia can vary from a mild and self-limited illness to a life-threatening disease. You will also find our regular features "Test Yourself" and "Product Profile" in this issue.

We hope that you will find this healthcare bulletin both interesting and informative.

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

Thank you !

Omar Akramur Rab

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Key title: The square (Dhaka)
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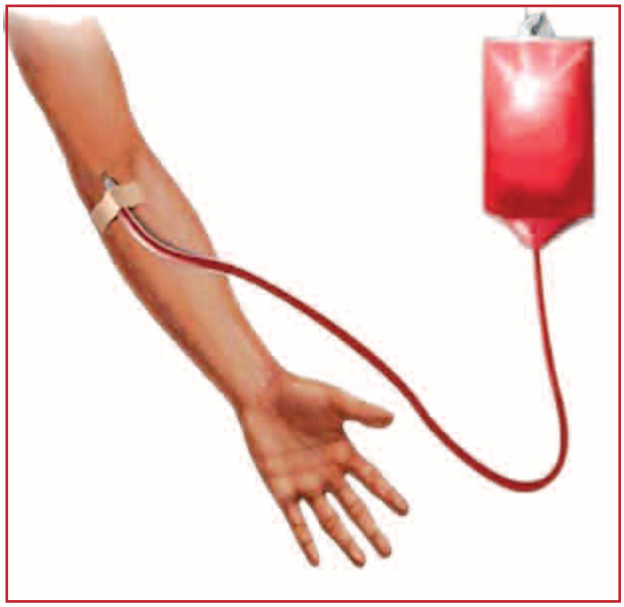
Safe Blood Transfusion

There is much data internationally and locally which confirms that regular voluntary, non-remunerated blood donors are the safest as they have the lowest prevalence of transfusion transmissible infections (TTIs). In accordance with internationally accepted guidelines and ethics, all blood for transfusion should be collected from voluntary non-remunerated blood donors from low risk population groups and strategies should be implemented to encourage regular voluntary non-remunerated blood donation. According to the International Society of Blood Transfusion (ISBT) Code of Ethics which was also adopted by the World Health Organisation (WHO), a donation is considered voluntary and non-remunerated if the person gives his/her blood of his/her own free will, without any coercion and receives no payment for it either in the form of cash or in kind, which could be considered a substitute for money. This would include time off work other than that reasonably needed for the donation and travel. Small tokens, refreshments and re-imbursement of direct travel costs are compatible with voluntary non-remunerated blood donation. Family replacement blood donation (where family or other community members donate blood for the patient or to replace that provided to the patient) will be gradually phased out to achieve 100% voluntary non-remunerated blood donation in the country.



Blood must never be collected from paid donors. Other forms of blood donation such as directed donation (where blood is donated for a specific patient and must be used by that patient only) and pre-deposit autologous blood donation (where patients donate their own blood in advance of planned surgery are generally discouraged). Autologous donation is encouraged as part of intra-operative cell salvage. Directed donations are acceptable only where medically indicated such as in patients with allo-antibodies. Where indicated, directed donations must fulfill the same blood donation criteria of voluntary non-remunerated blood donors and the ABO and RhD group from the potential donors and recipient should be determined by the unit requesting directed donation prior to donor venesection.

The guidelines for safe blood transfusion are developed to protect both the blood donor and the recipient.

Blood Donor Education

The potential donor must be educated and provided with information on blood donation to enable him/her make an informed decision on blood donation. This should include the following:

a) Who is eligible to donate

b) Reasons for giving blood

c) How much blood will be collected

d) Tests to be carried out

e) Risks of blood donation

f) Potential donors must sign a consent form for taking blood, testing and use by patients and must understand that once donated the blood becomes property of the blood bank and cannot be returned to the blood donor.

Assessment of Fitness for Donation

Clinical assessment of the donor's fitness for donation should be conducted at each donation session. Potential donors should complete a questionnaire with standard question to understand all the information on the donor questionnaire. Assessment should be confidential and in private to ensure that donors understand the importance of honesty: how non disclosure of certain information can put blood donors themselves as well as recipients of the blood at risk and be given an opportunity to self exclude from donating blood. Blood donors must only be allowed to donate blood if they meet the minimum donation criteria specified below:

Donor Age

Donors should be of age from 16 to 65 years

Regular donors between 65 and 70 year can be allowed to donate if medically fit

Frequency of Donation

Blood can be donated every 3 months for males and 4 months for females

Weight

Potential blood donors must weigh at least 42 kg

Medical and Social History

Blood donors with the following conditions shall be permanently deferred :

a) Cardiovascular disease

b) Epilepsy

c) Mental illness

d) Malignancy

e) Diabetes (on insulin)

f) HIV

g) Hepatitis B

h) Hepatitis C

i) Syphilis

Blood donors with the following conditions shall be temporarily deferred :

a) Antibiotic use (7 days from the day of completing short acting antibiotics)
b) Pregnancy (6 months post delivery if not lactating)
c) Lactation (can donate after one year of lactation)
d) Abortion (6 months)
e) Major surgery (12 months)
f) Minor surgery (6 months)
g) Malaria (3 weeks after getting well)
h) Blood transfusion (12 months)
i) Jaundice (6 months)
j) Hormonal contraceptives (acceptable at all times)
k) On aspirin (acceptable for all blood components except for platelet production)
l) Unwell and/or under any medical investigation (defer until condition is known to decide subsequent periods of deferral)

Potential blood donors who practice any of the following must be permanently deferred :

a) Have multiple sexual partners
b) Have received payment for or have paid for sex
c) Men who have sex with men
d) Abuse intravenous drugs

Potential blood donors with conditions not highlighted above shall be discussed with a trained medical officer before accepting their donations.

Haemoglobin

Haemoglobin must be at least 12g/dl

Blood Pressure

At rest blood pressure should fall within the following range: 100/60 mmHg to 160/ 100 mmHg.

Pulse Rate

At rest pulse rate should be within 50 -100 beats per minute. Very fit blood donors (such as long distance runners) may be allowed to donate blood with a lower pulse rate.

Premises for Blood Donation

A place suitable for carrying out a blood donation clinic must meet the following minimum requirements:

a) Sufficient space to cater for donor registration, health check and drawing of blood
b) A private area for confidential counseling
c) A separate area for provision of refreshments
d) Non slippery floor
e) Adequate lighting
f) Toilet facilities for staff and donors
g) Waste disposal facilities

Blood Collection

Blood must be collected in a manner that is safe for the blood donor and the phlebotomist. Proper procedures for blood mixing to avoid clot formation and low platelets yield are also important for patient safety and the efficacy of the transfused blood product.

Preparation of Blood Pack

The pack shall be inspected for the presence of any defect and should not be used if the following defects are present including:

a) Moisture on the surface of the pack
b) Anticoagulant solution that is not clear
c) Holes or broken tubing

Blood Donation

a) Asceptic technique and infection prevention measures must be adhered to during phlebotomy
b) Strict sterile procedures, using disposable single use pyrogen free blood bags must be adhered to at all times
c) Blood must be collected from a suitable vein in the ante-cubital fossa which is free of skin lesions
d) Veins may be made prominent by appropriate venous occlusion
e) Blood of volume 450 ml may be collected from donors who weigh 45 kg and above
f) Blood of volume 250 ml from donors who weigh between 42 and 44 kg
g) The blood and anticoagulant must be gently mixed together every minute during collection by manual inversion of the blood pack
h) The donor may be given a stress ball to squeeze through out phlebotomy to facilitate blood flow
i) Blood flow must not be interrupted and must be completed within 15 minutes
j) During collection, the blood pack must be on a scale to monitor the weight / volume of blood collected
k) On completion of donation, the pressure cuff must be deflated, the needle removed from the arm and immediate pressure applied to the veinpuncture site
l) The donor must be monitored regularly during the donation by a medically qualified person
m) The arm and well being of the donor should be assessed before leaving the premises
n) Blood unit and specimen labels must be labeled with a unique donation (pack) number

Post Donation Advice

The donor must be offered post donation advice on fluid intake, vein puncture site care and physical activity.

Donor Adverse Reactions

All adverse reactions should be noted, managed, documented and reported to the manager.

Blood Donor Records

Blood donor records must be kept confidentially. The records must be kept in such a way as to allow transfusion audit trail in case of an adverse transfusion reaction. Records must be kept for 5 years at the site and sent to National Archives thereafter.

Blood Storage and Transportation from Blood Donor Clinics

Blood must be allowed to cool to ambient temperature before putting in the refrigerator or cold chain box for transportation. Once collected, blood should be transported to the laboratory within 6 -10 hours. The blood cold chain must be maintained at all times.

Testing and Processing Blood

The purpose of laboratory testing is to ensure that blood and blood products meet specified standards of safety and efficacy. All laboratory tests must be conducted according to well validated and documented techniques and in accordance with national standards and policy.

Test equipment and reagents must be validated before being introduced into routine use. Procedures must be in place to ensure that test systems, reagents and equipment are able to produce consistent and valid results.

Reception

All specimens of blood received in the laboratory for testing and processing must be clearly labeled and documented. Each donation pack and connected satellite pack must be identified by a unique donation (pack) number applied at the time of donation.

Quarantine

Units of blood and blood components which have not yet been tested or are being tested must be kept in a well labeled area completely separate from the area designated for issuable units. This area is called quarantine.

Storage in Quarantine

a) Whole blood, which are intended for processing components (platelets; fresh frozen plasma; cryo-precipitate) must be stored at ambient temperature and processed within 6 hours of collection.

b) The blood components made from these must also be kept in the appropriate quarantine as follows:

   i) Platelet concentrates in quarantine platelet agitator at 20-24°C

   ii) Fresh frozen plasma in blood bank deep freezers/freezer rooms at -25 °C or below

   iii) Units earmarked for red cell and whole blood production must be stored in quarantine blood bank fridges or cold rooms at 2 - 6°C

Storage after Testing

A designated storage area, appropriate for each type of blood component, must be provided for units that have passed the mandatory tests and can be issued. Consequently, those that have failed the test(s) must be labeled and separated in quarantine in readiness for disposal.

Testing

Mandatory Donor Testing

Laboratory tests must be performed on samples taken from the blood donor which have been labeled with a unique donation (pack) number. The results of the tests are used to ensure safety and correct labeling of all units of blood intended for transfusion and for compatibility testing purposes. The following are mandatory and must be carried out before blood is transfused:

a) ABO and RhD grouping

b) Transfusion transmissible infections testing (TTIs) and

c) Compatibility testing

ABO Grouping

The ABO blood group must be determined on each blood donation using the results obtained by testing the red blood cells with standardized antisera and testing the serum or plasma with known A, B and O cells for the reverse grouping.

RhD Grouping

The RhD blood group must be determined on each blood donation based on the results of testing for the D red cell antigen using standardized antisera. Those units which are negative for this test must be investigated for D variant.

Transfusion Transmissible Infection Testing

A Transfusion Transmissible Infection (TTI) is a blood borne infection that is capable of being transmitted by blood transfusion. Therefore, each donation of blood must be subjected to government approved test methods for the following infectious markers.

Human Immunodeficiency Virus (HIV)

Each donation must be screened for HIV I & II using tests which will determine both antibody and antigen.

HBV

Each donation must be screened for Hepatitis B surface antigen.

HCV

Each donation must be screened for Hepatitis C antibodies.

Syphilis

Each donation must be screened for syphilis antibodies.

Malaria

Each donation must be screened for malaria parasites.

Use of Test Results

a) Any unit of blood found positive for any of the mandatory serological tests must not be issued and must be disposed of using recommended means.

b) For the purposes of informing the donor about results of the above infections (except for HIV), when units are found serologically positive, each unit must be retested in duplicate.

c) In accordance with the national HIV policy, supplementary or confirmatory testing must be carried out for HIV, before test results are disclosed to blood donors.

d) Malaria positive units should be labeled and stored. Such blood may be transfused to non-high risk patients.

A Note on HCV Testing

Care must be taken when interpreting and using HCV ELISA test results as the available tests tend to produce a high false positive rate in low prevalence populations. Tested donor samples must be kept frozen for 5 years before final disposal. This will help in case of later investigations or approved research.

Specialized Testing

Specialized immunohematological tests such as antibody screening and identification may be carried out.

Labeling

Only units which have been tested and passed as issuable must be labeled. Units which have not passed must be discarded with a biohazard sticker label only. The label must specify the following :

a) Name of component
b) Blood group
c) Expiry date
d) Unique donation (pack) number
e) Storage conditions

Any other relevant information may be added. Labels containing any additional information must not be superimposed on other labels.

Blood Components : Preparation and Storage

The following blood components can be prepared and issued for clinical use. There must be quality control procedures in place to demonstrate the meeting of blood product specifications, storage and transportation conditions.

Platelet Concentrates

Random donor platelet concentrates are made from the buffy coats of single donor whole blood donations. They must meet the following minimum specifications:

a) Volume: 50-70 ml
b) Platelet yield: ≥55x109
c) They must be stored at 20 - 24°C in a platelet agitator. There is no alternative piece of equipment for the storage of platelets
d) They must never be refrigerated nor frozen
e) They must be transported at ambient temperatures and used up to 5 days after production

Cryo-precipitate

a) Cryo-precipitate must be made by separating the precipitate that forms when plasma freshly frozen at -65°C or below is thawed overnight for 24 hours.
b) It must meet the following minimum specifications:
   i. Volume 30-40 ml
   ii. Factor VIII yield: 80iu/pack
c) It must be stored at -25 to -30°C in a plasma freezer or freezer room for a maximum of one year.
d) Freezer compartments of domestic fridges are not suitable for the storage of cryoprecipitate as their temperature rarely goes below -20°C.
e) It must be transported frozen at least at -18°C and returned to storage temperature within 24 hours.

Fresh Frozen Plasma

a) Fresh frozen plasma is made by rapidly freezing plasma at -30°C or below.
b) It must meet the following minimum specifications :
   i. Volume 200-300 ml
   ii. Factor VIII yield 0.7iu/ml
c) It must be stored at -25 to -30°C in a plasma freezer or freezer room for a maximum of one year.
d) Freezer compartments of domestic fridges are not suitable for the storage of cryoprecipitate as their temperature rarely goes below -20°C.
e) It must be transported frozen at least at -18°C and returned to storage temperature within 24 hours.

Red Cell Suspensions

a) Red cell suspensions are made by adding an additive solution to packed cells.
b) The haematocrit must be between 50-70%.
c) It must be stored at 2 - 6°C in a blood bank fridge or cold room for up to 42 days.
d) They must be transported at between 2 - 10°C and returned to storage temperature within 24 hrs.
e) Red cell suspensions are also referred to as red cells in additive solution.

Whole Blood

a) Whole blood is made by collecting blood in an anticoagulant preservative solution.
b) The expiry date depends on the solution used.
c) Most current blood bags contain Citrate Phosphate Dextrose-Adenine 1 (CPDA1), conferring the longest storage period of 35 days.
d) Whole blood must be stored at 2-6°C in a blood bank fridge or cold room.
e) It must be transported, at a maximum 10°C and returned to 2-6°C within 24 hrs.

Arrangement of Blood Products in Storage Facility

Blood components must be stored in an orderly manner such as according to blood groups and/or cross-match status. Blood components must be arranged in a manner that allows for air circulation in cubicles or trays.

Use of Household (Domestic) Fridge

a) Domestic refrigerators are not intended for blood component storage.
b) They have no fan for uniform air circulation, have no alarm for warning when temperature is outside range and have no temperature display.
c) Red cell products may only be stored in domestic refrigerators in exceptional circumstances.
d) They must be placed in the middle of the fridge compartment,
e) Blood must not be placed near the back as the temperature may be lower than 2°C and not near the door, as the temperature may be higher than 6°C.
f) Blood stored in domestic refrigerators may only be stored for a maximum of 7 days.
g) A thermometer should be placed in the middle compartment of the fridge to monitor the temperature. The temperature must be documented at least twice per day.
h) Fresh frozen plasma and cryoprecipitate must never be stored in the freezer compartment of a household fridge.

Cross-Border Movement of Blood

Cross-border movement or exchange of blood and components shall be with the explicit approval of the Ministry of Health and in line with international health regulations.

Hospital Blood Bank Processes

Health facility blood banks collect blood, store, prepare for issue, issue for transfusion and carry out transfusions in individual patients. Proper hospital blood bank processes are important for blood transfusion safety.

Requirements for a Health Facility Blood Bank

The following are minimum requirements for operations of a blood bank:

a) Room with at least 3 x 3 meters of space
b) At least a 3 meter bench
c) Adequate lighting
d) Proper ventilation
e) Provision of a sink
f) Blood grouping and cross matching equipment and reagents
g) Storage facilities for reagents, specimens and blood components.
h) Qualified laboratory medical and nursing personnel registered with the relevant regulatory bodies
i) If a refrigerator/deep freezer (as opposed to a cold/freezer room) is used to store blood components, make provision for an air conditioner
j) Blood cold chain box
k) Back-up power source

Management of Hospital Blood Bank Stock

Ordering of Blood From Source

a) Blood should be obtained from the first priority source.
b) Individual healthcare facilities should order blood in order to maintain agreed minimum stock levels and to cover known demand (such as for planned surgery).
c) A minimum stock level of the daily average demand+25% should ensure that blood is available roughly 90% of the time.
d) The quantity of blood ordered should reflect actual demand as described above.
e) Blood must only be ordered by approved blood banks.
f) A formal order must be issued from the blood bank before blood will be released from source.
g) Following collection, healthcare units are responsible for tracking the subsequent use or disposal of all blood products.
h) Both source and health facility blood banks must keep written records of all blood products ordered.

Documentation on Receipt

On reception of blood and blood products, laboratory must check and document the following:

a) Date and time of reception
b) Pack number
c) Blood group
d) Temperature of (transportation) blood cold chain box
e) Integrity of pack and contents
f) Expiry date
g) A declaration that blood has been screened for TTIs
h) Name and signature of person registering receipt of blood

Storage/Stock Control

After reception, blood and blood products must be stored according to specifications. Individual healthcare facilities should have Standard Operating Procedures (SOPs) detailing : management of blood storage. These should include :

a) Temperature records
b) Recording of stock levels
c) Arrangement of blood products in storage facility
d) Separate storage of directed/replacement donor blood
e) De-reserving unused cross-matched blood
f) Crossover of unused directed donor blood

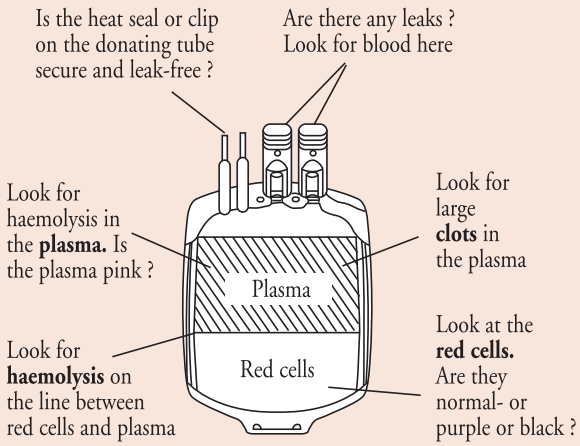
Mandatory documentation should include daily temperature records and stock levels.

Blood banks should be able to account for every unit received and its fate.

Disposal

Blood which is unsuitable for transfusion must be disposed of according to the National Infection Prevention Guidelines. The date of disposal, pack number and reason for disposal must be recorded.

Checklist for Signs of Deterioration in Blood and Plasma



Pre-Transfusion Testing

The purpose of pre-transfusion testing is to ensure transfused blood is safe for the intended recipient. This includes serological compatibility, microbiological safety, product integrity and prevention of misidentification errors. The commonest cause of serious transfusion reactions is the recipient receiving incompatible blood meant for another patient.

It is essential that procedures for ensuring correct identification are followed strictly at all points of the transfusion process. The requirements for identification and documentation are an integral part of the safety system.

Ordering of Blood from the Hospital Blood Bank

Blood must be ordered under the authority of a registered clinician. All samples should be accompanied by a request form specifying the tests or investigation required and the signature and name of person requesting the test.

All requests must contain the following minimum information :

a) Surname and first name of the intended recipient

b) A second point of identification (date of birth or hospital number)

c) Ward Blood product required

d) Time blood products are needed

e) Date and time of blood specimen collection

f) Name and signature of person ordering the test

g) Name and signature of person taking the blood sample, if this is different from the person ordering the test

Health facility blood banks should not process requests which do not have all of the above information.

Health facilities should have written procedures for communicating and dealing with incomplete hospital blood requests.

It is good practice to include the following when ordering blood from the blood bank:

a) Reason for request

b) Hb level of the patient

c) Details of any previous transfusions if known

d) Patient's blood group if known

e) If there is a directed donation for the patient

Sample Requirements

Potential recipients require a blood sample for ABO and RhD grouping and cross-matching. Samples must have the following minimum information written on the tube:

a) First name and surname

b) A second point of identification

c) Ward

Healthcare facilities should develop written procedures for communicating and dealing with inadequately labeled samples. Individual laboratories should have SOPs to cover specimen reception.

These should include:

a) Documentation of time and date of specimen receipt.

b) Issuing a unique specimen identification number for each sample.

c) Checking that identification information is adequate and consistent with the request form.

d) Visual inspection of sample to determine unsuitability for testing.

e) Incorrect or damaged specimen tube.

f) Presence of hemolysis/lipemia/clots.

g) Low sample volume.

h) Procedure for dealing with unsuitable specimens or requests.

Compatibility Testing (Cross-Matching)

a) Compatibility testing is the set of procedures required to ensure that there are no antibodies in the patient's serum that could cause a haemolytic transfusion reaction.

b) ABO blood group compatibility is the most important determinant of compatibility but there are other antibodies that can cause transfusion reactions even where the ABO groups are compatible.

c) Cross-matching between donor red cells and recipient serum/plasma is therefore necessary in addition to blood group determination to ensure safety.

d) Tests must be performed using donor red cells from the originally attached pilot tube on the blood bag, and recipient's serum/plasma sample no older than 48 hours.

e) A fresh sample must be taken from the patient if the patient has been transfused more than 48 hours previously.

f) Cross-match samples should be stored at 4°C for 7 days after sampling for investigation of transfusion reactions.

Routine Cross-Matching

Minimum mandatory cross-matching processes must include:

a) Review of readily available transfusion records

b) Forward ABO grouping on recipient and donor specimens

c) Confirmation of recipient ABO group by reverse grouping

d) RhD determination

e) Saline cross-match will detect IgM incompatibility only and offers a second check that blood is ABO compatible

f) Indirect antiglobulin Test (IAT) allows for detection of many clinically significant (IgG) antibodies which cannot be detected with a saline cross match

Emergency Cross-matching

a) In emergency situations where there is insufficient time to perform an IAT cross-match, blood may be released after the saline cross-match only. This should make the blood available after 15 minutes.

b) The IAT cross-match should still be performed and positive results actively notified to the clinicians.

c) In extreme emergencies, where there is insufficient time to perform, the emergency cross match, uncross-matched group O Rh (D) negative blood may be issued, clearly labeled as uncross-matched blood.

d) In this case a signed declaration from the clinician accepting responsibility for the transfusion should be obtained. Full compatibility testing should be performed while the blood is being transfused and positive results actively notified to the clinicians.

Post Cross-Match Labeling

Compatible blood must be labeled with the following as a minimum:

a) First name and surname of recipient

b) A second point of identification

c) Pack number

d) Laboratory number
e) Blood group of unit
f) Blood group of recipient
g) Ward
h) Name of person cross-matching blood
i) Date and time of cross-matching
j) Expiry date
k) Any special information (for example if recipient and unit have different blood groups)

Uncross-matched blood issued in extreme emergencies can be released marked as such without further labelling. The laboratory compatibility records should include all of the above information.

Issuing of Blood and Blood Products

Product Selection

Red Cell Suspension / Whole Blood

a) Whole blood and red cell suspension can be issued interchangeably for treatment of anaemia. For paediatric patients where blood is prescribed by volume, an equivalent red cell dose should be issued (10ml red cell suspension is equivalent to 15 ml whole blood).
b) RhD negative recipients should receive RhD negative products.
c) An uncertain RhD result ("weak D expression") in the recipient should be treated as RhD negative.
d) In life threatening emergencies where RhD negative products are unavailable, RhD positive products may be issued upon request from a senior clinician.
e) IAT cross-match must be performed either prospectively or retrospectively.

Fresh Frozen Plasma

a) Fresh frozen plasma (FFP) should be ABO group compatible with the patient.
b) Because plasma is being transfused, compatibility is opposite to red cell transfusion (Group AB plasma may be given to recipients of all groups; Group O should only be given to group O).
c) FFP must be thawed before transfusion.
d) Once thawed, FFP must never be refrozen for storage. It can be stored at 2 to 6°C for 24 hours only for fibrinogen replacement therapy as most labile clotting factors (factor VIII & V) will have deteriorated.
e) Water baths at 30 to 35°C. Can be used to thaw FFP. This is fast and takes about 15 minutes to thaw one unit.
f) Where this is not feasible tap water in plastic pails/basins can be used. This is slower and takes about 30-40 minutes to thaw 1 unit.
g) Care must be taken to avoid contact of the transfusion ports with thawing water (particularly water bath water) as this can lead to bacterial contamination of the plasma and septicaemia in the recipient.

Cryo-precipitate

a) If possible, it should be ABO group compatible with the patient as for FFP but this is not necessary.
b) Cryo-precipitate must be thawed before transfusion.
c) Once thawed it must never be refrozen for storage.
d) It can be stored at 2 to 6°C for 24 hours only for fibrinogen replacement therapy as factor VIII will have deteriorated.
e) Water baths at 30 to 35°C can be used to thaw FFP.
f) Where this is not feasible tap water in plastic pails/basins can be used. As units of cryoprecipitate have smaller volume, they thaw much faster than FFPs.

Platelet Concentrates

a) These should be of the same ABO group as the patient and RhD compatible.
b) ABO mismatched platelets may be given if ABO compatible platelets are unavailable but may be less effective.
c) RhD positive platelets should not be given to RhD negative women of childbearing age.
d) Avoid giving group O platelets to non-O infants.

Procedures for Issuing Blood

a) The person collecting the blood from the blood bank should bring documentation to identify the patient including full name and a second unique identifier.
b) Both blood bank staff and individual collecting blood should check that the patients name and other identification information agree with the blood request form, compatibility label and laboratory record.

Checks must be made to ensure that :

a) All required tests for transfusion transmissible infections have been performed and are negative
b) Blood is compatible by checking the blood group on the request form, compatibility label and compatibility register
c) Blood is not expired
d) Blood has no signs of deterioration or loss of integrity
e) The date and time of issue must be written in the laboratory record
f) The technician issuing blood and individual collecting blood should sign the laboratory record

Blood Administration

There should be national guidelines on the appropriate clinical use of blood and blood products guiding all the clinical aspects of blood transfusion including indications for use, maximal blood ordering schedules, the role of hospital transfusion committees, patient monitoring and management of transfusion reactions.

Non-Transfusion Use of Blood and Blood Products

Acceptable non-transfusion use of blood and blood products shall include: preparation of controls, reagent cells and approved research. Ministry of Health approval must be sought if blood is going to be used for purposes other than those outlined above patients with cerebral palsy.

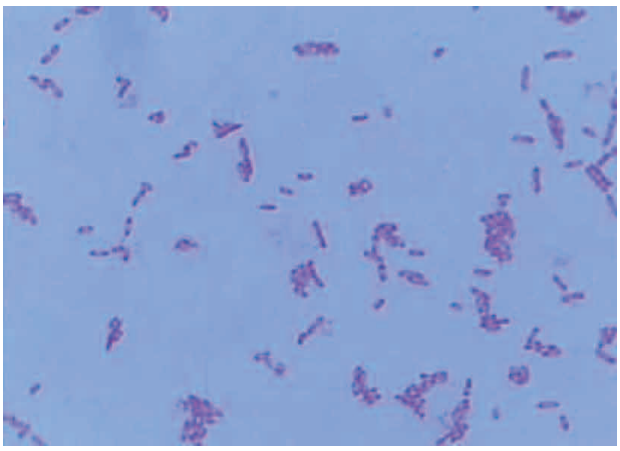
References :

www.transfusionguidelines.org.uk
www.bbts.org.uk
www.blood.co.uk
www.shotuk.org

Melioidosis is an infectious disease that can affect humans and many species of animals. The name "Melioidosis" is derived from the Greek 'melis' meaning "a distemper of asses" with the suffixes -oid meaning "similar to" and -osis meaning "a condition", that is, a condition similar to glanders. It is also called Whitmore's disease after Captain Alfred Whitmore, who first described the disease. It is also known as pseudoglanders, Nightcliff gardener's disease (Nightcliff is a suburb of Darwin, Australia where melioidosis is endemic), Paddy-field disease etc. Domestic and farm animals susceptible to melioidosis include sheep, goats, swine, horses, cats and dogs. Cattle and water buffalo are considered to be relatively resistant to melioidosis despite their constant exposure to mud. Strains which cause disease in humans differ from those causing disease in other animals.

Causative Organism

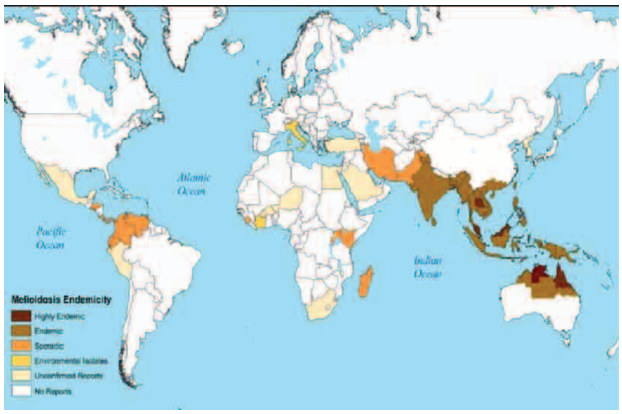
The disease is caused by *Burkholderia pseudomallei* (previously known as *Pseudomonas pseudomallei*). It is a *motile aerobic gram*-negative bipolar rod-shaped saprophytic bacterium. It is phylogenetically related closely to *B. mallei* (agent of glanders- a disease in animals) as well as to *B. thailandensis* and *B. oklahomensis*. It measures 2-5µm in length and 0.4-0.8 µm in diameter. The majority of strains are capable of fermentation of sugars without gas formation. It is able to polymerise actin and spread from cell to cell, causing cell fusion and the formation of multinucleate giant cells. *Burkholderia pseudomallei* genome carries constant region and variable regions. The later contains multiple genomic islands containing DNA acquired from other bacteria.



Burkholderia pseudomallei

Geographical Distribution

Melioidosis is primarily a disease of tropical and sub-tropical climate. Optimal proliferation temperature for the causative organism is reported around 40°C in pH-neutral or slightly acidic environments (pH 6.8-7.0). It is endemic in parts of Southeast Asia, Taiwan and northern Australia. Northeast Thailand has the highest incidence of melioidosis recorded in the world (21.3 cases of melioidosis per 100,000 people per year) where 80% of children are positive for antibodies against *B. pseudomallei* by the age of 4 years. In the United States, confirmed cases reported in previous years have ranged from zero to five and have occurred among travelers and immigrants coming from places where the disease is widespread.



Geogrpahical distribution of melioidosis

a. The greatest numbers of melioidosis cases are reported in Thailand, Malaysia, Singapore, Taiwan and Northern Australia.

b. Though rarely reported, cases are thought to frequently occur in Papua New Guinea, most of the Indian subcontinent, Southern China, Hong Kong, Vietnam, Indonesia, Cambodia, Laos and Myanmar.

c. Outside of Southeast Asia and Australia, cases have been reported in Southern Pacific, Sri Lanka, Mexico, El Salvador, Panama, Ecuador, Peru, Guyana, Puerto Rico, Martinique, Guadeloupe, Brazil, Parts of Africa and the Middle East.

There is recent news stating that *B. pseudomallei* has been isolated from the soil of Bangladesh. This suggests that melioidosis is endemic to Bangladesh and that there is a problem of underdiagnosis or under-reporting there which is most likely due to a lack of adequate laboratory facilities in affected rural areas.

Transmission

The organism can survive for months or years in soil and water. It usually resides below the surface of soil during the dry season. After heavy rainfall it is found in surface water and mud and may become airborne. So, infection most commonly occurs during the rainy season(75%). Severe weather events such as flood, tsunamis, cyclones and typhoons may also increase transmission. It can spread to humans and animals by direct contacts with contaminated water and soil (especially through open skin wounds) or inhalation of contaminated dust or rarely ingestion of contaminated water. It is very rare for people to get the disease from another person or animals. Although vertical transmission has rarely been proven, a few cases of melioidosis have been described in newborns. Another infant was thought to be infected by nursing contaminated milk. Sexual transmission has been suggested in some cases, but it has not been proven yet. Transmission from humans to animals is theoretically possible. Melioidosis can occur as sporadic cases or as outbreaks. The time between an exposure to the bacteria that causes the disease and the emergence of symptoms (incubation period) is not clearly defined, but may range from one day to many years; generally symptoms appear 2 to 4 weeks after exposure. A few cases have remained subclinical for up to 29 years, and one infection apparently became symptomatic after 62 years. Infections from aerosolized forms in biological weapons are expected to have an incubation period of 10 to 14 days.

Risk Factors

Melioidosis is primarily an opportunistic infectious disease. More than 50 percent cases of melioidosis occur in presence of some risk factors. The single most important risk factor for developing severe melioidosis is diabetes mellitus. Other risk factors include heavy alcohol use, thalassaemia, chronic kidney disease, chronic liver disease, malignant conditions, certain occupations (*rice/paddy farmers*), immunosuppression(high-dose glucocorticoid therapy), bronchiectasis and cystic fibrosis. HIV infection does not predispose to melioidosis. Incidence is highest between 40 and 60 years of age, but melioidosis is well recognized in children.

High risk occupation of melioidosis

Pathogenecity

Burkholderia pseudomallei contains flagella which play role in the motility and invasion of host cells. It also contains three type III and six type VI secretion systems that are implicated in virulence, intracellular survival and delivery of bacterial effector molecules into the host cell cytoplasm. Other putative virulence factors include surface capsular polysaccharide, lipopolysaccharide, exotoxin, endotoxin, fimbriae, pilli and adhesins. The bacterium also expresses a toxin called lethal factor 1 which is similar to *Escherichia coli* cytotoxic necrotizing factor 1. This factor interferes with the initiation of translation, leading to alteration of actin cytoskeleton and ultimately to cell death. The mutation rate in the multiple genomic islands is high and the organism continues to evolve even after infecting the host. These genomic islands are likely to be associated with virulence and the potential for infection, although specific associations with clinical outcomes have not yet been elucidated. Pattern recognition receptors e.g., TLRs, NLRs function in the uptake of the organism.The immune response initiated by pattern-recognition receptors play a critical role in early bacterial containment. Activation of innate immunity results in apoptosis, complement activation and activation of coagulation whereas adaptive immunity results in cell-mediated and antibody mediated response. The organism can survive and replicate in different cells including phagocytes by incompletely understood mechanisms (may be by way of escaping from endocytic vacuoles or intracellular compartment).

Clinical Presentation

A history of occupational or recreational exposure to soil or surface water is almost invariable in patients with melioidosis. But sometimes the patient cannot recall the event of exposure (as the incubation period may be long).While some infections are subclinical, others result in acute or chronic suppurative infections. The disease may be localized or the organism may disseminate through the blood to affect other body sites e.g., lungs, heart, brain, liver, spleen, kidneys, bones, joints where abscesses are usually formed. Another important point is that *Burkholderia pseudomallei* is one of the important causes of community-acquired sepsis which subsequently develops into septic shock.

A. Acute Melioidosis

- Pulmonary disease is the most common form of melioidosis (51%) that can occur as either the primary syndrome from inhalation or as a component of septicemia. The symptoms usually include fever, dyspnoea, productive cough, pleuritic chest pain and in some cases, hemoptysis. Ulcerative lesions and nodules are sometimes found in the nose and the septum may perforate. Pulmonary signs can develop suddenly or may occur gradually after a prodromal syndrome characterized by headache, anorexia and generalized myalgia. Complications include pneumothorax, empyema and pericarditis. Untreated cases often progress to septicemia.
- Acute localized skin infections(13%) occur at the site of inoculation or by hematogenous spread from other sites. In the skin, infections appear as gray or white, firm nodules and ulcers. The nodules may caseate and are often surrounded by inflammation. Regional lymphadenopathy and lymphangitis may also be seen.
- Other forms of acute localized disease include parotid abscess, destructive corneal ulcers after corneal trauma, cellulitis & necrotizing fasciitis.
- Genitourinary infections(14%) often manifest as prostatic abscess.
- In up to 25% of patients, no focus of infection is found.
- Localized infections can disseminate, but systemic infections are not always preceded by localized signs
- Neurological involvement (meningitis, brain-stem encephalitis, myelitis, cranial nerve palsies) may occur in 3% cases.
- Septicemia is the most serious form of melioidosis which can occur without prior localized infections. The onset is usually acute with high fever but may also develop more gradually, with a fluctuating fever often associated with severe weight loss. Common symptoms of septicemic melioidosis include fever, severe headache, disorientation, pharyngitis, upper abdominal pain, diarrhea, jaundice, muscle tenderness, dyspnea, arthritis and others. Some patients have a disseminated pustular rash with regional lymphadenopathy, cellulitis or lymphangitis. Septic shock is common and it is usually fatal once it develops.

B. Chronic Melioidosis

Chronic melioidosis is usually defined by persistence of symptoms more than 2 months and occurs in approximately 10% of patients and mimic cancer or tuberculosis. The clinical presentation is protean and includes such presentations as chronic skin infection, skin ulcers, lung nodules, chronic pneumonia closely mimicking tuberculosis, tuberculous pericarditis etc.

In more chronic forms, multiple abscesses occur in liver, spleen, prostate gland, subcutaneous tissues, bones, joints, lymph nodes and testes. Rarely, melioidosis can result in brain abscesses. Fever may or may not be present in chronic melioidosis. Some infected patients remain asymptomatic for years. These chronic carriers may eventually develop clinical disease, typically when they become immunosuppressed from other conditions.

Laboratory Diagnosis

Clinical specimens that can be used for the diagnosis of melioidosis are blood, sputum, throat swab, urine or a swab from an abscess or non-healing ulcer. The soil and/ or water may also be sampled during outbreaks.

- Culture

A culture from any clinical sample is the sine qua non for the diagnosis of melioidosis. A complete screen (blood culture, sputum culture, urine culture, throat swab culture and culture of any aspirated pus) should be performed on all patients with suspected melioidosis. *B. Pseudomallei* grows on most media including blood agar. Selective medium containing gentamicin such as Ashdown's medium is also used frequently. Mature colonies often have a wrinkled form; these colonies may be mixed with smooth colonies. *B. pseudomalle* colonies have a characteristic putrid, earthy odor. In the septicemic form, blood cultures may be negative until just before death. A new medium derived from Ashdown medium known as Francis medium may help differentiate *B. pseudomallei* from *B. cepacia* and may help in the early diagnosis of melioidosis, but has not yet been extensively clinically validated. Cultures typically become positive in 24 to 48 hours (this rapid growth rate differentiates the organism from *B. mallei*, which typically takes a minimum of 72 hours to grow)

- Staining and microscopy

On microscopic examination, the organisms are motile, short gram-negative bacilli, with bipolar or irregular staining in young culture.

- Serological tests

Antigens of *B. pseudomallei* can be identified directly in specimens by direct immunofluorescence,indirect hemagglutination or latex agglutination tests. Most people in endemic areas are sero-positive which limits the value of antibody detection. But antibody detection may be helpful in some circumstances, particularly when paired sera are available. However a high single titer or rising titer in paired sera in the presence of clinical signs may be suggestive. Cross-reactions can occur in serological tests with closely related organisms including *B.mallei, B. cepecia* and *B. thailandensis*. False positives have also been reported from other gram negative bacteria including Legionella.

- Genetic techniques

Gene detection of *B. pseudomallei* by PCR assay has been reported, and may be able to differentiate the DNA of *B. mallei* from that of *B. pseudomallei*. Other genetic techniques used to distinguish these two organisms include RFLP, pulse-field gel electrophoresis, 16S rRNA sequencing, variable number tandem repeat polymorphism, and multi-locus sequence typing (MLST). These specialized genetic techniques may be mainly available in research laboratories.

- Imaging tests

It is not possible to diagnose melioidosis on the basis of imaging studies alone, but imaging is routinely performed to assess the full extent of disease. Imaging of the abdomen using CT scan or ultrasound is recommended routinely, as abscesses may not be clinically apparent and may coexist with disease elsewhere. Australian authorities suggest imaging of the prostate specifically due to the high incidence of prostatic abscesses in northern Australian patients. A chest x-ray is also considered routine, with other investigations as clinically indicated. The presence of honeycomb abscesses (hypoechoic, multi-septate, multiloculate on CT) in the liver are considered characteristic, but are not diagnostic.

Treatment

The principal mode of treatment is antibiotic therapy. Sometimes surgical intervention is encountered.

A. Antibiotic Treatment

Burkholderia pseudomallei is inherently resistant to many antimicrobials e.g., penicillin G, ampicillin, 1st & 2nd generation cephalosporins, aminoglycosides, macrolides, fluoroquinolones and polymyxin (by various mechanisms e.g., efflux pumps, enzymatic inactivation, alteration of permeability, alterations in the antibiotic target sites etc). Of the newer antibiotics, ertapenem, tigecycline and moxifloxacin have limited in vitro activity against clinical isolates of *Burkholderia pseudomallei*. The treatment of melioidosis is divided into two stages: an intravenous high intensity phase which is followed by an eradication phase to prevent recurrence.

- Intravenous high intensity phase:

In the acute illness, prompt treatment without waiting for confirmation by culture may be life-saving. A misdiagnosis may be fatal. Intravenous Ceftazidime as mono-therapy is the current drug of choice for acute melioidosis but intravenous Meropenem is routinely used in Australia. Imipenem and Cefoperazone-Sulbactam are also effective. Intravenous Co-amoxiclav may be used if none of the above four drugs are available, but it produces inferior outcomes.

Name of antibiotics	Dosage
Ceftazidime*	50 mg/kg body weight (or up to 2 g) 6-8hourly
Meropenem	25 mg/kg body weight (or up to1 g) 8-hourly
Imipenem	25 mg/kg body weight (or up to1 g) 6-hourly

* Drug of choice

Ceftazidime should be replaced by Meropenem if clinical conditions worsen, new focus of infection develops or repeated blood cultures at 7 days remain positive. The duration of treatment should be at least 10-14 days but 4 or more weeks of parenteral therapy may be necessary in patients with severe diseases (septic shock, deep-seated organ abscess, septic arthritis, osteomyelitis, neurologic melioidosis). Even with appropriate antibiotic therapy, fevers often persist for weeks or months, and patients may continue to develop new lesions even while on appropriate treatment. The median fever clearance time in melioidosis is 10 days: and failure of the fever to clear is not a reason to alter treatment.

- Eradication Phase

Intensive intravenous therapy is followed by oral maintenance therapy for eradication of the organism and prevention of relapse. Co-trimoxazole and Doxycycline had been used combindly in the past. The current recommendation is to use only Co-trimoxazole as 1st line drug for this phase because there is evidence of antagonistic activity between Co-trimoxazole and Doxycycline in in-vitro test. The 2nd line options are Doxycycline and Co-amoxiclav but are less effective to prevent relapse. Co-amoxiclav is safer in pregnancy. Chloramphenicol is no longer routinely recommended for this purpose.

Name of antibiotics	Dosage
Co-trimoxazole* (TMP-SMX)	• 160/800 mg 12 hourly in <40 kg body weight • 240/1200 mg12 hourly in 40–60kg body weight • 320/1600 mg 12 hourly in >60 kg body weight
Doxycycline	200 mg daily
Co-amoxiclav	(20+5) mg/kg body weight every 8 hourly

* Drug of choice

Duration of treatment of this phase should be 3-6 months but in severely ill patients, duration of treatment should be up to 12 months. Lifelong monitoring is often recommended as relapses may occur after apparently successful treatment.

B. Surgical Treatment

A careful search for internal-organ abscesses is recommended, such as with the use of CT/USG of abdomen and pelvis. Abscesses should be drained and usually indicated for prostatic abscesses, septic arthritis and parotid abscesses. With pulmonary involvement of melioidosis, if cultures remain positive for six months, surgical removal of the lung abscess with lobectomy is considered.

Prognosis

Untreated melioidosis is fatal. With appropriate antibiotics, the mortality rate is about 10% for uncomplicated cases but up to 30-47% for acute severe cases. In septicemic cases, fatality may be 80% even with antibiotics and greater than 90% in untreated cases. Once septic shock develops, the case fatality rate is approximately 95%. It is certain that access to intensive care facilities is also important to reduce mortality. In endemic areas, recurrence occurs in 10 - 20% of patients which may be due to re-infection, particularly after 2 years. Risk factors for recurrence include more severe disease, positive blood cultures, multifocal disease, ineffective antibiotic for eradication therapy, poor compliance with eradication therapy and duration of eradication therapy less than 8 weeks.

Prevention

- Melioidosis is potentially preventable.
- In endemic areas, gloves and rubber boots are recommended for anyone doing agricultural work. Skin wounds including abrasions or burns should be promptly and thoroughly cleansed. Veterinarians should take precautions to avoid exposure, including the use of gloves and protective clothing, when working with infected animals or collecting diagnostic samples. In addition, people who process meat should also wear gloves and disinfect knives regularly. Although small numbers of organisms may survive, chlorination of the water supply decreases the risk of infection. People with diabetes mellitus, cystic fibrosis, chronic kidney disease, malignant conditions, immunosuppressive therapy should take special precautions to avoid contact with soil and contaminated water, especially in farm areas. It is also recommended that they should stay indoors during periods of heavy rainfall and wind, when aerosolization of *B. pseudomallei* is possible.
- Laboratory workers may be exposed to clinical samples from patients, even where melioidosis is not endemic. Practices such as sniffing opened culture plates should be discouraged. Post-exposure prophylaxis may be given after inadvertent laboratory exposure. Co-trimoxazole or doxycycline twice daily orally at usual dose for 3 weeks is recommended and should be started as early as possible. The exposed workers should be instructed for self-recording of temperature twice daily for 21 days and they should seek medical attention if become ill.
- There is no vaccine currently licensed for the prevention of melioidosis.
- It is stated to be susceptible to numerous disinfectants including 1% sodium hypochlorite, 70% ethanol, glutaraldehyde and formaldehyde but can remain viable for some time in 0.3% chlorhexidine. Chlorination reduces the number of *B. pseudomallei* in water, but small numbers of bacteria have been isolated from water containing up to 1000 ppm free chlorine. *B. pseudomalle* is resistant to UV light. Moist heat of 121°C (249°F) for at least 15 min or dry heat of 160-170°C (320-338°F) for at least one hour can also kill this organism.

Agent of Bioterrorism

B. pseudomallei carries the potential to be developed as a biological weapon. It is classed by the US Centers for Disease Control (CDC) as a Category B agent of bioterrorism i.e., one of the second highest priority agents that are moderately easy to disseminate, result in moderate morbidity rates & low mortality rates and require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance. *B. pseudomallei*, like its relative *B. mallei*, was studied by some superpowers as a potential biological warfare agent, but was never weaponized.

References :

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Diabetes mellitus is one of the most common medical complications of pregnancy. Gestational diabetes mellitus (GDM) represents approximately 90% of these cases. Pre-existing diabetes mellitus complicates 0.2% to 0.3% of pregnancies. The importance of diabetes in pregnancy stems from the fact that it carries a significant risk to both the foetus and the mother. Despite major advances in clinical management, we are still facing a higher incidence of malformations and perinatal morbidity compared to the non-diabetic population. However, during the past decade, type 2 diabetes in pregnancy has emerged and is certain to become a prominent concern.

Normal Glucose Regulation during Pregnancy

Metabolic changes occur in normal pregnancy in response to the increase in nutrient needs of the foetus and the mother. There are two main changes which are seen during pregnancy. Progressive insulin resistance begins near mid-pregnancy and progresses through the third trimester to the level that approximates the insulin resistance seen in individuals with type 2 diabetes mellitus. The insulin resistance appears to result from a combination of increased maternal adiposity and the placental secretion of hormones (progesterone, cortisol, placental lactogen, prolactin and growth hormone).

The fact that insulin resistance rapidly abates following delivery suggests that the major contributors to this state of resistance are placental hormones. The second change is the compensatory increase in insulin secretion by the pancreatic beta-cells to overcome the insulin resistance of pregnancy. As a result, circulating glucose levels are kept within normal. If there is maternal defect in insulin secretion and in glucose utilisation, then GDM will occur as the diabetogenic hormones rise to their peak levels.

Risks to the Foetus & the Neonate

If the mother has hyperglycaemia, the foetus will be exposed to either sustained hyperglycaemia or intermittent pulses of hyperglycaemia; both situations prematurely stimulate foetal insulin secretion. Foetal hyperinsulinaemia may cause increased foetal body fat (macrosomia) resulting in difficult delivery.

Table 1 : Foetal complications in diabetic pregnancy.

- Congenital anomalies: cardiovascular, central nervous system, skeletal (sacral agenesis) and genito-urinary
- Excessive foetal growth (macrosomia)
- Foetal growth retardation (in diabetic pregnancy complicated by nephropathy)

It may also cause inhibition of pulmonary maturation of surfactant resulting in respiratory distress of the neonate. Foetal organogenesis is completed by seven weeks post-conception and there is an increased prevalence of congenital anomalies and spontaneous abortions in diabetic women with poor glycaemic control during this period.

Pre-pregnancy counselling and planning should occur in women of child-bearing age who have diabetes. Pregnancy in patients with diabetes is associated with a six-fold increase in perinatal mortality and a two fold increase in the rate of major congenital malformations and an eight fold increase in preterm delivery compared to the general population. There is also an increase in neonatal hypoglycaemia which may cause permanent neurologic damage, hyperbilirubinaemia, respiratory distress and stillbirth. The associated increase of congenital anomalies for the foetus and spontaneous abortion in women with poor glycaemic control appears to be related to maternal glycaemic control rather than to the mode of anti-diabetic therapy during early pregnancy. The normalisation of maternal glucose before and throughout pregnancy can decrease pregnancy-related complications to those seen in non-diabetic pregnancies.

Table 2 : Neonatal complications in diabetic pregnancy.

- Traumatic delivery
- Pulmonary surfactant deficiency
- Hypoglycaemia
- Polycythaemia
- Hypocalcaemia
- Hypomagnesaemia
- Hyperbilirubinaemia

Risks to the Mother

Maternal diabetic complications are frequent in women with both type 1 and type 2 diabetes. Diabetic retinopathy and diabetic nephropathy may progress or start. Pre-eclampsia occurs in both type 1 and type 2 diabetes mellitus and is high as it affects approximately 20% of cases. Other complications including polyhydramnios and worsening of chronic hypertension are not uncommon.

Table 3 : Maternal complications in diabetic pregnancy.

- Diabetic ketoacidosis
- Hypoglycaemia
- Visual deteriorations (retinopathy)
- Deterioration of nephropathy
- Vomiting (gastric neuropathy)
- Miscarriages
- Pre-eclampsia
- Polyhydramnios
- Premature delivery

Management of Pregnancy with Pre-existing Diabetes

Pre-pregnancy planning (Table 4) is essential to achieve a healthy baby and avoid maternal morbidity such as adverse pregnancy outcomes and progression of chronic diabetes complications. Ideally this is carried out by a team, which includes an obstetrician and a diabetologist for optimum care. Blood glucose control in the pre-conception period and during the first trimester of pregnancy have demonstrated striking reductions in rates of malformation compared with infants of diabetic women who did not participate in pre-conception care.

Counselling about the risk of malformations associated with unplanned pregnancies and poor metabolic control and the use of effective contraception at all times unless the patient is in good metabolic control and actively trying to conceive.

Table 4 : Pre-pregnancy assessment.

- Glycaemic control/appropriate medication
- Weight and diet
- Blood pressure/appropriate medication
- Review of diabetes complications
- Retinopathy/nephropathy/autonomic neuropathy
- Coronary artery disease
- Smoking
- Rubella status
- Folic acid supplementation

Optimise Glycaemic Control : In preparation for pregnancy, oral hypoglycaemic agents should be discontinued and insulin started if needed. Statins and ACE-inhibitors should also be discontinued. Hypertension should be controlled with safer drugs like Methyldopa, Nifedipine or Labetalol. Diabetic complications should be assessed and treated. Regular self-monitoring should be encouraged to optimise control. Folic acid should be started at least four weeks pre-conception. Glycaemic control should be optimised with the aim of pre-prandial blood glucose < 5.5 mmol/L (<95mg/dl) and HbA1c < 7%.

Diabetes Ante-natal Care : This should be provided in a special hospital and the team caring for pregnant women should ideally include a Diabetologist, Obstetrician, Dietician and a Diabetes Specialist Nurse. The aim of ante-natal care is to maintain tight glycaemic control and to monitor the mother for diabetes complications. Tighter glycaemic control has an impact on maternal and foetal complications, therefore, excellent glycaemic control should be continued throughout pregnancy, fasting blood glucose should be kept < 5.5 mmol/L (<95mg/dl), post-prandial glucose < 7.8 mmol/lL (<140 mg/dl) and HbA1c <7%. Tighter glycaemic control may lead to an increase in episodes of severe hypoglycaemia and worsening of hypoglycaemia unawareness. The patient should be aware of subtle signs of hypoglycaemia, and the patient's family should be taught the proper treatment of severe hypoglycaemia (i.e. Glucagon).

Glucose Monitoring : Home blood glucose monitoring is an essential part of maintaining euglycaemic state and its goal is to detect glucose concentration to allow fine-tuning of insulin adjustment. Post-prandial glucose levels have been shown to correlate more with macrosomia than do fasting levels. Diabetes in early pregnancy studies found that third trimester post-prandial glucose levels were the strongest predictors of percentile birth weight.

Dietary Advice : The goal of diet in pregnancy is to provide adequate nutrition for the mother and the foetus, provide sufficient calories for appropriate maternal weight gain, maintain normal glycaemia and avoid ketosis. Eating three small to moderate size meals and three snacks per day is appropriate. Monitoring with a pre-breakfast ketone measurement is recommended for patients who are on a hypo-caloric or carbohydrate restricted diet.

Insulin Therapy : Insulin regimes should be individualised but in type 1 patients multiple injection/ basal bolus regime of human insulin is preferable and in type 2, twice-daily injections may be appropriate.

The aim is to achieve blood glucose as near normal as possible without excessive risk of hypoglycaemia.

Hypoglycaemia : Hypoglycaemia is common in pregnancy, particularly in the first trimester. Education of patients and their families in the recognition and management of hypoglycaemia is vital.

Ketoacidosis : Ketoacidosis is a preventable condition but potentially lethal to the foetus at any stage of pregnancy. Women should be instructed to test their urine for ketones if their blood glucose readings are high or if they feel unwell.

Retinopathy : Diabetic retinopathy may accelerate during pregnancy. Fundoscopy is necessary before conception and once in each trimester of pregnancy for all women with diabetes.

Nephropathy : Baseline assessment of renal function by serum creatinine and some measure of urinary protein excretion (urine albumin/creatinine ratio or 24-hour albumin excretion) should be undertaken before conception. Women with microalbuminuria may experience transient worsening during pregnancy; however, those with established nephropathy with overt proteinuria are at increased risk of pre-eclampsia and intra-uterine growth retardation and premature delivery.

Hypertension : Hypertension is a frequent concomitant of diabetes. Patients with type 1 diabetes frequently develop hypertension in association with diabetic nephropathy, as manifested by the presence of overt proteinuria. Patients with type 2 diabetes more commonly have hypertension as a concomitant disease. In addition, pregnancy induced hypertension is a potential problem for women with diabetes. Hypertension contributes to worsening of diabetic nephropathy and retinopathy in pregnancy. ACE-inhibitors, beta-blockers and diuretics should be avoided in women contemplating pregnancy if they are being used for hypertension. Methyldopa or Labetalol may be substitute.

Foetal Monitoring : The major risks for the foetus of a diabetic woman are congenital malformations, intra-uterine death, usually after 30 weeks and macrosomia, which may result in significant problems in labour for both mother and baby. Ante-natal foetal surveillance must be planned so that each risk is addressed efficiently and in a timely manner. Ultrasound scanning must be available for assessing gestational age, examining for congenital abnormalities and monitoring foetal growth and liquor volume. All diabetic patients should be counselled about the possibility of a neural tube defect and offered serum alpha-fetoprotein blood test between 15 and 19 weeks gestation. A detailed ultrasound scan at between 20 and 22 weeks for careful assessment of foetal anatomy is mandatory. The risk of intrauterine foetal death is increased by approximately three times, mostly confined to the third trimester. Although strict control of maternal blood glucose levels will reduce this risk, but not as low as that of the general population.

Ultrasound assessment should be carried out at each visit from 26 weeks. The programme of surveillance must be modified if there are additional recognised risk factors, such as hypertension or renal disease.

Unlike in the non-diabetic, it is excessive foetal growth rather than retarded growth that may be associated with the greatest risk. Increasingly large abdominal circumference in relation to the bi-parietal diameter can be easily monitored by serial ultrasound scans and these two parameters should be measured and documented at each visit, in association with assessment of liquor volume.

Management of Labour and Delivery

Table 5 : Maternal risk factors for gestational diabetes.

- Obesity
- Diabetes in first-degree relative
- Previous infant with macrosomia
- Previous diagnosis of GDM
- Age more than 35 years
- Polycystic ovary syndrome
- Multiparity
- Member of high risk population (e.g. Asian or African descent)

Uncomplicated case with no evidence of obstetrical or foetal complications, spontaneous delivery at term is standard practice. Pregnancy can be continued to at least 38 weeks if everything is alright. When there are maternal complications of diabetes, complications of pregnancy, previous stillbirth or evidence of abnormal foetal growth, each case must be considered in its own merit with timely delivery in hospital. Delivery by elective Caesarean section should be considered if the ultrasound estimated foetal weight is > 4kg. In the absence of these or other obstetric contraindications a spontaneous vaginal delivery should be possible, with induction of labour as required.

Glucose control during labour is very important (1-2 hourly blood glucose estimation to keep blood glucose between 3.9 - 6.7 mmol/L.) It is necessary to administer IV insulin and Dextrose to prevent ketoacidosis and to maintain the blood glucose as near normal as possible. After delivery of placenta insulin requirements falls and blood glucose reaches quickly to about the pre-pregnancy level.

Neonatal Management : Hyperglycaemia in later weeks or during delivery may cause neonatal hypoglycaemia due to hyperinsulinism in foetus. Common neonatal problems include hypoglycaemia, respiratory distress syndrome, jaundice, hypocalcaemia etc. Routine blood glucose monitoring of the baby should be performed for the first 12 hours. 5-10 gm glucose/hour in I/V infusion, insulin if needed in a separate set at a rate of 0.02-0.04 unit/hour/kg (1.4-2.8 unit/hour) may be followed. Other problems should address properly and management to be done immediately.

Table 6 : Perinatal complications of gestational diabetes mellitus

- Death (still birth and neonatal death)
- Shoulder dystocia
- Bone fracture
- Nerve palsy
- Neonatal hypoglycaemia

Gestational Diabetes Mellitus

GDM is defined as a glucose intolerance that begins or is first detected during pregnancy. The prevalence may range from 1-14% of all pregnancies, depending on the population sample, with 2 - 5% being the most common rate. GDM develops when a woman is unable to secrete sufficient insulin to compensate for the increased insulin resistance during pregnancy. Women who develop GDM are at increased risk for type 2 DM in latter life. Impact of GDM on pregnancy is similar to that of pregestational DM, though complications are fewer and less severe. GDM is seldom symptomatic and need for screening.

Screening of High Risk Group

- Bad obstetrical history-still birth, abortion, recurrent UTI, etc
- Obesity
- Age > 35 yrs
- Multiparity
- Previous H/O of GDM
- H/O of DM in 1st degree relatives
- Fasting or repeated glycosuria
- High RBS (> 7.8 mmol/L)
- H/O of birth of previous large baby (> 4kg)
- Patient own birth wt > 9 lb
- Congenital malformation - Macrosomia (present/past)
  - Polyhydramnios (present/past)

Screening : All pregnancy-screening at 24-28 weeks. High risk group-screning at presentation, if not then check at 28 weeks if not then recheck at 32 weeks.

Management of GDM

Treatment of GDM can substantially reduce perinatal morbidity (table 6) from 4% to 1%. Women diagnosed with GDM should receive dietary advice and calorie intake should be reduced if overweight. Such measures will achieve metabolic control in the majority of women. They should monitor their own blood glucose levels and, if the pre-prandial glucose levels are consistently above 5.5mmol/L (95 mg/dl), insulin should be commenced with the aim of keeping pre-prandial blood glucose below 5.5 mmol/L (95 mg/dl), and two hour post-prandial below 7.8mmol/L (140 mg/dl). They should be advised to make life style changes to reduce their risk of subsequent type 2 diabetes mellitus.

References :

www.idf.org
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www.ljm.org.ly
http://www.diabetes.niddk.nih.gov
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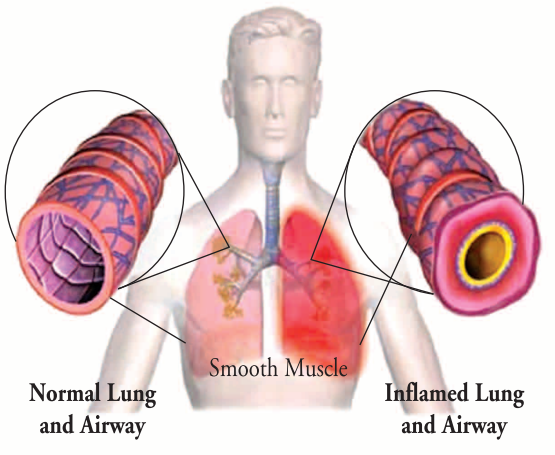
Viral Pneumonia

Viral pneumonia is the inflammation of the lungs' parenchyma due to viral infection. Viruses are one of the two major causes of pneumonia, the other being bacteria; less common causes of pneumonia are fungi and parasites. Viruses are the most common cause of pneumonia in extremes of age (children and elderly), while in adults, bacterial pneumonia are more common.



Causes

Both DNA and RNA viruses are involved in the etiology of viral pneumonia. Some are well-known lung pathogens that produce common clinical and radiologic manifestations. Others are rarely involved as lung pathogens.

Etiologic Viruses Include Various Families

- Adenoviridae (adenoviruses)
- Coronaviridae (coronaviruses)
- Bunyaviridae (arboviruses) -Hantavirus
- Orthomyxoviridae (orthomyxoviruses) - Influenza virus
- Papovaviridae (polyomavirus) - JC virus, BK virus
- Paramyxoviridae (paramyxoviruses) -Parainfluenza virus (PIV), respiratory syncytial virus (RSV), human metapneumovirus (hMPV), measles virus
- Picornaviridae (picornaviruses) - Enteroviruses, coxsackievirus, echovirus, enterovirus 71, rhinovirus
- Reoviridae (rotavirus)
- Retroviridae (retroviruses)- Human immunodeficiency virus (HIV), human T-cell lymphotropic virus type 1 (HTLV-1)

Most of the members of Herpesviridae family are documented lung pathogens in hosts with compromised cell immunity and include the following:

- Herpes simplex virus 1 (HSV-1) and herpes simplex virus 2 (HSV-2), also called human herpesvirus 1 (HHV-1) and human herpesvirus 2 (HHV-2), respectively
- Herpesvirus 6, herpesvirus 7, and herpesvirus 8
- Varicella-zoster virus (VZV)
- Cytomegalovirus (CMV)
- Epstein-Barr virus (EBV)

Serious viral pneumonia is more likely to happen in those with a weakened immune system, such as :

- Babies who are born too early
- Children with heart and lung problems
- HIV infection
- People receiving chemotherapy for cancer, or other medications that weaken the immune system
- Organ transplant recipients

Influenza virus, respiratory syncytial virus, adenovirus, parainfluenza virus, coronavirus, rhinovirus, and human metapneumovirus may cause community-acquired viral pneumonia.

Influenza Virus

The influenza viruses are enveloped, single-stranded, RNA viruses of the family Orthomyxoviridae and are the most common viral cause of pneumonia. Three serotypes of influenza virus exist: A, B, and C.

Influenza type A can alter surface antigens and infect livestock; perhaps, this characteristic accounts for its ability to create a reservoir for infection and cause epidemics in humans. The virus is spread by means of small-particle aerosol and targets the columnar epithelial cells along the entire respiratory tract.

Influenza type B causes illness that usually is seen in relatively closed populations such as boarding schools. Influenza type C is less common and occurs as sporadic cases.

Influenza type A is usually the most virulent pathogen. The influenza virus has 2 envelope glycoproteins, hemagglutinin (H) and neuraminidase (N), which are important for a number of reasons. The hemagglutinin initiates infectivity by binding to cellular sialic acid residues, whereas the N protein cleaves newly synthesized virus from sialic acid on cell surfaces, thus allowing spread of the virus to other cells.

The influenza virus maintains its infectivity by undergoing antigenic drift (small number of amino acid substitutions) and shift (large number of amino acid substitutions) due to changes in the protein structure of the surface protein, hemagglutinin. Epidemics occur when a viral drift occurs, and pandemics are seen with viral shift (2 influenza A viruses exchange H or N genes during infection of the same hosts) because most people have no prior immunity to the virus.

Two influenza types have emerged of particular importance: H5N1 avian influenza strain and the novel H1N1 swine influenza strain.

Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) is the most frequent cause of lower respiratory tract infection among infants and children and the second most common viral cause of pneumonia in adults. It is a medium-sized virus of the Paramyxoviridae family that consists of only 1 serotype. Structurally, RSV has 10 unique viral polypeptides, 4 of which are associated with virus envelope, and 2 of these (F and G) are important for infectivity and pathogenicity. Classic RSV infection causes syncytia formation in cell culture, giving the virus its name.

RSV is highly contagious, spreading via droplet and fomite exposure. Most children are infected before age 5 years-the infection rate during an epidemic approaches 100% in certain settings such as daycare centers-but the resulting immunity is incomplete.

Reinfection in older children and young adults is common but mild. However, the likelihood of more severe disease and pneumonia increases with advancing age.

Adenoviruses

Adenoviruses are enveloped DNA viruses that cause a wide spectrum of clinical illnesses depending on the serotype of the infecting agent. These include asymptomatic illness, conjunctivitis, febrile upper respiratory disease, pneumonia, gastrointestinal illness, hemorrhagic cystitis, rash, and neurologic disease. Pneumonia is less common in adults outside of military recruit camps and similar facilities, but fulminant disease has been described in infants and in the immunocompromised population and can occur in apparently healthy hosts.

Although 52 serotypes exist, classified into 7 subgroups or species (A-G), pulmonary disease is predominantly caused by serotypes 1, 2, 3, 4, 5, 7, 14, and 21. Type 7 viruses can cause bronchiolitis and pneumonia in infants. Types 4 and 7 viruses are responsible for outbreaks of respiratory disease in military recruits.

Spread of adenovirus is by respiratory secretions, infectious aerosols, feces, and fomites. Neonates may acquire infection from exposure to cervical secretions at birth.

Contaminated environmental surfaces can harbor virus capable of causing infection for weeks. The virus is resistant to lipid disinfectants but is inactivated by heat, formaldehyde, and bleach.

Adenoviruses are extremely contagious. Studies of new military recruits have shown seroconversion rates of 34-97% over a 6-week period. The majority of children have serologic evidence of prior adenovirus infection by the age of 10.

Parainfluenza Virus

Parainfluenza virus (PIV) is a common virus that infects most persons during childhood. PIV is second in importance to only RSV in causing lower respiratory tract disease in children (pneumonia) and bronchiolitis in infants younger than 6 months. Transmission is through direct person-to-person contact or large-droplet spread.

PIV is characterized by nucleocapsids, which develop in the cytoplasm of infected cells, with hemagglutinin present in the virion envelope.

There are 4 subtypes of PIV, based on antigenic characteristics. PIV type 3 is endemic year-round, while types 1 and 2 peak during the fall season. Immunity is short term, and recurrent upper or lower respiratory tract infections occur throughout life. The infections vary from a mild illness to life-threatening croup, bronchiolitis, or pneumonia. Infection in immunocompromised hosts can result in life-threatening pneumonia with lung injury and respiratory failure. In one study, 44% of hematopoietic stem cell transplant (HSCT) patients with PIV progressed to develop pneumonia, of which 37% died.

Rhinovirus

According to some authors, rhinovirus accounts for up to 30% of cases of all virus-related pneumonia. Clinical studies show that rhinovirus is the second most frequently recognized agent associated with pneumonia and bronchiolitis in infants and young children. Rhinovirus infection is linked to asthma hospitalizations in both adults and children.

A study of 211 French children with rhinovirus infection revealed bronchiolitis or bronchitis in 25.6% and pneumonia in 6.2%, after cases of dual bacterial or viral infections were eliminated.

A study from the Netherlands showed that rhinoviruses cause 32% of all lower respiratory tract infections with an identified pathogen in the elderly (> 60 y) symptomatic population. Rhinoviruses were identified more frequently than coronaviruses (17%) or influenza viruses (7%).

Human Metapneumovirus

Human metapneumovirus (hMPV) is a relatively newly discovered respiratory pathogen, initially described in the Netherlands in 2001. hMPV is in the Paramyxoviridae family (like RSV and PIV) and is a pleomorphic-shaped virus surrounded by surface protein projections. This virus is a ubiquitous organism, and most surveys indicate that by age 5 years, almost all children have been exposed to it. However, reinfection occurs throughout life, including in adults. This virus is spread via droplet and fomite exposure.

As a human pathogen, hMPV may have been underestimated for a long time. In children and infants, hMPV was reported to be a notable cause of lower respiratory tract infections such as bronchiolitis (59%), croup (18%), asthma (14%), and pneumonia (8%).

As with other viruses, the severity of infection increases with older age and with comorbid (cardiopulmonary disease) or immunosuppressive conditions. The most common diagnoses associated with adult hospitalizations with hMPV infection are chronic obstructive pulmonary disease (COPD) exacerbations, bronchitis, and pneumonia. In immunocompromised hosts (eg, hematologic malignancies), severe pneumonitis requiring intensive care or resulting in death has been reported.

Coronavirus

Coronaviruses are from the family Coronaviridae and are single-stranded RNA viruses, the surface of which is covered by crownlike projections, giving the virus its name. This virus is spread via droplet and fomite exposure. Long known to cause upper respiratory infections, coronaviruses were not felt to significantly cause pneumonia until relatively recently. However, the severe acute respiratory syndrome (SARS) pandemic in 2003 brought the ability of this virus to cause life-threatening pneumonia to worldwide attention.

Four human coronaviruses (HCoVs) have now been identified: HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1. These HCoVs appear to be established human pathogens with worldwide distribution, causing upper and lower respiratory tract infections, especially in children. Typically, HCoV infection follows a seasonal pattern similar to that of influenza, although Hong Kong researchers found that HCoV-NL63 infections mainly occurred in early summer and autumn.

Avian Influenza

In Hong Kong in 1997, an influenza virus (H5N1 virus) previously known to infect only birds was found to infect humans. Manifestations included pneumonia, which in some cases led to fatal acute respiratory distress syndrome (ARDS) or multisystem organ failure.

Prior to the human outbreak, the H5N1 virus caused widespread deaths in chickens on 3 farms in Hong Kong. Epidemiologic investigations of this outbreak demonstrated that individuals in close contact with the index case or with exposure to poultry were at risk of being infected.

Concern is growing that avian influenza, which is a subtype of influenza A, may result in a worldwide pandemic in the near future. The avian influenza virus A/H5N1 has several ominous characteristics, including increased virulence and human-to-human transmission in several cases, rather than bird-to-human transmission, as is usually necessary. The disease causes high mortality as a result of pneumonia and respiratory failure.

The 1997 outbreak in Hong Kong was thought to be controlled by depopulating 1.5 million chickens in local farms and markets. However, human infections occurred in 2001 through 2003 in other parts of Asia, and the virus has been found in poultry and birds in Europe.

The rising incidence and widespread reporting of disease from H5N1 influenza viruses can probably be attributed to the increasing spread of the virus from existing reservoirs in domestic waterfowl and live bird markets, leading to greater environmental contamination. As of August 2010, 504 cases of H5N1 human infections have been reported from 15 countries since 2003, with 299 deaths (59% mortality).

Severe Acute Respiratory Syndrome

Severe acute respiratory syndrome (SARS) was due to a novel coronavirus (CoV) that crossed the species barrier through close contact between humans and infected animals. Viral isolation and genomic sequencing have revealed that the SARS virus originated in the masked palm civet cat (*Paguma larvata*), raccoon dog (*Nyctereutes procyonoides*), and possibly the Chinese ferret-badger (*Melogale moschata*), with subsequent interspecies jumping, during which a partial loss of genome probably led to more efficient human-to-human transmission.

Horseshoe bats (*Rhinolophus sinicus*) have also been found to harbor SARS-like coronaviruses (more distantly related to SARS-CoV than that of the palm civets), raising the possibility of bats being a reservoir for future SARS infections.

SARS was a particularly challenging disease because its long incubation period allowed seemingly healthy travelers who were infected with the virus to spread it. The SARS coronavirus (SARS-CoV) quickly spread from China to the rest of the world over a period of 1 year, affecting more than 8000 patients in 29 countries and resulting in 774 deaths.

Global transmission of SARS was halted in June 2003 after the World Health Organization instituted traditional public health measures, including finding and isolating case-patients, quarantining contacts, and using enhanced infection control. No cases of SARS have been reported since 2004.

H1N1 (swine) Influenza

Initially reported as an outbreak in Mexico and subsequently the United States, infection from a novel swine-origin influenza A (H1N1) virus rapidly spread to become a worldwide pandemic in 2009. The World Health Organization declared an end to the pandemic in August 2010.

Virus-associated hemophagocytic syndrome may play an important role in development of multiorgan failure and ensuing death in H1N1 infection.

Epidemiology

Viral pneumonia occurs in about 200 million people per year which includes about 100 million children and 100 million adults. Traditionally, viruses were felt to cause approximately 8% of cases of community-acquired pneumonia for which patients are hospitalized. More recent investigations have shown viruses to play a larger role, causing 13-50% of pathogen-diagnosed community-acquired pneumonia cases as sole pathogens and 8-27% of cases as mixed bacteria-virus infections.

Influenza virus types A and B account for more than 50% of all community-acquired viral pneumonias in adults. Various studies have reported differing frequencies of the other viruses causing community-acquired pneumonias, with RSV ranging from 1-4%, adenovirus 1-4%, PIV 2-3 %, hMPV 0-4%, and coronavirus 1-14% of pathogen-diagnosed pneumonia cases.

Viral Pneumonia in Immunocompromised Hosts

Although immunocompromised patients are at higher risk for viral pneumonia from CMV, VZV, HSV, measles, and adenoviruses, seasonal viruses (influenza, RSV, PIV) remain a major cause of pneumonia. Hematopoietic stem cell transplant (HSCT) and Solid organ transplant (SOT) recipients are particularly at risk for acquiring lower respiratory tract infection due to CMV and RSV.

CMV pneumonia has been observed in 10-30% of patients with HSCT and 15-55% of heart-lung transplant recipients, making this virus the most common cause of viral pneumonia in the former patient group. After CMV, the frequency of viruses isolated from HSCT patients vary, with influenza virus ranging from 14-52%, RSV 14-48%, adenovirus 2-21%, and PIV 11-49% of viral isolates.

Although HSV has been shown to cause pneumonia in this patient population, it is relatively rare when compared with the other viral pathogens, with one study showing HSV to cause 5% of nonbacterial pneumonias in HSCT recipients, compared with 46% for CMV.

Viral Pneumonia in Pregnancy

Acute viral pneumonia is common and often underdiagnosed in pregnancy. Although the severity of bacterial pneumonia does not seem to be increased in pregnancy, viral pneumonia can have a serious clinical evolution. Among the viral pathogens, influenza virus, VZV, and measles virus are reported as etiologic agents in severe lower respiratory tract infection.

The infection may result in acute respiratory decompensation; respiratory failure; and/or ARDS, which can lead to materno-fetal hypoxia, preterm labor, multisystem organ failure and even death.

Pathophysiology

Viruses must invade cells in order to reproduce themselves. Typically, a virus will reach the lungs by traveling in droplets through the mouth and nose via inhalation. There, the virus invades the cells lining the airways and the alveoli. This invasion often leads to cell death either through direct killing by the virus or by self-destruction through apoptosis.

Further damage to the lungs occurs when the immune system responds to the infection. White blood cells, in particular lymphocytes, are responsible for activating a variety of chemicals (cytokines) which cause leaking of fluid into the alveoli. The combination of cellular destruction and fluid-filled alveoli interrupts the transporta-tion of oxygen into the bloodstream.

In addition to the effects on the lungs, many viruses affect other organs and can lead to illness affecting many different bodily functions. Viruses also make the body more susceptible to bacterial infection; for this reason, bacterial pneumonia often complicates viral pneumonia.

Symptoms

Symptoms of viral pneumonia often begin slowly and may not be severe at first.

The most common symptoms are:

- Cough (with mucus or even bloody mucus)
- Fever, which may be mild or high
- Chills and rigors
- Shortness of breath

Other Symptoms Include :

- Confusion, especially in older people
- Excessive sweating and clammy skin
- Headache
- Loss of appetite, low energy and fatigue
- Sharp or stabbing chest pain that gets worse on deep breath or cough

Investigations

Depending on the severity of illness, tests may be done to diagnose viral pneumonia, including:

- Chest x-ray
- Complete blood count (CBC)
- CT scan of the chest
- Blood cultures
- Blood tests to diagnose specific viruses
- Bronchoscopy (rarely needed)
- Nasal swab test to check for viruses such as the flu
- Open lung biopsy (only done in very serious illnesses when the diagnosis cannot be made from other sources)
- Sputum culture

Treatment

Antibiotics do not treat viral pneumonia. Antiviral medication only works against influenza pneumonia and some causes by the herpes family of viruses.

Treatment may also Involve :

- Corticosteroids
- Increased fluids
- Oxygen
- Use of humidified air

Treatment at Home :

- Fever should be controlled with paracetamol, aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen or naproxen). Aspirin should be avoided in children.
- Plenty of fluids intake could help loosen secretions and bring up phlegm.
- Rest.
- Sometimes, anti-tussive could be used.

Prognosis

The prognosis is good in the vast majority of patients with viral pneumonia. It is guarded in elderly or immunocompromised patients. Some adenovirus serotypes, especially 2, 3, 7 and 21 have been the cause of serious chronic morbidity after acute respiratory illness, including irreversible atelectasis, bronchiectasis, bronchiolitis obliterans and unilateral hyperlucent lung. An estimated 14-60% of these children will suffer some degree of permanent lung damage. Many of these patients presented with pharyngitis, tonsillitis and bronchitis. Adenovirus 14 has a high fatality and morbidity rate in healthy patients. Serious sequelae occurred in those who survived. Viral pneumonia may leave patients with residual disability from interstitial fibrosis. Infants hospitalized with lower lung infection due to RSV are much more likely to later develop asthma.

Complications

More serious infections can result in respiratory failure, liver failure, and heart failure. Sometimes, bacterial infections occur during or just after viral pneumonia, which may lead to more serious forms of pneumonia.

Prevention

- By washing hands often, especially after blowing nose, going to the bathroom, diapering a baby, and before eating or preparing foods.
- Smoking should be prohibited. Tobacco damages lungs' ability to ward off infection.
- Vaccines may help prevent pneumonia in children, the elderly, and people with diabetes, asthma, emphysema, HIV, cancer, or other chronic conditions.
- A drug called palivizumab is given to some children under 24 months old to prevent pneumonia caused by respiratory syncytial virus.
- Flu vaccine prevents pneumonia and other problems caused by the influenza virus. It must be given each year to protect against new virus strains.

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eMedicine-Medscape
http://www.nlm.nih.gov/medlineplus/ency/article/000073.htm
http://en.wikipedia.org/wiki/Viral_pneumonia
http://www.drugs.com/cg/viral-pneumonia.html

Test Yourself - 32

Correct Answers :

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

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Test Yourself - 33

1. The followings are true for Pregnancy and Diabetes except:
a. Congenital anomalies and foetal growth retardation are the only foetal complications in diabetic pregnancy.
b. Diabetic keto-acidosis, hypoglycaemia, miscarriages, pre-eclampsia are among the maternal complications in diabetic pregnancy.
c. Maternal diabetic complications are frequent in women with both type 1 and type 2 diabetes.
d. Bone fracture, nerve palsy, neonatal hypoglycaemia are among the perinatal complications of gestational diabetes mellitus.

2. All the followings are correct for Melioidosis except:
a. It is caused by B. pseudomallei bacterium.
b. Infections most commonly occur during winter season.
c. The single most important risk factor for developing severe melioidosis is diabetes mellitus.
d. Acute localized skin infection is the most common form of melioidosis.

3. All the below are true for Safe Blood Transfusion except:
a. Donors should be of age from 16 - 65 years.
b. Potential blood donors must weigh at least 50kg.
c. 450ml of blood should be drawn from donors weighing 45 kg and above.
d. 250ml of blood should be drawn from donors weighing 42 - 44kg.

4. All the followings are correct for Viral Pneumonia except:
a. Both DNA and RNA are involved in the oetiology of viral pneumonia.
b. Respiratory syncytial virus(RSV) is the most frequent cause of upper respiratory tract infection in infants and children.
c. More serious infections can result in respiratory failure, liver failure and heart failure.
d. Antibiotics do not treat viral pneumonia.

5. The followings are right for Melioidosis except:
a. B. pseudomallei is inherently resistant to ampicillin, 1st and 2nd generation cephalosporins, fluoroquinolones among the antimicrobials.
b. Intravenous meropenem is the drug of choice for acute illness.
c. The duration of antimicrobial treatment should be at least 10 - 14 days.
d. Co-trimoxazole is currently recommended as 1st line drug for eradication phase.

6. All the followings are correct for Safe Blood Transfusion except:
a. Blood donors only with cardiovascular diseases, epilepsy, mental illness must be permanently deferred.
b. Haemoglobin of the donors must be at least 12g/dl.
c. Fresh frozen plasma is made by rapidly freezing plasma at - 50° C or below.
d. Red cell suspensions are made by adding an additive solution to packed cells.

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Product Profile- Comet™

Comet™
Metformin HCl

500 mg Tablet
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850 mg Tablet
1 gm Tablet
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First-line therapy for Type-2 Diabetes

COMPOSITION
Comet™ 500: Each film coated tablet contains Metformin Hydrochloride BP 500 mg. **Comet™ 750**: Each film coated tablet contains Metformin Hydrochloride BP 750 mg. **Comet™ 850**: Each film coated tablet contains Metformin Hydrochloride BP 850 mg. **Comet™ 1 gm**: Each film coated tablet contains Metformin Hydrochloride BP 1 gm. **Comet™ XR 500**: Each extended release tablet contains Metformin Hydrochloride BP 500 mg. **Comet™ XR 1 gm**: Each extended release tablet contains Metformin Hydrochloride BP 1 gm.

PHARMACOLOGY
Metformin is an antihyperglycemic agent that improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Unlike sulfonylureas, Metformin does not produce hypoglycemia in either patients with type 2 diabetes or normal subjects and does not cause hyperinsulinemia.

INDICATION AND USAGE
Comet™ (Metformin Hydrochloride tablet) is indicated as an adjunct to diet and exercise to improve glycemic control in children and adults with type 2 diabetes mellitus.
Comet™ XR (Metformin Hydrochloride extended release tablet) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

DOSAGE AND ADMINISTRATION
Dosage of **Comet™** or **Comet™ XR** must be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended daily dose. The maximum recommended daily dose of **Comet™** is 2550 mg in adults and 2000 mg in pediatric patients (10-16 years of age); the maximum recommended daily dose of **Comet™ XR** in adults is 2000 mg. **Comet™** should be given in divided doses with meals while **Comet™ XR** should generally be given once daily with the evening meal. **Comet™ XR** tablet must be swallowed whole and never be crushed or chewed. **Comet™** or **Comet™ XR** should be started at a low dose, with gradual dose escalation, both to reduce gastrointestinal side effects and to permit identification of the minimum dose required for adequate glycemic control of the patient.

Recommended Dosing Schedule
a) *Adults*: The usual starting dose of **Comet™** is 500 mg twice a day or 850 mg once a day, given with meals. Dosage increases should be made in increments of 500 mg weekly or 850 mg every 2 weeks, up to a total of 2000 mg per day, given in divided doses. Patients can also be titrated from 500 mg twice a day to 850 mg twice a day after 2 weeks. Doses above 2000 mg may be better tolerated given three times a day with meals. The usual starting dose of **Comet™ XR** is 500 mg once daily with the evening meal. Dosage increases should be made in increments of 500 mg weekly, up to a maximum of 2000 mg once daily with the evening meal. If glycemic control is not achieved on **Comet™ XR** 2000 mg once daily, a trial of **Comet™ XR** 1000 mg twice daily should be considered. Patients receiving **Comet™** treatment may be safely switched to **Comet™ XR** once daily at the same total daily dose, up to 2000 mg once daily.

b) *Pediatrics*: The usual starting dose of **Comet™** is 500 mg twice a day, given with meals. Dosage increases should be made in increments of 500 mg weekly up to a maximum of 2000 mg per day, given in divided doses. Safety and effectiveness of **Comet™** in pediatric patients below 10 years have not been established.

USE IN PREGNANCY
Pregnancy Category B. Most experts recommend that insulin should be used during pregnancy to maintain blood glucose levels as close to normal as possible. Both Metformin immediate and extended release tablets should not be used during pregnancy unless clearly needed.

USE IN NURSING MOTHERS
Because the potential for hypoglycemia in nursing infants may exist, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

PRECAUTION
Metformin is known to be the substantially excreted by kidney and the risk of Metformin accumulation and lactic acidosis increases with the degree of impairment of renal function. Thus, patients with serum creatinine levels above the upper limit of normal for their age should not receive Metformin. In patients with advanced age, Metformin should be carefully titrated to establish the minimum dose for adequate glycemic effect, because aging is associated with reduced renal function.

CONTRAINDICATION
Metformin is contraindicated in patients with:
1. Renal disease or renal dysfunction (e.g., as suggested by serum creatinine levels > 1.5 mg/dL [males], > 1.4 mg/dL [females] or abnormal creatinine clearance).
2. Known hypersensitivity to Metformin hydrochloride. 3. Acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma.

ADVERSE EFFECTS
Diarrhea, nausea, vomiting, flatulence, asthenia, indigestion, abdominal discomfort, headache etc.

WARNINGS
Lactic acidosis can occur due to Metformin accumulation during treatment with Metformin. The reported incidence of lactic acidosis in patients receiving Metformin is very low.

DRUG INTERACTION
No information is available about the interaction of Metformin and furosemide when co-administered chronically. Nifedipine appears to enhance the absorption of Metformin. Metformin had minimal effects on nifedipine. Cationic drugs (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, or vancomycin) that are eliminated by renal tubular secretion theoretically have the potential for interaction with Metformin by competing for common renal tubular transport systems. Metformin had no effect on cimetidine pharmacokinetics. Certain drugs tend to produce hyperglycemia and may lead to loss of glycemic control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid.

STORAGE
Store at cool and dry place and keep away from light. Keep out of reach of children.

HOW SUPPLIED
Comet™ 500: Each box contains 100 tablets in blister pack.
Comet™ 750: Each box contains 60 tablets in blister pack.
Comet™ 850: Each box contains 50 tablets in blister pack.
Comet™ 1 gm: Each box contains 30 tablets in blister pack.
Comet™ XR 500: Each box contains 50 tablets in blister pack.
Comet™ XR 1 gm: Each box contains 30 tablets in blister pack.

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500 mg IM/IV
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Neonates and children (up to 2 months)	:	25 to 60 mg/kg/day in 2 divided doses
Infants and children (over 2 months)	:	30 to 100 mg/kg/day in 2 to 3 divided doses
Adults	:	1 to 6 gm per day 8 or 12 hourly
Patients over 65 years of age	:	1 gm 12 hourly

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Escitalopram 5 & 10 mg tablet

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- Capsule (200 mg and 400 mg)
- Powder for Suspension (100 mg/5 ml)
- Forte Powder for Suspension (200 mg/5 ml)

- Superior to current oral Cephalosporins against clinically important bacteria
- Excellent efficacy in MDR enteric fever
- Drug of choice for the treatment of RTI
- Shows excellent efficacy in UTI
- First-line therapy for the treatment of gonorrhea

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