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**PROPHYLAXIS OF
TUBERCULOSIS**

Prophylaxis of tuberculosis:

- ✓ **Social,**
- ✓ **Infectious control,**
- ✓ **Sanitary,**
- ✓ **BCG vaccination,**
- ✓ **Preventive Chemotherapy**

Social prophylaxis

Principles of prophylactic orientation, state character, toll-free medi-care are fixed in basis of social prophylaxis.

It is carried out due to the measures of socio-economic character of state scale.

A social prophylaxis is directed on:

- ✓ making healthy of environment;**
- ✓ it is an increase of financial welfare of population;**
- ✓ it is strengthening of health of population;**
- ✓ it is an improvement of feed and vitally domestic terms;**
- ✓ it is development of physical education and sport;**
- ✓ are measures on a fight against alcoholism, drug addiction, smoking, other harmful habits.**

BCG VACCINE

Bacillus Calmette–Guérin (historically Vaccin Bilié de Calmette et Guérin commonly referred to as Bacille de Calmette et Guérin or BCG) is a vaccine against tuberculosis that is prepared from a strain of the

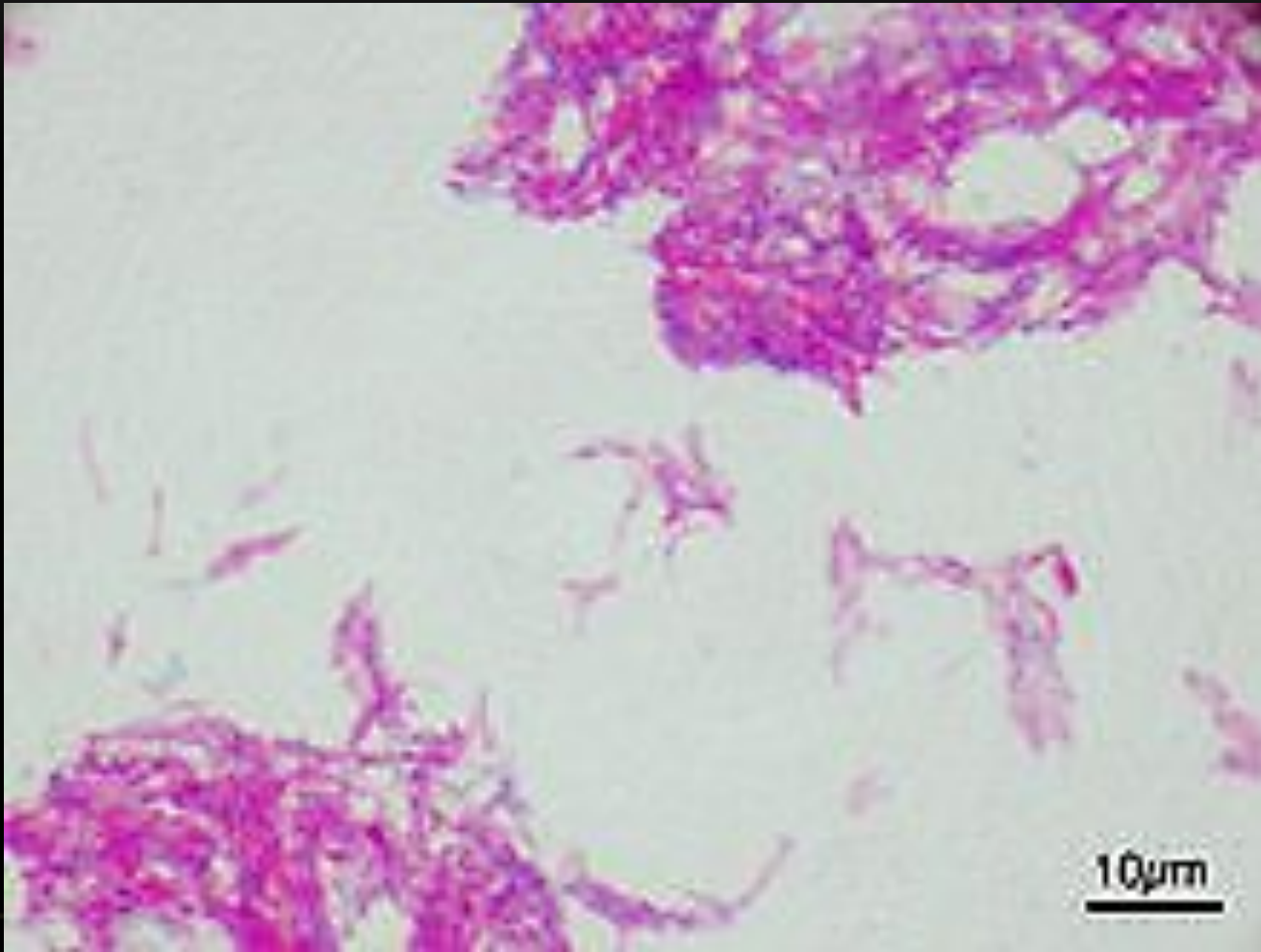
attenuated (virulence-reduced) live bovine tuberculosis bacillus, *Mycobacterium bovis*, that has lost its virulence in humans by being specially subcultured in a culture medium, usually Middlebrook 7H9.



Because the living bacilli evolve to make the best use of available nutrients, they become less well-adapted to human blood and can no longer induce disease when introduced into a human host. Still, they are similar enough to their wild ancestors to provide some degree of immunity against human tuberculosis.

The BCG vaccine can be anywhere from 0 to 80% effective in preventing tuberculosis for a duration of 15 years.

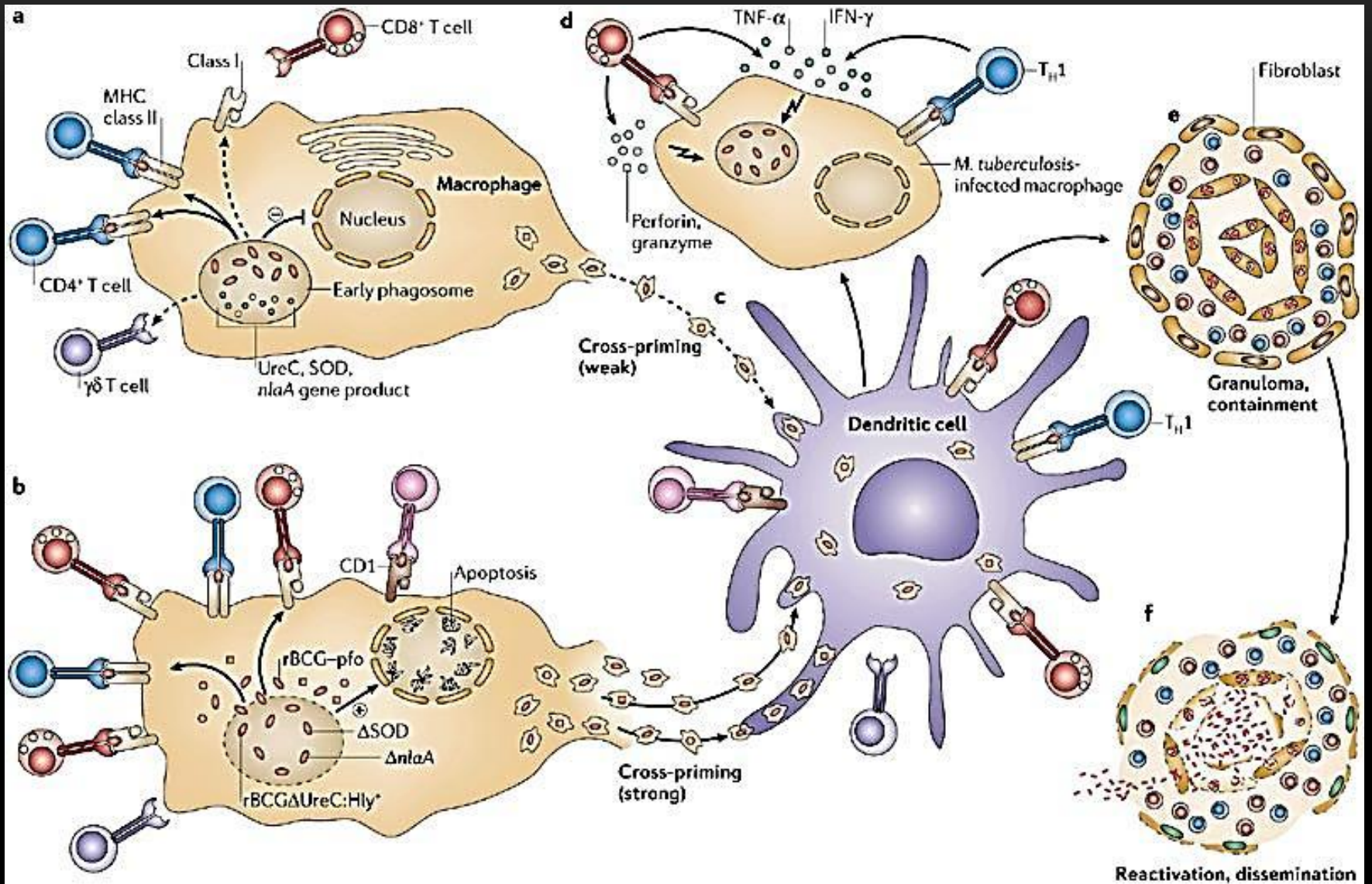
**Microscopic image of the Calmette-Guérin bacillus,
Ziehl-Neelsen stain, magnification:1,000**



The bacille Calmette-Guérin (BCG) vaccine has existed for 80 years and is one of the most widely used of all current vaccines, reaching >80% of neonates and infants in countries where it is part of the national childhood immunization programme. BCG vaccine has a documented protective effect against meningitis and disseminated TB in children. It does not prevent primary infection and, more importantly, does not prevent reactivation of latent pulmonary infection, the principal source of bacillary spread in the community. The impact of BCG vaccination on transmission of MTB is therefore limited.

The biological interaction between MTB and the human host is complex and only partially understood. Recent advances in areas such as mycobacterial immunology and genomics have stimulated research on numerous new experimental vaccines, but it is unlikely that any of these urgently need vaccines will be available for routine use within the next few years. In the meantime, optimal utilization of BCG is encouraged.

RECOMBINANT BCG VACCINE



Tuberculosis vaccine (BCG)

is used for active specific prophylaxis of tuberculosis – dry for intracutaneous transfusion.

These are live mycobacteria of vaccine strain, lyophilically dried in 1,5 % solution of sodium glutamate. It looks like a white dried mass.

It is manufactured in ampullas of 1 mg of vaccine, which contains 20 doses, each of 0,05 mg of the preparation. BCG vaccine is used intracutaneously in a dose of 0,05 mg in the volume of 0,1 ml.

The primary vaccination is done to healthy, delivered at the right time newly borns on the 3-5th day of their life.

BCG-M vaccine

is manufactured in a half dose (0,5 mg in an ampulla, which contains 20 doses, each of 0.025 mg of the preparation)

is meant for vaccinating prematurely newly borns and children who were not immunised at birth in connection with contraindications, as well as for vaccination and revaccination of children, who live in the territories (areas) contaminated with radionuclides (III-IV zone).

BCG-STRAINS

There have been many (WHO estimated 40 or more in 1999) manufacturers of BCG around the world. The most widely-used strains in international immunization programmes include: “Danish 1331” strain; “Moscow” strain, and “Tokyo 172” strain. The use of other strains is largely limited to their country of origin, e.g. “Moreau” strain (Brazil) or “Tice” strain (USA).

- **when the vaccine had been administered in infancy, as is recommended by WHO and widely practiced, use of presence or absence of BCG scar years later was not a highly sensitive and reliable indicator of prior vaccination status.**

There is also no evidence of a correlation between increased BCG scar size and protection against either tuberculosis.

VACCINATION PROCEDURE

BCG is given as a single intradermal injection at the insertion of the deltoid



THE RULES OF TRANSFUSION

▶ The dry vaccine (1 ampulla) is dissolved in 2 ml of isotonic solution and the cultivation is the result, i.e. 1 dose in 0,1 ml of the solution.

▶ The vaccine is used during 2-3 hours, the remnant is destroyed by boiling.

▶ 0,2 ml of the dissolved vaccine is taken into 1-gram syringe after mixing, the air and part of the preparation up to 0,1 ml mark is evacuated through the needle.

▶ The vaccine is injected strictly intracutaneously on the limit between the upper and the *middle third* part of the shoulder, having previously rubbed the skin with 70° spirit.

▶ At the proper technique a whitish papule of 5-6 mm in diameter is formed, which resolves in 15-20 minutes.

IN 4-6 WEEKS



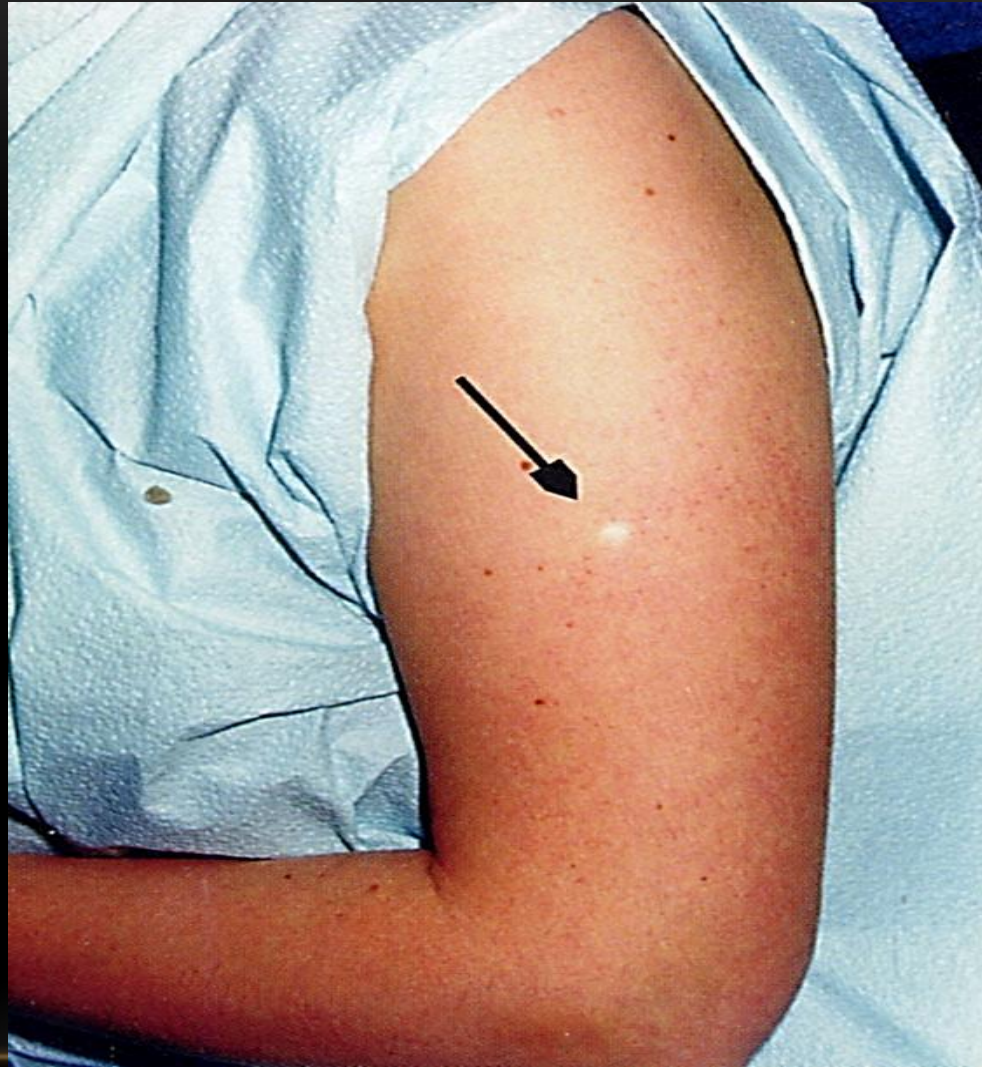
pustule

IN 6-8 WEEKS



crust

IN 2-4 MONTHS



cicatrix

BCG IN ADOLESCENTS AND ADULTS

- **There is no evidence that revaccination with BCG affords any additional protection, and general revaccination is therefore not recommended.**
- **However, given the serious consequences of developing multidrug-resistant disease and the low reactogenicity of the vaccine, BCG vaccination may be considered for all HIV-negative, unvaccinated, tuberculin-negative persons who are in an unavoidable close exposure to multidrug-resistant tuberculosis (MTB) (e.g. health care workers in facilities still lacking of proper TB infection control measures in place).**

BCG IN HIV-INFECTED NEWBORNS

- **In children who are known to be HIV-infected, BCG vaccine should not be given.**
- **In infants whose HIV status is unknown and who are born to HIV-positive mothers and who lack symptoms suggestive of HIV, BCG vaccine should be given after considering local factors. Such factors are likely to be important determinants of the risk-benefit balance of such an approach and include: coverage and success of the prevention of mother to child transmission of HIV programme; possibility of deferring BCG vaccination in HIV-exposed infants until HIV infection status has been established; availability of early diagnosis of HIV infection in infants; and, provision of early ART to HIV-positive infants.**

COMPLICATIONS (BCG-RELATED DISEASES)

CLASSIFICATION (*WHO, 1984*)

- **Local (the most frequent) – cold abscess, ulcer, regional lymphadenitis.**
- **Disseminated BCG-infection (osteitis, lupus).**
- **Generalized BCG-infection with lethal outcomes.**
- **Post-BCG syndrome (cheloid cicatrix, nodular erythema, allergic rash).**

BCG LYMPHADENITIS



- The term "BCG lymphadenitis" is usually coined when ipsi-lateral axillary, supraclavicular or lower cervical lymph node enlargement developing after BCG vaccination is severe enough to arouse significant concern from the child care provider to seek medical attention.

BCG LYMPHADENITIS



- There are two forms of BCG lymphadenitis.
- The **nonsuppurative form** (simple form) is characterised by a benign clinical course and the lesion resolves spontaneously without any sequelae over a period of weeks.
- The **suppurative form** is marked by the progressive enlargement of regional lymph nodes leading to a collection of suppurative material, with recognisable fluctuation in the swelling.

BCG LYMPHADENITIS



Overlying skin changes is universal, with erythema, edema, increased pigmentation and pustule formation. If left untreated, the suppuration will eventually rupture, leading to persistent caseous discharge and sinus formation.

Wound healing inevitably takes several months, which is unpleasant to both patients and their care providers. Frequent and meticulous wound dressing is required, and secondary bacterial infection, unsightly scarring or keloid formation are not uncommon sequelae.

BCG LYMPHADENITIS

Three treatment options have been described for BCG lymphadenitis.

Antibiotic Therapy

Several antibiotics (e.g. erythromycin) and antituberculous medications (e.g. isoniazid and rifampicin) have been used.

It should also be noted that BCG is generally not susceptible to pyrazinamide, a first-line agent for treating TB. Antibiotic therapy is, however, often indicated for treatment of suppurative lymphadenitis proven to be caused by superinfection with pyogenic bacteria such as *Staphylococcus aureus* or *Streptococcus pyogenes*, as definitive therapy or an adjunct to surgical intervention.

Needle Aspiration

For suppurative BCG lymphadenitis, given time there is almost universal development of spontaneous perforation and sinus formation if left untreated. Recent studies have shown that needle aspiration can help to prevent this complication and shorten the duration of healing, apart from offering valuable diagnostic information.

Surgical Excision

Surgical excision is a definitive way to remove the affected lymph node(s) and promote early cure and better wound recovery.

COMPLICATION: ULCER



- developing 3-4 weeks after vaccination

COMPLICATION: CHELOID CICATRIX



DISSEMINATED BCG-INFECTION

- **Osteitis after BCG vaccination is a rare condition, with an incidence of approximately 0.39/1,000,000, depending on the bacillus used.**
- **Bone involvement occurs due to lymphohematogenous dissemination, and the lesion site is not necessarily associated with the injection site. The sites most often affected are the tibia, femur, vertebrae, sternum and ribs.**



DISSEMINATED BCG-INFECTION

- **Clinical manifestations usually occur 18 months after vaccination, this interval can range from a few months to 5 years.**
- **The initial symptoms are sensitivity, pain and limited movement of the affected region. When present, fever is low and does not affect the general status of the individual.**
- **On X-rays, lytic lesions with a sclerotic halo can be seen, as can periosteal reaction and periarticular osteoporosis.**
- **Histopathological studies show granulomatous inflammation with epithelioid cells, with or without caseous necrosis. Acid-fast bacilli are detected in approximately half of all cases, and most present strongly positive PPD reactions.**
- **It recommends treatment with isoniazid and rifampin for 12 months.**
- **In most cases, long-term antituberculosis therapy and surgical drainage are necessary for remission. Fortunately, the prognosis is good, with a low frequency of complications. Therefore, the use of BCG vaccine should be maintained in countries with a high incidence of TB.**

GENERALIZED BCG-INFECTION

- Generalized infection due to BCG vaccination has also been reported, sometimes being fatal. Systemic BCG-itis is a recognized but rare consequence of BCG vaccination, and traditionally has been seen in children with severe immune deficiencies. A recent multi-centre study has identified the syndrome in children with severe combined immunodeficiency (SCID), chronic granulomatous disease, Di George syndrome and homozygous complete or partial interferon gamma receptor deficiency (Jouanguy, 1996; Jouanguy 1997; Casanova, 1995). Its frequency is reported as less than 5 per million vaccine recipients, reflecting the rarity of the underlying conditions (Lotte, 1988). If not properly managed, these cases may be fatal.
- According to Mande, 1980, the first case was reported in 1953, 30 years after BCG had first been applied to man. Between 1954 and 1980, 34 cases were published in the global literature, and the Lotte et al. study estimates the incidence as 2.19 per one million vaccine recipients. Nevertheless, three recent Canadian cases were reported in 1998. Severe and generalized BCG infection that may occur in immunocompromised individuals should be treated with anti-tuberculous drugs including isoniazid and rifampicin (Romanus et al., 1993).

LATENT TB INFECTION

- **Latent tuberculosis infection (LTBI) is defined as a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB .**
- **One third of the world's population is estimated to be infected with M. tuberculosis. The vast majority of infected persons have no signs or symptoms of TB disease and are not infectious, but they are at risk for developing active TB disease and becoming infectious. The lifetime risk of reactivation TB for a person with documented LTBI is estimated to be 5–10 %, with the majority developing TB disease within the first five years after initial infection.**
- **However, the risk of developing TB disease following infection depends on several factors, the most important one being the immunological status of the host.**

PREVENTIVE CHEMOTHERAPY

- **Guidelines on the management of latent tuberculosis infection were developed in accordance to the requirements and recommended process of the WHO Guideline Review Committee, and provide public health approach guidance on evidence-based practices for testing, treating and managing LTBI in infected individuals with the highest likelihood of progression to active Disease.**
- **The guidelines are also intended to provide the basis and rationale for the development of national guidelines. The guidelines are primarily targeted at high-income or upper middle-income countries with an estimated TB incidence rate of less than 100 per 100 000 population.**
- **Resource-limited and other middle-income countries that do not belong to the above category should implement the existing WHO guidelines on people living with HIV and child contacts below 5 years of age.**

PREVENTIVE CHEMOTHERAPY

- **Systematic testing and treatment of LTBI should be performed in people living with HIV, adult and child contacts of pulmonary TB cases, patients initiating anti-tumour necrosis factor (TNF) treatment, patients receiving dialysis, patients preparing for organ or haematologic transplantation, and patients with silicosis. Either interferon-gamma release assays (IGRA) or Mantoux tuberculin skin test (TST) should be used to test for LTBI.**

(Strong recommendation, low to very low quality of evidence)

PREVENTIVE CHEMOTHERAPY

- **Systematic testing and treatment of LTBI should be considered for prisoners, health-care workers, immigrants from high TB burden countries, homeless persons and illicit drug users. Either IGRA or TST should be used to test for LTBI.**

(Conditional recommendation, low to very low quality of evidence)

PREVENTIVE CHEMOTHERAPY

- **Systematic testing for LTBI is not recommended in people with diabetes, people with harmful alcohol use, tobacco smokers, and underweight people provided they are not already included in the above recommendations.**

(Conditional recommendation, very low quality of evidence)

PREVENTIVE CHEMOTHERAPY

- **Individuals should be asked about symptoms of TB before being tested for LTBI. Chest radiography can be done if efforts are intended also for active TB case finding. Individuals with TB symptoms or any radiological abnormality should be investigated further for active TB and other conditions.**

(Strong recommendation, low quality of evidence)

PREVENTIVE CHEMOTHERAPY

- **Either TST or IGRA can be used to test for LTBI in high-income and upper middle-income countries with estimated TB incidence less than 100 per 100 000**
(Strong recommendation, low quality of evidence).
- **IGRA should not replace TST in low-income and other middle-income countries.**
(Strong recommendation, very low quality of evidence)

**FOR RESOURCE-LIMITED COUNTRIES AND OTHER
MIDDLE-INCOME COUNTRIES THAT DO NOT BELONG TO THE
ABOVE CATEGORY**

- **People living with HIV and children below 5 years of age who are household or close contacts of people with TB and who, after an appropriate clinical evaluation, are found not to have active TB but have LTBI should be treated.**

(Strong recommendation, high quality of evidence)

PREVENTIVE CHEMOTHERAPY

- Treatment options recommended for LTBI include:
- 6-month isoniazid, or
- 9-month isoniazid,
- or 3-month regimen of weekly rifapentine plus isoniazid,
- or 3–4 months isoniazid plus rifampicin, or 3–4 months rifampicin alone.

(Strong recommendation, moderate to high quality of evidence).

MDR-TB CASES

- **Strict clinical observation and close monitoring for the development of active TB disease among contacts of multidrug-resistant TB (MDR-TB) cases preferably for at least two years over the provision of preventive treatment.**
- **Clinicians can consider individually tailored treatment regimens based on the drug susceptibility profile of the index case, particularly for child contacts below 5 years of age, when benefits can outweigh harms with reasonable confidence.**

RISK OF DRUG RESISTANCE FOLLOWING LTBI TREATMENT

A systematic review was conducted to determine whether LTBI treatment leads to significant development of resistance. The systematic review considered the following treatment regimens:

- **Isoniazid for 6- to 12-month** duration: Thirteen studies comparing 6- to 12-month isoniazid preventive therapy versus no treatment or placebo were included in the systematic review (seven involving HIV uninfected populations); no difference in the risk of resistance among incident TB cases was found (risk ratio = 1.45 (95% CI: 0.85–2.47)). There was little evidence of heterogeneity ($p=0.923$) and the risk ratio for HIV-uninfected and HIV-infected populations was comparable. The quality of the evidence was moderate.
- **Isoniazid for 36 months in HIV-infected individuals**: Three studies comparing 36- and 6-month isoniazid were reviewed but only one study provided resistance rates, and no significant Difference in drug resistance was found (risk ratio = 5.96 (95% CI: 0.24–146) (24). The two other studies reported that the observed proportion of resistant cases were similar to the expected rate in the background population, but did not provide a direct comparison of resistance rates between those receiving 36 months compared to those receiving 6 months treatment (25,26). Therefore, it was concluded that there is no evidence to indicate whether or not continuous use of isoniazid increases the risk of isoniazid resistance.

INFECTION CONTROL OF TUBERCULOSIS

HIERARCHY OF INFECTION PREVENTION & CONTROL

- **Administrative controls**
 - Reduce risk of exposure, infection and disease thru policy and practice
- **Environmental (engineering) controls**
 - Reduce concentration of infectious bacilli in air in areas where air contamination is likely
- **Personal respiratory protection**
 - Protect personnel who must work in environments with contaminated air

ADMINISTRATIVE CONTROLS

- **Develop and implement written policies and protocols to ensure:**
 - Rapid identification of TB cases (e.g., improving the turn-around time for obtaining sputum results)
 - Isolation of patients with PTB
 - Rapid diagnostic evaluation
 - Rapid initiation treatment
- **Educate, train, and counsel HCWs about TB**
- **To the extent possible, avoid mixing TB patients and HIV patients in the hospital or clinic setting**

ENVIRONMENTAL CONTROLS: VENTILATION AND AIR FLOW

- **Ventilation is the movement of air**
- **Should be done in a controlled manner**
- **Types**
 - Natural
 - Local
 - General
- **Simple measures can be effective**

EVIDENCE FROM PERU

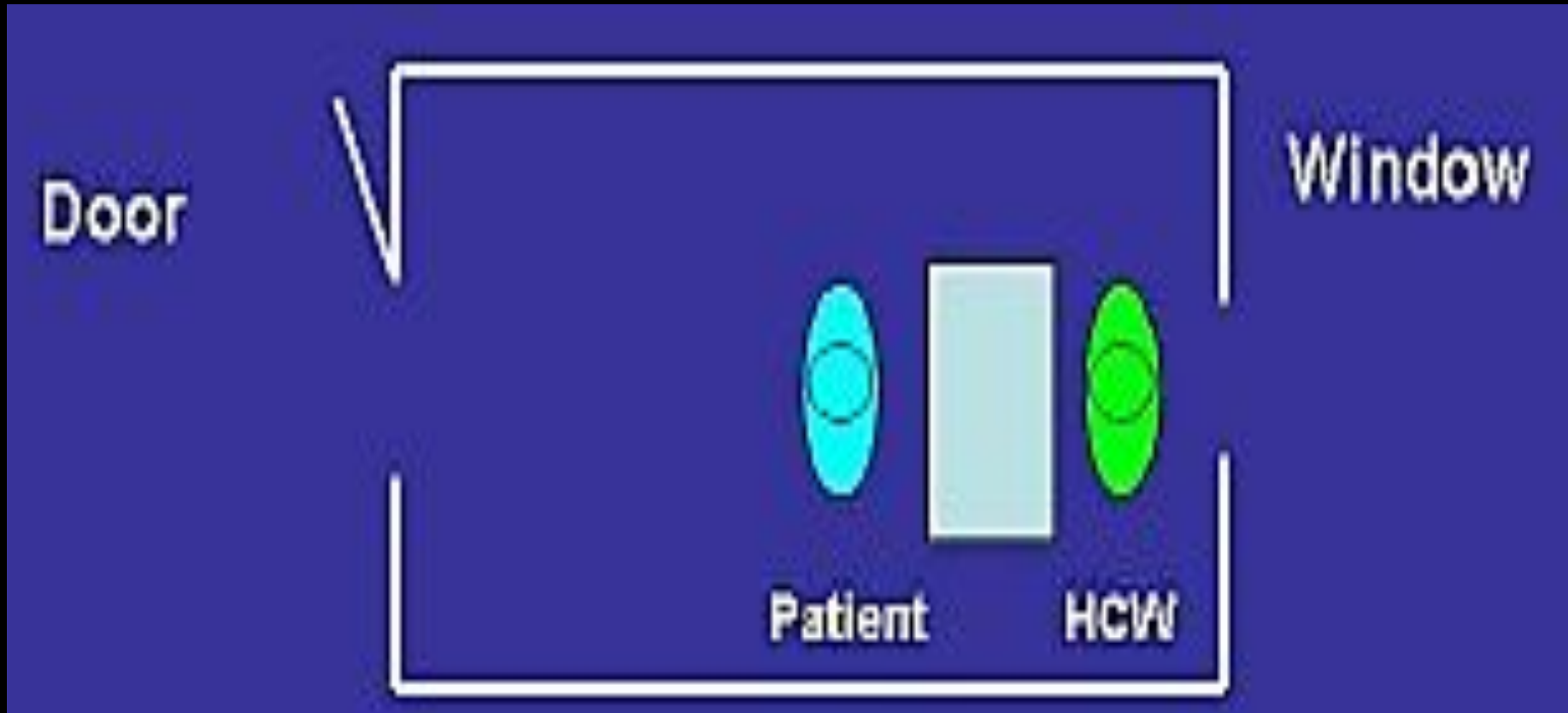
- Open windows and doors produced 6x greater air exchanges than mechanical ventilation and 20x greater air changes per hour than with windows closed
- Natural ventilation in “old-style” hospitals and clinics resulted in much better ventilation and much lower calculated TB risk, despite similar patient crowding
 - More likely to have larger, higher ceilings; larger windows; windows on opposite walls allowing through-flow of air

ESTIMATED RISK OF AIRBORNE TB INFECTION

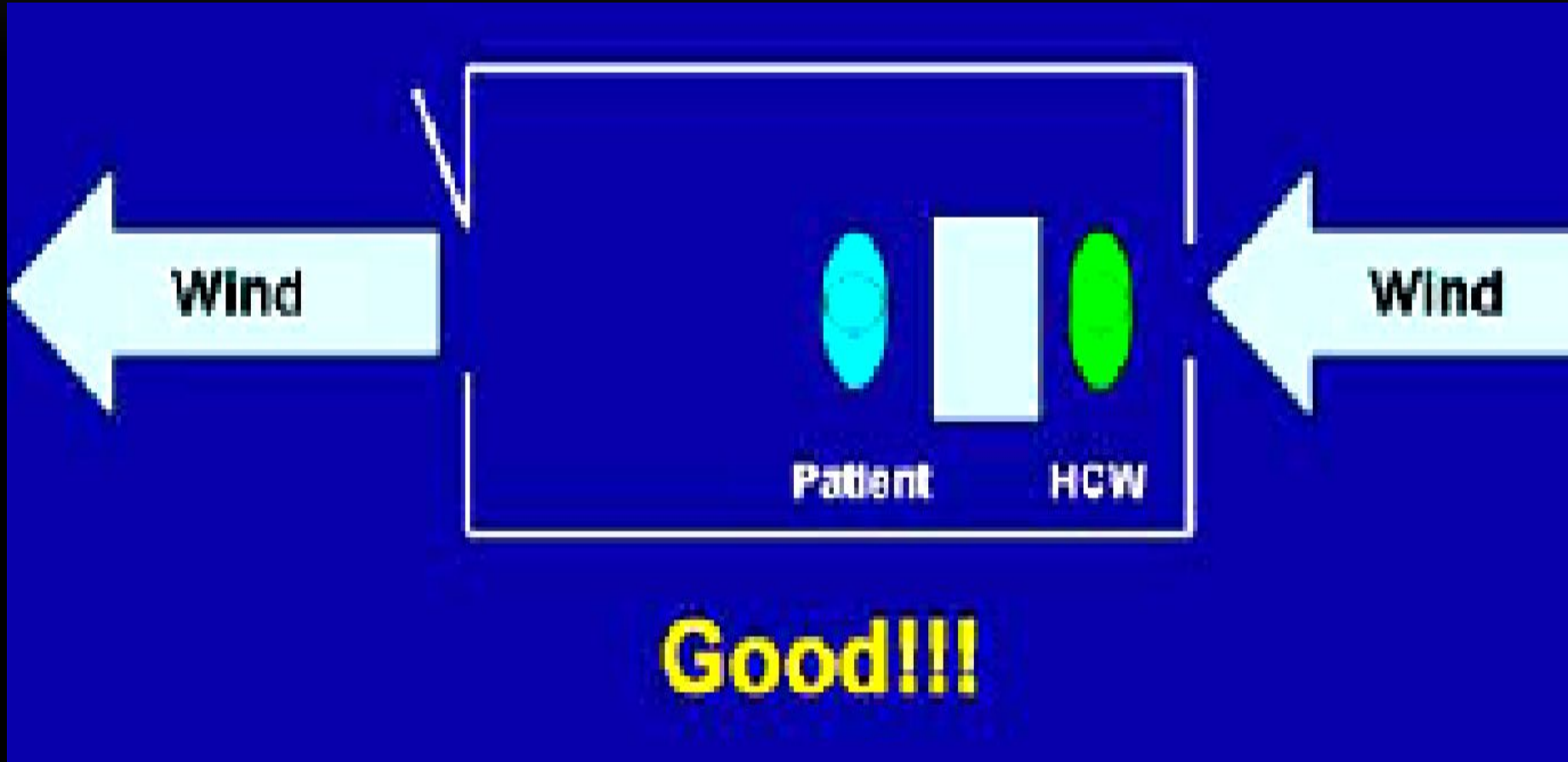
- Naturally ventilated, windows closed - **97%**
- Mechanically ventilated with neg pressure (ACH 12) - **39%**
- Naturally ventilation, windows and doors fully open:
 - Modern (1970-1990) - **33%**
 - Old-fashioned (pre-1950) - **11%**

Direction of Natural Ventilation and Correct Working Locations

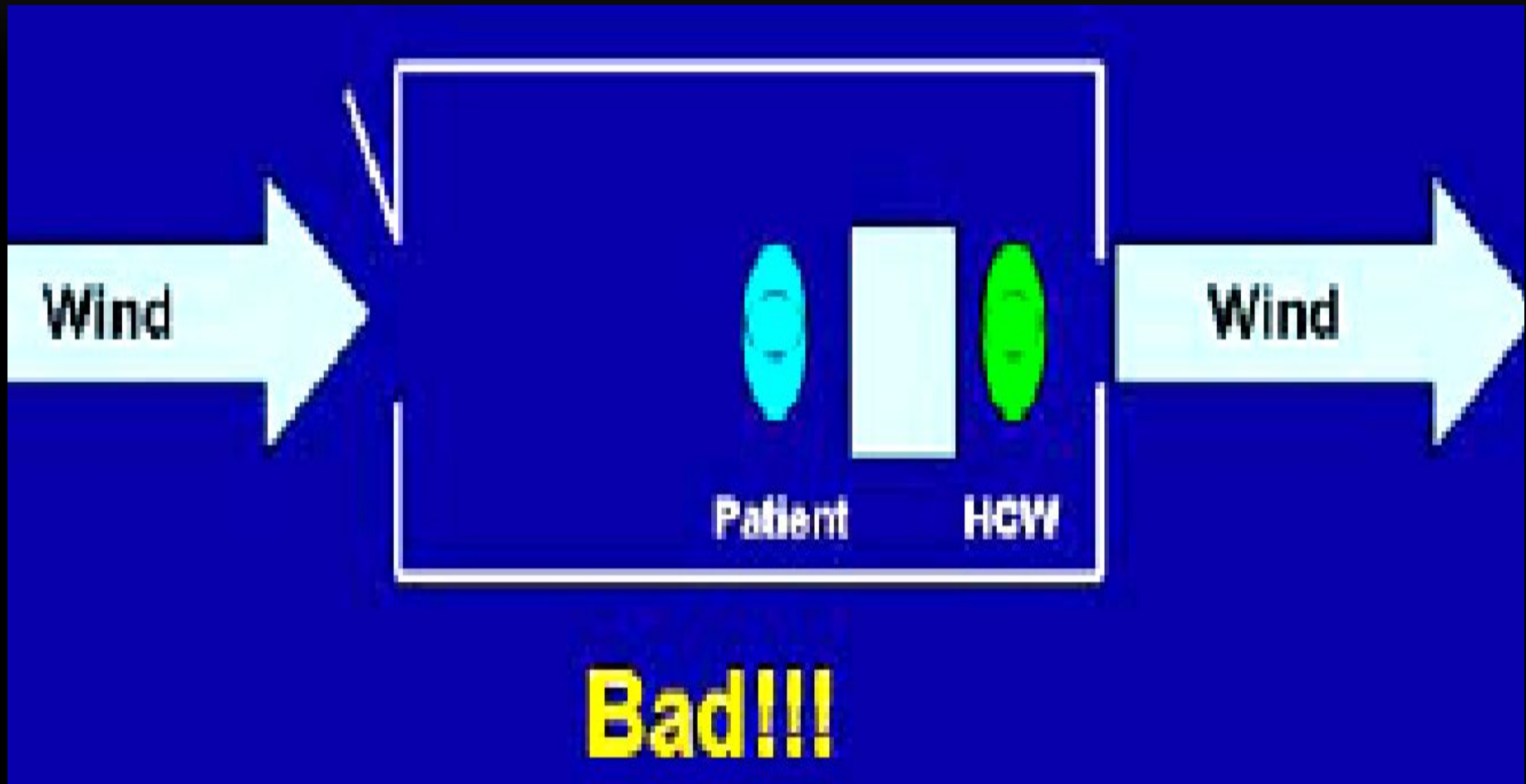
When increasing ventilation and air flow, care should be taken as to the appropriate positioning of the windows, doors, the patient and the HCW to control infection



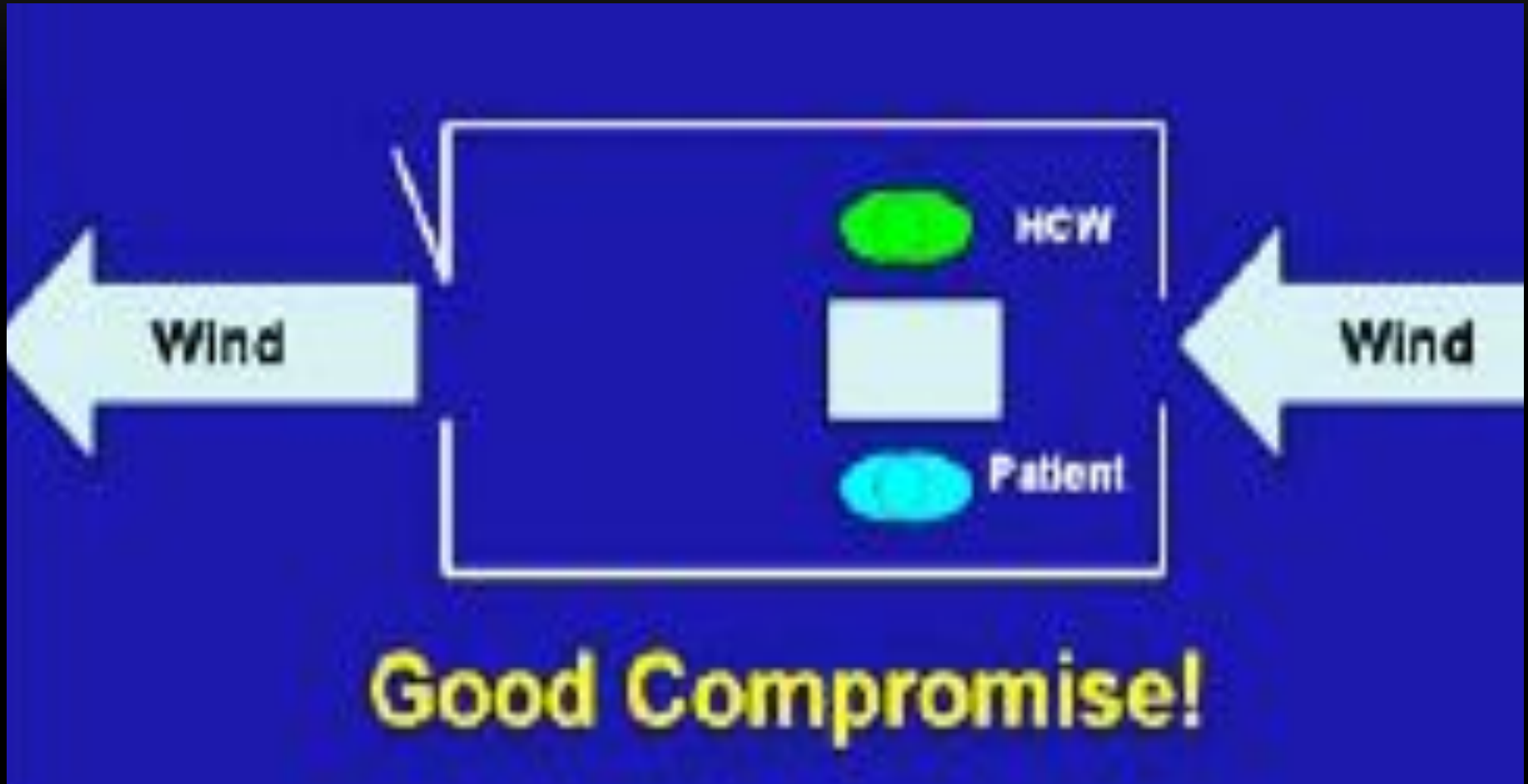
Direction of Natural Ventilation and Correct Working Locations



Direction of Natural Ventilation and Correct Working Locations



Direction of Natural Ventilation and Correct Working Locations



Remember, the patient is the one that is infected and might pass on TB to the
HCW

HIGH-RISK PROCEDURES

- Sputum induction or sputum collection
- Aerosol breathing treatments
- Pentamidine treatment (on any patient)

SPECIAL VENTILATION PRECAUTIONS USED

Local exhaust ventilation booth or tent

Local exhaust ventilation hood

AllR with 6*-12 air changes per hour (ACH) exhausted directly outdoors away from operable windows, doors, and air intake vents (using HEPA filtration if possible, where human traffic may exist)

Performed outdoors only (sputum collection only)

- Bronchoscopy
- Airway suctioning

AllR with 6*-12 ACH exhausted directly outdoors away from operable windows, doors, and air intake vents (using HEPA filtration if possible, where human traffic may exist)

- Processing specimens for mycobacteriology studies

Class I or Class II biological safety cabinet (BSC) in a room with All environmental controls

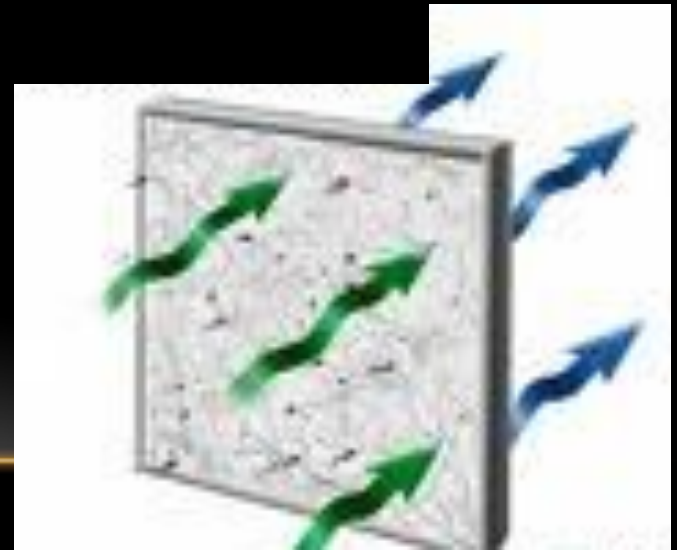
ENVIRONMENTAL CONTROLS

Both indirect ultraviolet irradiation of air and HEPA filters have been used in some high-risk settings to reduce the concentration of infectious TB particles in the ambient air

Ultraviolet Light



HEPA (high efficiency particulate air) filters



PERSONAL RESPIRATORY PROTECTION

- **Respirators:**
 - Can protect HCWs
 - Should be encouraged in high-risk settings
 - May be unavailable in low-resource settings
- **Face/surgical masks:**
 - Act as a barrier to prevent infectious patients from expelling droplets
 - Do not protect against inhalation of microscopic TB particles

N95 RESPIRATOR DOS AND DON'TS

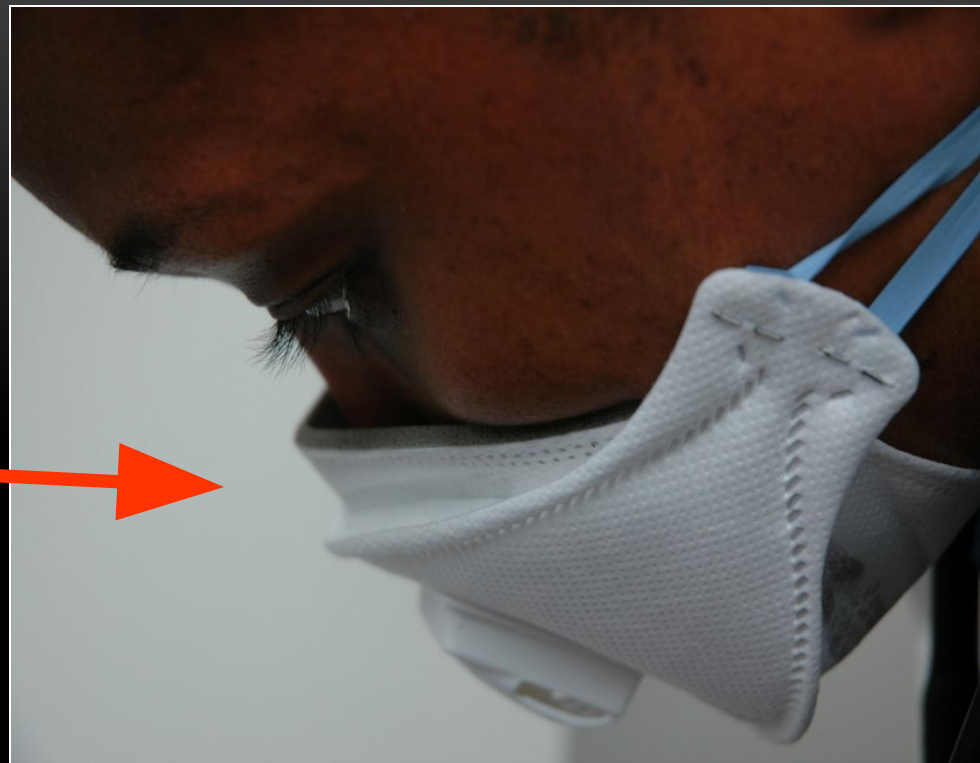


**Be sure your
respirator is
properly fitted!**

**It should fit
snugly at nose
and chin**



**Note poor fit at the
bridge of nose**



**Note poor fit at the
chin**

**Respirator should
cover chin and
create a seal**



High efficiency particulate air (HEPA) filters

HEPA filters or absolute filters are those able to remove 99.97 % of particles with a diameter larger than $0.3 \mu\text{m}$ which pass through them. They can be placed in exhaustion ducts, in room ceilings or in movable filtration units

The use of HEPA filters and/or UV light is strongly recommended for rooms where the following procedures take place:

- ✓ bronchoscopy,
- ✓ induced sputum,
- ✓ pentamidine nebulization,
- ✓ necropsy,
- ✓ isolation.

The combination of an adequate number of air changes with negative pressure and a HEPA filter or UV light minimizes the risk of transmission in the environment in which the TB patient is assisted and in the area where the air is exhausted. The germicidal efficiency of the UV light is limited to its area of direct incidence and decreases with time

HEPA filters are used:

- To purify the exhaustion of air of contaminated environments
- To recirculate the air inside the room or to other rooms facilitating the number of air changes per hour.

DON'T FORGET TO WEAR IT!

Remember, respirators and masks don't do you any good if kept in your pocket or purse!



THANK YOU FOR YOUR ATTENTION!