Prevention of Healthcare-associated Infections in Neonatology

Pan American Health Organization

World Health Organization
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LATIN AMERICAN CENTER FOR PERINATOLOGY
WOMEN AND REPRODUCTIVE HEALTH · CLAP/WR

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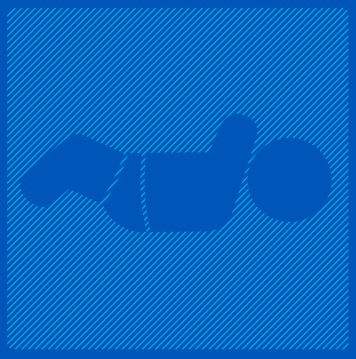

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Summary

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Introduction

Advances in neonatology in recent decades have enabled the survival of preterm and extremely low birthweight newborns, as well as newborns with some malformations. However, with this improvement in initial survival, other problems have emerged, including an increase in health-care-associated infections (HAIs), which has become one of the factors limiting survival of these children [1].

Modes of transmission of infection

Intrauterine colonization or infection of the fetus can occur through the placenta or through ascending infection when there is premature rupture of the membrane and childbirth does not occur immediately.

After birth, the process of colonization continues through direct contact with the mother, family members, and nursery personnel, or through indirect contact with inanimate objects such as thermometers, stethoscopes, and transducers. Infection resulting from colonization depends on the degree of immunity of the newborn and the virulence of the microorganism.

In addition to contact, which is the most common and important mechanism of colonization and/or infection of newborns, other forms of transmission should be considered: contaminated fluids, such as blood and blood products, medications, parenteral nutrition, breast milk, and infant formulas; the respiratory tract, mainly in outbreaks of viral infections such as influenza and adenovirus; and vectors capable of transmitting dengue, malaria, and yellow fever, although occurrences of these are rare in hospital neonatal units.

All the situations noted above refer to the exogenous sources most frequently responsible for epidemic outbreaks. In addition, the newborn's microbiota, which suffers direct action of selective pressure of antibiotics, is responsible for the continued endemicity of hospital-associated infections in neonatal units.

Definition of HAI in the neonatal period

The Pan American Health Organization considers all infections occurring in the neonatal period to be HAIs, except for those transmitted prenatally. HAIs are classified as "early" when they manifest in the first 48 hours of life, and "late" when they manifest more than 48 hours after birth.

Many countries in the Region of the Americas have their own definitions of HAI that should be followed by the hospitals in these countries.

It is essential to establish national criteria for HAI that can be used in all of a country's neonatal care services in order to standardize the collection of epidemiological data, monitor these infections, and establish prevention and control strategies.

In this document we will address aspects of HAI prevention in the hospital environment, including birth, rooming-in, and the neonatal hospitalization unit.

Risk factors for HAI in newborns [1,3]

The main risk factors for infection in newborns include low birthweight, weak immune defenses, the need for invasive procedures, and alteration of the bacterial flora through acquisition of hospital flora.

In addition to risk factors inherent in newborns, other risk factors for HAI correspond to the institution where the newborn is admitted:

- the number of newborns admitted is disproportion to the number of professionals on the health team;
- number of inpatients exceeding the capacity of the institution.

Strategies for prevention of HAI in neonatology

The strategies for prevention of HAI include administrative measures, general and specific measures for prevention and control, including good birth practices [4, 5], and incentives for breast-feeding [6, 7].

To reduce neonatal morbidity and mortality, care for newborns should follow good evidence-based practices.

Physical structure and material and human resources

The physical environment and the availability of human resources in neonatal care units should be aligned with current legislation.

- For clinical situations in which breast-feeding is not possible, it is important to ensure the supply of pasteurized breast milk or milk formula coming from a human milk bank or a milk preparation unit, respectively, with adherence to good practices of preparation, storage, and administration, in accordance with current legislation.

- The supply of parenteral nutrition and intravenous drugs is another critical point for infection. The hospital pharmacy should validate its suppliers and assume responsibility for safe drug storage and dispensing. In hospitals with pharmacies that dispense single doses of drugs, the pharmacy team should also assume responsibility for good preparation practices, in accordance with their country's health legislation.

- With regard to human resources, in addition to maintaining an adequate balance between the number of personnel and the number of newborns served in intensive or intermediate care units, it is fundamental to have a trained team of nurses and nursing technicians, pharmacists, physical therapists, and physicians who can carry out all necessary newborn care procedures using appropriate techniques and following all safety standards. The staffing ratio can vary in accordance with the level of complexity, following the legislation of each country. Evidence points to an increase in the number of hospital infections with higher patient-nurse ratios in neonatal units.

- The occupational health of these professionals is another point to be emphasized. Great care should be taken with skin injuries, especially on the hands, and with acute infectious conditions, especially upper respiratory tract infections, conjunctivitis, and diarrhea. Professionals with these diseases can infect newborns. They should be treated appropriately and kept away from patients during the acute phase of the disease.

- Standardization of routines is essential, including protocols to prevent cross-transmission of microorganisms in the hospital environment (hand hygiene and standard precautions), good practices in invasive procedures, and rational use of antibiotics. All these are important in the prevention of HAI in the neonatal period.

- In addition to standardizing routines for direct care, it is important to consider the structure of healthcare delivery, including the standardization of routines for cleaning and disinfection of the environment, materials, and equipment used in the care of newborns. Work processes should be organized to ensure safe practices in the use of drugs and in parenteral and enteral nutrition of newborns; supplies and equipment appropriate for neonatal care; laboratory support for timely diagnosis; and a trained team with sufficient personnel to carry out these activities.

In short, all these aspects aimed at improving work processes and safety in neonatal care are critical for the reduction of deaths and morbidities resulting from infections and other adverse events associated with healthcare.

This document sets forth practical guidelines for the health team responsible for direct or indirect newborn care. The objective is for all health professionals to adhere to safe practices in providing care, thus contributing to the prevention and control of infections and, consequently, to the reduction of infant mortality from HAI.

Clinical Diagnosis and Laboratory Diagnosis

Infection in neonatology: When should it be considered?

The diagnosis of infection in newborns is difficult, since symptoms are nonspecific and can form part of the clinical picture of multiple diseases.

Symptoms indicating early or late infection include hypoactivity, thermal instability, glucose intolerance/hyperglycemia, apnea, respiratory distress, food intolerance, bleeding, and hemodynamic instability, among others.

The clinical picture can be difficult to differentiate from other conditions that affect newborns, and any one symptom by itself has low positive predictive value, the highest being 31% for hypotension[12]. For this reason, pediatricians need to know the differential diagnosis for each symptom that can be part of the clinical picture of infection so that they can evaluate suspected cases and confirm or disconfirm the diagnosis with greater confidence.

General decline: also reported as hypoactivity/lethargy by the medical team. This is a nonspecific and subjective sign of neonatal sepsis. However, the sleep-wakefulness cycle can often be confused with hypoactivity, given that newborns, especially in the first month, spend most of their time sleeping when not in discomfort. Newborns can appear underactive for several reasons, including:

General decline: also reported as hypoactivity/lethargy by the medical team. This is a nonspecific and subjective sign of neonatal sepsis. However, the sleep-wakefulness cycle can often be confused with hypoactivity, given that newborns, especially in the first month, spend most of their time sleeping when not in discomfort. Newborns can appear underactive for several reasons, including:

- the newborn is sleeping;
- the newborn has just breast-fed;
- the newborn has been handled a lot;
- the newborn is hypothermal;
- the newborn is on sedatives;
- the newborn has an infection.

Conclusion: Before considering infection, think about other factors that might be causing hypoactivity. Do not appraise this symptom in isolation, but reevaluate the child repeatedly. A well-trained nursing team is important in this process, since these professionals spend more time with each child and are better able to evaluate its behavior.

Temperature instability: Temperature instability is defined as cutaneous temperature less than 36.0 ºC (hypothermia) or greater than 37.5 ºC (hyperthermia).

In infection patterns, the temperature of newborns can be normal, high, or low. Hypothermia is more frequent as an indicator of infection in preterm newborns, while hyperthermia is observed most frequently in full-term newborns. In the presence of hyperthermia, before considering infection, first rule out other possibilities, such an overheated incubator, especially in preterm newborns, and excessive clothing and/or low nutritional intake, especially in full-term newborns during the summer months.

Hyperglycemia: This is defined as glucose concentrations higher than 125 mg/dL in whole blood or 145 mg/d in plasma. This occurs especially in preterm newborns, in cases of sepsis and in neonatal diabetes mellitus. Sepsis is associated with an inadequate response to insulin. Secondary hyperglycemia is related to surgical stress due to an increase in the hormonal secretion of adrenaline, glucocorticoids, and glucagon associated with insulin suppression; use of theophylline and caffeine to stimulate glycogenolysis; exogenous infusion of glycose or lipids to stimulate glyconeogenesis; and hypoxia, by alpha-adrenergic stimulation and decrease of the insulin response. Especially in preterm infants, the prescription of a glucose infusion rate above tolerated levels, or a serum drip or prolonged parenteral nutrition (PPN) containing glucose above the level prescribed, can lead to an increase in blood glucose without associated disease.

Conclusion: Hyperglycemia may be part of the clinical infection picture, but other causes should be ruled out first.

Apnea: Respiratory pause lasting more than 20 seconds, or with shorter duration associated with bradycardia (cardiac frequency <100 bpm) or cyanosis. Apnea can be primary or secondary, primary apnea being the most frequent in preterm newborns. It occurs in 25% of newborns with birthweight <2500 g and in 84% of newborns with birthweight <1000 g. Apnea may be secondary to several diseases or clinical situations, including:

- thermal instability (hypothermia or hyperthermia);
- hypoxemia associated with difficult breathing;
- airway obstruction;
- metabolic disturbances (hypoglycemia, hypocalcemia, hyponatremia, acidosis);
- hypovolemia, anemia;
- drugs (anesthetics, tranquilizers, anticonvulsants);
- persistent arterial duct;
- gastroesophageal reflux;
- pathologies of the central nervous system (CNS): meningitis, convulsions, CNS hemorrhage, convulsions and asphyxiation;
- sepsis.

Conclusion: Before considering apnea as a symptom of clinical infection, it is necessary to rapidly rule out other etiologies.

Respiratory distress: Usually characterized by coughing, tachypnea (increase in respiration rate), chest indrawing, and cyanosis. Especially in preterm or near-term newborns, distress soon after birth can be due to respiratory distress syndrome (hyaline membrane disease), transient tachypnea, or pneumonia of maternal origin. Initially it may be difficult to rule out infection, as it is necessary to know the maternal risk factors for infection and carry out screening for infection, including laboratory and radiological examinations.

Food intolerance: This is defined as the presence of one or more of the following signs: gastric residuals of 50% or more of volume administered (for large volumes of milk) or up to 5 ml twice or three times, bilious residuals, vomiting, abdominal distention, or visible raises in the abdomen. The signs of food intolerance may be present in serious infections with infectious ileus, as well as in other situations such as intestinal obstructions and metabolic disturbances such as hypopotassemia (presents symptom generally when K<2,5-3 mEq/L).

Disseminated intravascular coagulation (DIC): Localized or generalized signs of bleeding can be part of the clinical infection picture. Cases of serious sepsis can evolve with DIC, and in cases of necrotizing enterocolitis, the presence of blood in the stool is frequently observed. Remember that other situations, such as ingestion of blood by the newborn during childbirth, nipple fissures, deficiency of vitamin K, immune thrombocytopenia, or exogenous poisoning by heparin, can lead to vomiting with blood or blood in the stool without infection necessarily being present. Bleeding of vascular etiology can include central nervous system hemorrhage, pulmonary hemorrhage, arteriovenous malformations, and hemangiomas.

Hemodynamic instability/shock: This is a state of acute circulatory dysfunction that results in oxygen and nutrient transport that is insufficient to meet tissue needs. Organ dysfunction is due to inadequate blood flow and oxygenation, making cellular metabolism predominantly anaerobic, producing lactic and pyruvic acid; for this reason, the presence of metabolic acidosis often translates into inadequate circulation. In addition to tachycardia and hypotension, shock can manifest with cutaneous pallor, poor peripheral perfusion, cold extremities, decreased urine output, and lethargy. In preterm newborns, acute hypotension can occur with bradycardia without previous tachycardia.

Causes of shock: In the immediate postnatal period, the abnormal regulation of peripheral vascular resistance is a frequent cause of hypotension, especially in preterm newborns. Septic shock is considered a type of distributive shock, in which abnormal circulatory distribution can cause inadequate tissue perfusion. Among the factors involved in the circulatory dysfunction of septic shock are the direct depressor effect of microbial products, including endotoxins, and the release of other vasoactive agents, including nitric oxide, serotonin, and prostaglandins, among others. Although septic shock may be frequent in some neonatology services, other etiologies should be ruled out, such as cardiogenic shock, neurogenic shock, and hypovolemic shock, the latter resulting from the loss of whole blood, plasma, or extracellular fluid.

Conclusion: In response to clinical signs and symptoms suggestive of infection, once other possible causes have been ruled out, complementary research should be undertaken along with laboratory examinations, with a view to initiating treatment as soon as possible.

Laboratory diagnosis of early and late infections [13,14,15]

Hemogram: Especially in the first 72 hours of life, the hemogram can be altered by perinatal influences. The alterations may or may not be linked with the presence of infection. The hemogram is important because of its high negative predictive value. Thrombocytopenia can be a late sign of sepsis.

C-reactive Protein (CRP): This increases within 24 hours of the onset of infection, reaches a maximum level in 2 to 3 days, remains high until the infection is controlled, and returns to normal with 5 to 10 days of appropriate treatment. This test can assist greatly in the diagnosis of bacterial infection because of its high negative predictive value (98%). From a practical standpoint, when the CRP at the time of screening is normal and serial tests remain normal even 2 to 3 days after the beginning of the clinical picture, the chance of infection is quite small (2%).

Hemocultures: Preferably take two samples, always from different vascular locations, with a minimum volume of 1 ml of blood per sample. In newborns with central venous access, samples can be collected in this way and a second sample can be taken from a peripheral vein. The collection of two hemoculture samples yields a more reliable diagnosis of the etiologic agent, especially in coagulase-negative staphylococcal infections. In these cases, a positive result in two samples, associated with clinical signs, corroborates the diagnosis of infection. Isolation of coagulase-negative staphylococcus in only one hemoculture sample requires evaluation of the clinical evolution of the patient, especially if there might be growth of the agent in the first 24 hours after collection. Growth in a single sample after 48 hours suggests contamination of the sample. Bacterial growth only in the sample collected from the central catheter, with a negative result in the peripheral blood sample, suggests colonization of the catheter.

Cerebrospinal Fluid (CSF): The collection of CSF for chemocytological examination and culture is recommended in investigation of early and late sepsis, since bacteremia may occur with a high incidence of meningitis, reaching 23% in some studies; in addition, 38% of meningitis cases can show negative hemocultures. However, when the condition of the newborn does not allow for this collection, the examination should be postponed, while beginning the treatment with an antibiotic suitable for coverage of the central nervous system [16].

Urine culture: This is especially recommended in investigation of late-appearing infections, usually in patients without invasive devices. The gold standard is collection by supra-pubic punc-

ture. Collection by vesical probe can be used if supra-pubic puncture is not possible. Samples collected in urine collection bags only have value when the result is negative.

Diagnostic imaging: In addition to laboratory tests, investigation to localize an infection should be completed with chest x-rays when there is suspicion of pneumonia, and abdominal x-rays when there is suspicion of abdominal infections such as enterocolitis or peritonitis. Other types of imaging, such as sonography and tomography, are important in investigation of endocarditis or abscesses, whether cerebral, visceral, or in joints.

Chest x-ray: This is indicated for diagnosis of pneumonia. Remember that the diagnosis of pneumonia is difficult in neonatology. X-rays may be indicated based on the following criteria: radiological test shows new or progressive infiltration, cavitation, consolidation, or pleural effusion, and at least one of the following:

a) increase in the production of respiratory secretion;
b) change in the appearance of the respiratory secretion, becoming more purulent;
c) positive hemoculture, presence of IgM or increase of 4 times the serum antibody titer IgG against the pathogen;
d) isolation of the etiologic agent through bronchoalveolar lavage or brushing or biopsy;
e) isolation of virus or viral antigen in the respiratory secretions;
f) histopathology showing pneumonia.

Notes:

1. The results from cultures of sputum and tracheal secretions should not be used as diagnostic criteria for pneumonia, except when it is possible to quantify the number of colonies.

2. The analysis of repeated x-rays is more useful than an isolated x-ray.

Early neonatal infection [10,16]

Definition: Early neonatal infections are those that appear in the first 48 hours of life 1. Transmission occurs during the passage through the birth canal, by chorioamnionitis, or by hematogenic dissemination. The most common agents are Streptococcus agalactiae (group B streptococcus), Listeria monocytogenes, gram-negative enteric bacilli, and enterococci.

Risk factors for perinatal infection: pregnant woman colonized by group B beta-haemolytic streptococcus (GBS) without intrapartum prophylaxis when indicated, chorioamnionitis, physiometry, peripartum maternal fever, maternal leukogram altered in prolonged membrane rupture, urinary infection and other foci of bacteremia with less than 48 hours of treatment.

Clinical picture: The clinical picture is usually multisystemic, with or without localization (pneumonia or meningitis). It is represented initially by vague and nonspecific symptoms, such as thermal instability, altered cutaneous coloration, hypoactivity, apnea, hepatomegaly, respiratory distress, hemorrhagic disturbances, alteration of skin perfusion, bradycardia/tachycardia, vomiting/gastric residuals/abdominal distention.

It is important to isolate other factors that can mimic the clinical picture of infection laid out in this chapter.

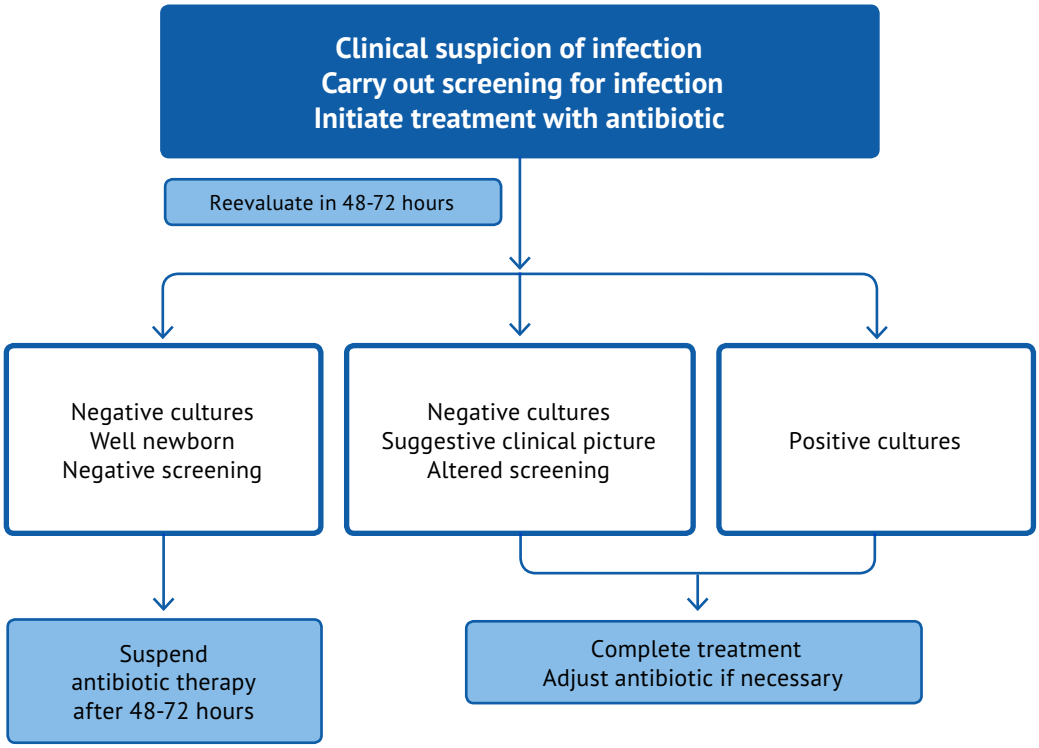
Laboratory investigation: Obtain hemogram, quantitative serial CRP levels (interval of 24 hours), two hemoculture samples, and cerebrospinal fluid for chemical analysis and culture.

It should be stressed that, along with the hemogram, the CRP can increase 100 to 1,000 times in bacterial infection or other inflammatory conditions, such as prolonged rupture of membranes, perinatal asphyxiation, respiratory distress syndrome, intracranial hemorrhage, meconium aspiration syndrome, and abdominal wall defects. In such these situations, evaluate critically the use of CRP in studies of early sepsis.

Altered initial CRP, with standardization in 48-72 hours, or normal serial CRP, with negative hemoculture and satisfactory clinical evolution, are suggestive of absence of bacterial infection.

Chest x-ray: This should be carried out in cases of respiratory distress, given the differential diagnosis of pneumonia. For confirmation of this diagnosis, serial examinations are needed, especially to rule out hyaline membrane disease, transient tachypnea, and meconium aspiration.

Management of newborns with suspicion of early sepsis [10]



Late neonatal infection [4, 16]

Late infections are those that appear after 48 hours of life and usually result from the impact on the newborn of microorganisms of its environment, varying from service to service.

Risk factors for late neonatal infection in newborns [1, 10]

Among the risk factors for HAI inherent in newborns are the following:

- Birthweight: the lower the child's weight, the greater the risk of infection.
- Weak immune defenses: the more preterm the newborn, the less humoral and cellular immunity it will have.
- Need for invasive procedures: the more preterm or the less healthy the newborn, the greater the need for invasive procedures, from the simplest ones, such as collection of blood for measuring blood glucose, to the most complex, such as tracheal intubation for mechanical ventilation, use of a central catheter, thorax drainage, use of H2 blockers, disease of the gastrointestinal tract, or surgical treatment.
- Alteration of the bacterial flora, once the hospitalized newborn is colonized by bacteria from the hospital environment, which are often resistant to antibiotics and highly virulent.
- In addition to risk factors related to the clinical condition of newborns themselves, other factors linked with the institution where they are located can elevate the risk for infection, in particular:
- disproportion between number of newborns admitted and number of professionals on the health team;
- number of inpatients exceeds capacity of the institution.

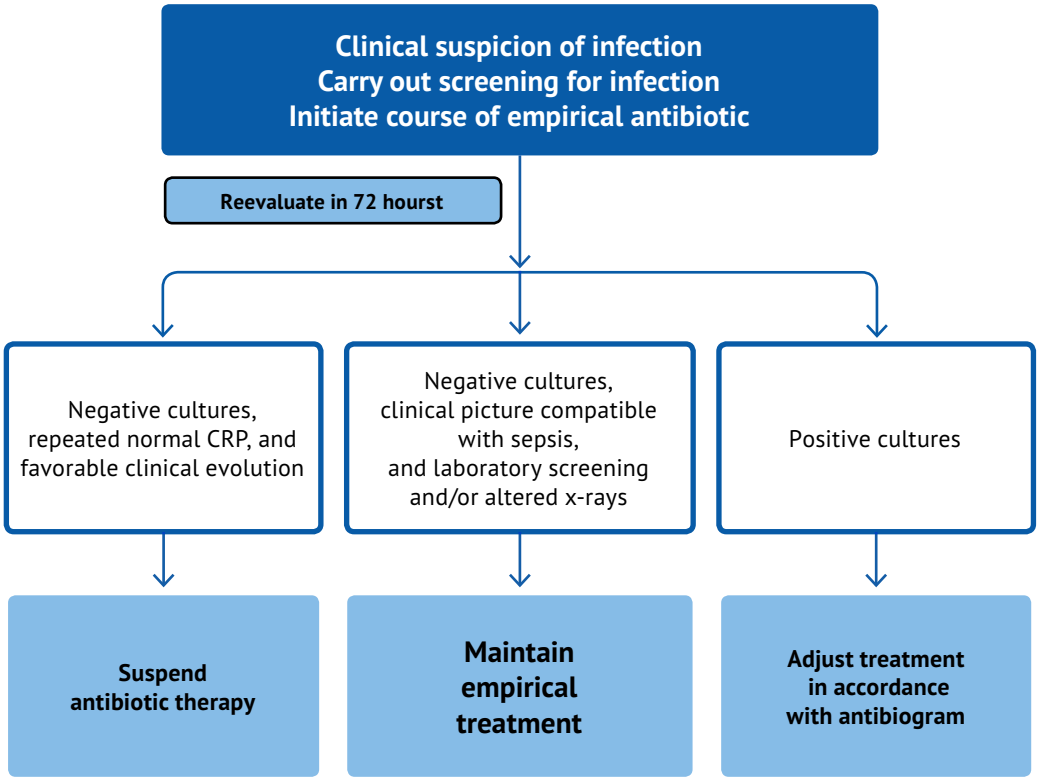
Diagnosis

Like early infections, late infections can be indicated by one or more signs, such as decline in general condition, hypothermia or hyperthermia, hyperglycemia, apnea, gastric residuals, respiratory insufficiency, shock, and bleeding.

Therefore, in addition to making a clinical assessment, the physician should obtain laboratory support, including a complete hemogram with blood platelets, C-reactive Protein (CRP), and collection of cultures, especially hemocultures, to better guide diagnosis and practice.

Diagnostic imaging: This is useful for investigating the localization of the infection. Use a chest x-ray on the suspicion of pneumonia, and an abdominal x-ray on suspicion of abdominal infections such as enterocolitis or peritonitis. Other imaging procedures, such as sonography and tomography, are important for investigating endocarditis and abscesses, whether cerebral, visceral, or in joints.

Management of newborns with suspicion of late neonatal Infection:



Management of laboratory-confirmed primary bloodstream infection [17]

Treatment time depends on the etiologic agent and whether the central catheter is removed or left in place. The central catheter should be removed in newborns with device-associated bloodstream infections caused by Staphylococcus aureus, gram-negative rods, enterococci, and fungi. It should be noted that bloodstream infections with coagulase-negative Staphylococcus can be successfully treated without removal of the catheter.

Although withdrawal of the central catheter is often recommended, depending on the etiologic agent isolated, this action is often postponed by the neonatologist, if the clinical condition of the newborn makes it difficult to establish new venous access. In the case of postponement, the following is recommended:

- Every newborn being treated for a bloodstream infection whose catheter was not removed should be monitored closely, with clinical assessment and additional hemocultures.
- The central catheter should be removed if there is clinical deterioration, persistence, or recurrence of the infection.

In bloodstream infections with *Staphylococcus epidermidis* or other coagulase-negative Staphylococcus that show good evolution and are not associated with the central catheter, or in cases where the catheter has been removed, treatment can be maintained for the minimum period indicated for the prescribed antibiotic (5 to 7 days). However, if the decision is made to keep the central catheter in place, the treatment time should be extended (10 to 14 days). Bloodstream

infections by *Staphylococcus aureus* require prolonged treatment (minimum of 14 days), even when the central catheter is removed, due to the greater risk of infectious complications. Bloodstream infections by other bacteria are usually treated successfully when the central catheter is removed. If the catheter is maintained, the treatment time should be extended.

Management of newborns at risk for Group B beta-hemolytic Streptococcus infection (*Streptococcus agalactiae*) [18,19]

For management of newborns at risk for Group B beta-hemolytic Streptococcus infection, the knowledge of the indications and contraindications for intrapartum antibiotic prophylaxis in pregnant women is important for prevention of GBS in preterm births.

Intrapartum prophylaxis for prevention of Group B Streptococcus infection is indicated in the cases described below:

- Prior invasive disease in newborn by GBS.
- Bacteriuria by GBS during any trimester of the current pregnancy*.
- Positive vaginal-rectal screening (culture) in the late phase † of the current gestation*.
- State of culture for GBS unknown at the beginning of labor (culture not carried out, incomplete, or with unknown result) and any one of the following factors:
  - childbirth with less than 37 weeks of gestation §
  - rupture of membranes ⩾ 18 hours
  - intrapartum maternal temperature ⩾ 38.0 °C
  - positive intrapartum nucleic acid amplification test (NAAT) for GBS **

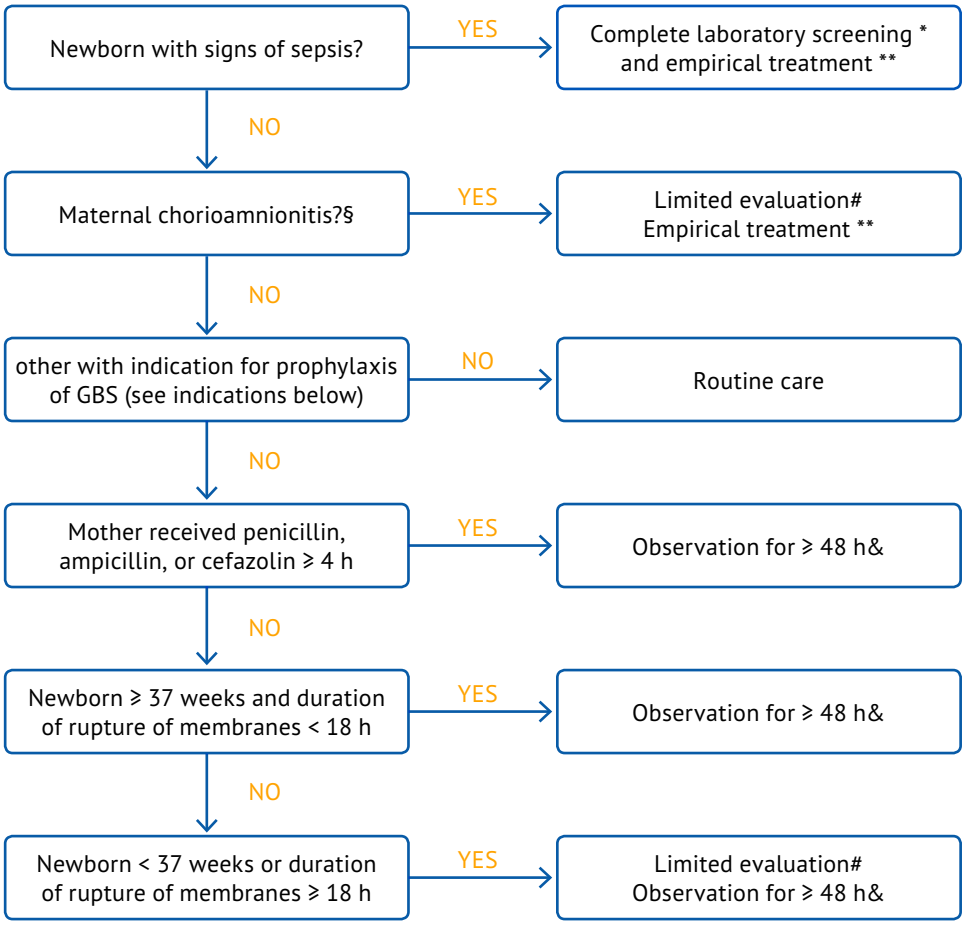
Prophylaxis for prevention of GBS infection **IS NOT** indicated in the following cases:

- colonization by GBS during previous gestation (unless there is an indication for prophylaxis in the current gestation);
- bacteriuria by GBS during previous gestation (unless there is an indication for prophylaxis in the current gestation);
- negative screening (culture) for GBS in the late phase † of the current gestation, regardless of the intrapartum risk factors;
- caesarean childbirth before the beginning of labor in a woman with intact amniotic membranes, regardless of the state of colonization by GBS or gestational age.

Note:

1. NAAT = Nucleic acid amplification test.
2. * Antibiotic prophylaxis is not indicated in this circumstance if the childbirth might have been by caesarean section before the beginning of labor in a woman with intact amniotic membranes.
3. † Prenatal screening for GBS should be carried out preferably between 35 and 37 weeks of gestation.
4. If there is suspicion of chorioamnionitis, wide-spectrum antibiotic therapy that includes a known active agent against GBS should replace prophylaxis.
5. ** The NAAT test for GBS is optional and may not be available in all facilities. If the test is negative, but there is any other intrapartum risk factor (childbirth < 37 weeks of gestation, rupture of membranes ⩾ 18 hours, temperature ⩾ 38.0° c), then prophylaxis is indicated.

Management of newborns at risk for Group B beta-hemolytic Streptococcus infection (*Streptococcus agalactiae*) [19]



* Complete laboratory screening: two hemoculture samples, complete hemogram, C-reactive Protein test, chest x-ray if indicated, and collection of cerebrospinal fluid (cytology, biochemistry, and culture) if the newborn is stable enough for puncture and there is suspicion of sepsis.

** The protocol of the US Centers for Disease Control (CDC) guides the use of wide-spectrum antibiotics for coverage of the most common causes of sepsis, including coverage for GBS with ampicillin EV and antibiotics for coverage of gram-negative bacilli as such as E. coli in newborns with signs of sepsis and in asymptomatic newborns of mothers with chorioamnionitis.

In asymptomatic newborns, the American Academy of Pediatrics recommends suspending the use of antibiotics after 48 hours, once infection has been ruled out.

According to the CDC, limited evaluation includes collection of hemocultures at birth, differential hemogram and blood platelet count at birth and/or within 6-12 hours of life.

If there are signs of sepsis: collect cultures and immediately begin antibiotic therapy. If the clinical picture is not confirmed clinically or by laboratory test, suspend antibiotics after 72 hours.

§ Clinical chorioamnionitis: nonspecific signs of peripartum maternal fever without a specific focus, uterus sensitive to the touch, physiometry.

** The CDC protocol recommends beginning empirical antibiotics in asymptomatic newborns of mothers with chorioamnionitis (A II). This decision should be made in consultation with the obstetrician in order to confirm that the condition of the mother is really considered chorioamnionitis (C III). In accordance with the American Academy of Pediatrics[15], the clinical picture of asymptomatic newborns of mothers with chorioamnionitis should be reevaluated in 48 hours to decide on the continuation or suspension of the use of antibiotic, in accordance with the clinical evolution and laboratory tests, including cultures.

The Royal Australasian College of Physicians [20] considers that in the management of GBS, asymptomatic newborns of mothers who are GBS-positive but received incomplete intrapartum prophylaxis and newborns of mothers with chorioamnionitis should be observed for a minimum of 48 hours. In accordance with this protocol, screening for infection and the beginning of treatment is only indicated if the newborn presents clinical symptoms of infection[20].

Conclusion: Considering the increase in adverse events resulting from the use of antibiotics in the first days of life as well as the increase in cases of enterocolitis and induction of bacterial resistance [21], we encourage neonatology services to adopt the following practice:

1. Investigate and initiate treatment for infection only in symptomatic newborns;
2. Discontinue the use of antibiotics after 48-72 hours in cases where infection can be ruled out based on the clinical evolution and screening tests (hemogram, CRP, hemocultures, CSF culture);
3. Observe clinically asymptomatic newborns of mothers with chorioamnionitis for 48-72 hours; conduct laboratory tests and initiate the use of antibiotics (penicillin or ampicillin and gentamicin or amikacin) if the newborn develops symptoms of infection.

Modes of transmission of infections [3,22]

Contact is the most common and important mechanism in colonization and/or infection of newborns, whether direct or indirect.

Direct contact: the fetus can be colonized or infected in the intrauterine environment through the placenta or through ascending infection, in cases of premature membrane rupture when childbirth does not occur immediately. After birth, the process of colonization continues through contact with the mother, family members, and health professionals who are sick or colonized and who provide care for the newborn.

Indirect contact: this involves inanimate objects such as thermometers, stethoscopes, blood pressure measurement equipment, and transducers, as well as people. In the hospital environment the principal mechanism for transmission of microorganisms is the hands of health professionals.

In addition to contact, which is the most common and important mechanism in colonization and/or infection of newborns, other forms of transmission to be considered include:

- contaminated fluids, such as blood and blood products, drugs, parenteral nutrition, breast milk, and infant formulas;
- through the respiratory tract, mainly in outbreaks of viral infection such as influenza and adenovirus;
- transmission by aerosols; this is infrequent in neonatal units, but the possibility of seasonal outbreaks of herpes zoster is worth noting;
- vectors capable of transmitting dengue, malaria, and yellow fever, although this occurs rarely in neonatal care units.

All the above-noted situations refer to exogenous sources frequently responsible for epidemic outbreaks. In addition, the microbiota of the newborn, which is subject to the direct impact of selective pressure from antibiotics, is responsible for continuing HAI endemicity in neonatal units.

Following are key recommendations for preventing the transmission of diseases in the hospital environment.

Access to the hospital unit [23, 24]

Professionals, parents, and family members seeking access to the neonatal hospital unit should be screened for the presence or risk of infectious diseases. In this regard, special attention should be given visits by siblings, since children are at greater risk for these diseases. No person with a respiratory or skin infection or diarrhea should have direct contact with a newborn.

Persons entering the unit should have short nails, cover up long hair, and remove bracelets, rings (including wedding rings), and watches. After taking these measures, disinfect the hands.

Hand hygiene [25, 26, 27]

Hand hygiene encompasses:

- simple hygiene: handwashing with water and common liquid soap;
- antiseptic hygiene: handwashing with water and antiseptic detergent solution (chlorhexidine or iodine-based products);
- antiseptic hand rub with 70% alcohol solution;
- surgical hand antisepsis: preoperative handwashing with water and antiseptic detergent solution by the surgical team.

Why is hand hygiene necessary?

The hands constitute the main form of transmission of microorganisms during patient care. The skin is a possible reservoir for various microorganisms that can be transferred from one surface to another.

The skin of the hands hosts two principal microorganism populations: those belonging to the resident microbiota and those belonging to transient microbiota.

Transient microbiota colonize the most superficial layer of the skin, which allows their mechanical removal by handwashing with water and soap, although they are eliminated more easily when an antiseptic solution is used. Typically, they include gram-negative bacteria such as enterobacteria (for example, *Escherichia coli*) and nonfermenting bacteria (for example, *Pseudomonas aeruginosa*), as well as fungi and viruses.

Resident microbiota are made up of low-virulence microorganisms, such as Staphylococcus, corynebacteria, and micrococci, which are rarely associated with hand-transmitted infections.

These are more difficult to remove by handwashing with water and soap, since they colonize internal skin layers.

What is handwashing good for?

Handwashing is intended to remove visible dirt and transient flora, scaly cells, sweat, and skin oils. In addition, when combined with use of an antiseptic, it also helps decrease resident flora. In neonatology units for general care of newborns, either simple handwashing (with plain soap) or antiseptic handwashing (with soap containing antiseptic) is used. However, before using invasive procedures, surgical hand antisepsis is recommended. The use of detergent with antiseptic is also recommended for handwashing in units at greater risk for infection, for example, neonatal ICUs.

How to disinfect the hands?

1. Simple handwashing (plain soap) or antiseptic handwashing (soap containing antiseptic)

1. Rub the hands with water and liquid soap or antiseptic detergent solution for approximately 15 seconds, including all the surfaces, spaces between the fingers, and nails. Also wash the forearms.
2. Rinse with running water.
3. Wipe with paper towel.

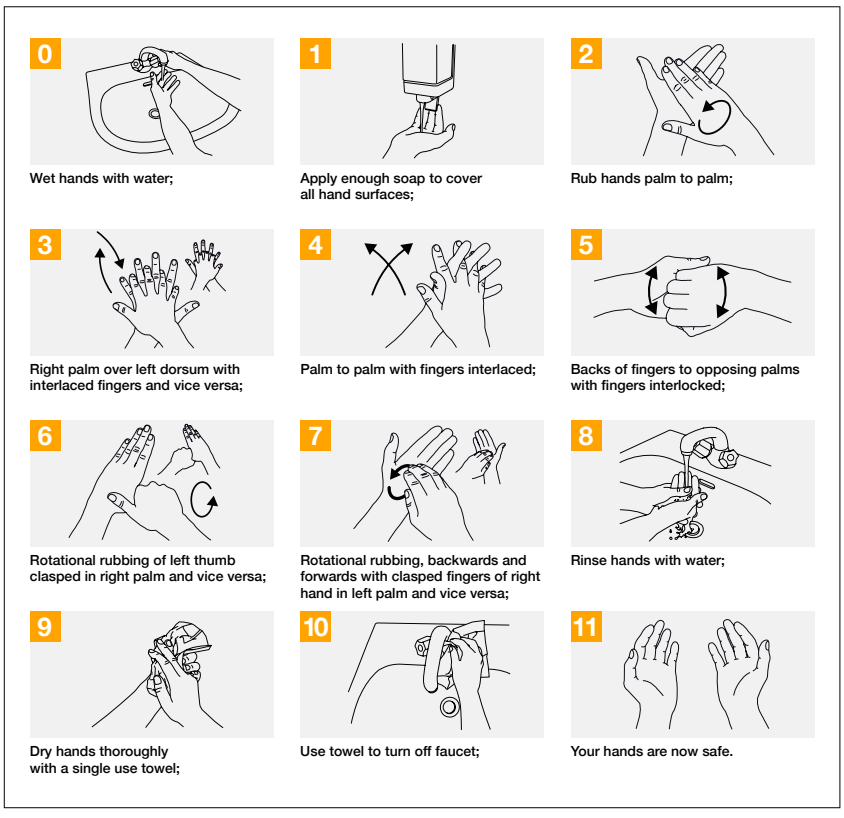


Figure 1: Handwashing with water and soap or antiseptic detergent (http://www.who.int/gpsc/5may/Hand_Hygiene_Why_How_and_When_Brochure.pdf)

2. Surgical hand antisepsis

- Rub the hands with water and antiseptic detergent solution, including all surfaces, spaces between the fingers, and nails; also wash the forearms.
- Rinse with running water.
- Wipe with sterile compress.

Note: this procedure should take 3 to 5 minutes for the first surgery and 2 to 3 minutes for subsequent surgeries.

3. Hand hygiene with alcohol gel or alcohol at 70% concentration with 2% glycerin (hand rubbing with antiseptic)

Hand hygiene with alcohol or alcohol at 70% concentration with 2% glycerin can replace handwashing with water and soap when there is no visible dirt, especially in procedures at low risk for infection or in emergency situations. In this procedure it is important to ensure the solution is rubbed on all surfaces of the hands, the fingers, and the spaces between the fingers, leaving the hands to dry spontaneously.

The use of antiseptic is an important strategy for control of infection since it is a simple procedure and reduces the risk of damaging the hands of the health professional by repeated handwashing with water and soap. In addition, it can be made available at the location of patient care.

The hygiene technique with alcohol gel is similar to simple hand hygiene, requiring use of the product on all surfaces of the hands, and spaces between the fingers, with care to await spontaneous drying.

Note: The use of gloves does not substitute for hand hygiene, which is necessary before and after wearing the gloves.

Products used for hand hygiene

Liquid soap with Triclosan (Irgasan DP300): The formulations usually marketed contain Triclosan in low concentrations, acting as a preservative for the product.

This is classified as a liquid soap with low antiseptic action, indicated for handwashing in areas at low risk for infection, such as rooming-in wards and clinics.

Chlorhexidine gluconate detergent (2% and 4%): This has bactericidal effect on gram-positive cocci and gram-negative bacilli, and is effective as a viricide against lipophilic viruses (influenza, cytomegalovirus, herpes, HIV) and as a fungicide, even in the presence of blood and other body fluids; its residual effect is approximately 6-8 hours for cumulative action. This is indicated for handwashing in hospital sectors at high risk for infection. In this context, its use is indicated for the neonatal unit (ICU) as a substitute for liquid soap and for handwashing before invasive procedures.

PVP-I detergent solution: This can be an option for use as an antiseptic for hand hygiene in the absence of chlorhexidine; however, its use should be avoided by health professionals, as it is less well tolerated by the skin.

Alcohol: this is effective at a 70% concentration and causes less dermatitis because it is less drying to skin. It has excellent bactericidal effects against vegetative forms of gram-positive and gram-negative microorganisms, but it is inactive against spores. It is effective against the tuberculosis bacillus, as well as against many fungi and viruses including respiratory syncytial virus, Hepatitis B, and HIV. Used in hand hygiene when the skin does not show visible dirt, it is an excellent alternative for handwashing since it is simple and saves time and resources.

When to disinfect the hands? [25,26,27]

The 5 key moments identified by the World Health Organization (WHO) 27 and other situations associated with care of newborns*.

1. Before contact with the patient.
2. After contact with the patient.
3. Before invasive procedures.
4. After contact with secretions and body fluids.
5. Whenever preparing materials or equipment that are or have been in contact with patients and after contact with areas close to the patient.

* Whenever entering or leaving the hospital unit or isolation area.
* Before the preparation of materials and equipment.
* Before the preparation and administration of medication.

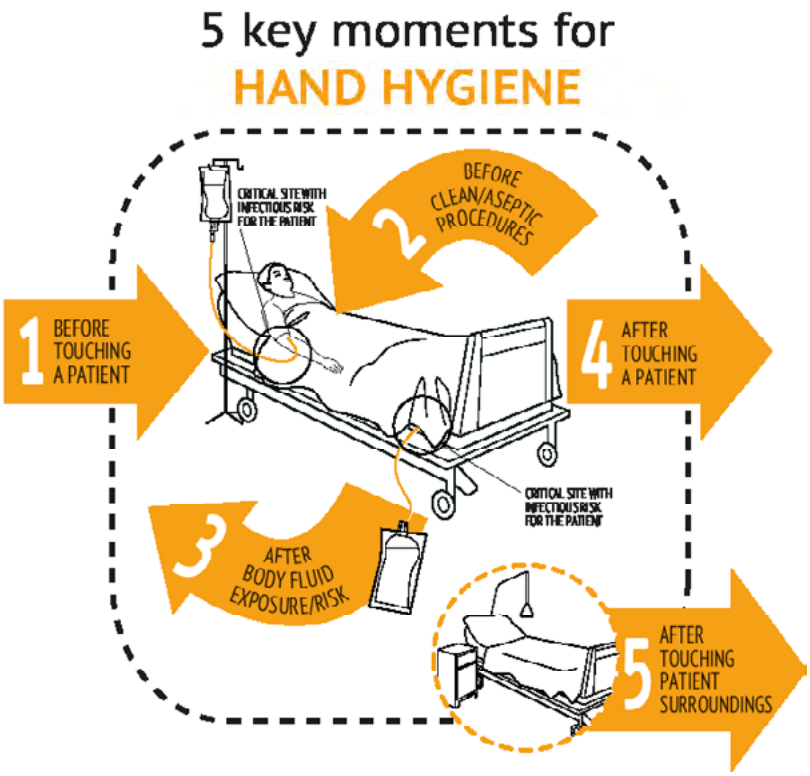


Figure 2: Five key moments for hand hygiene (WHO 2009) [27]

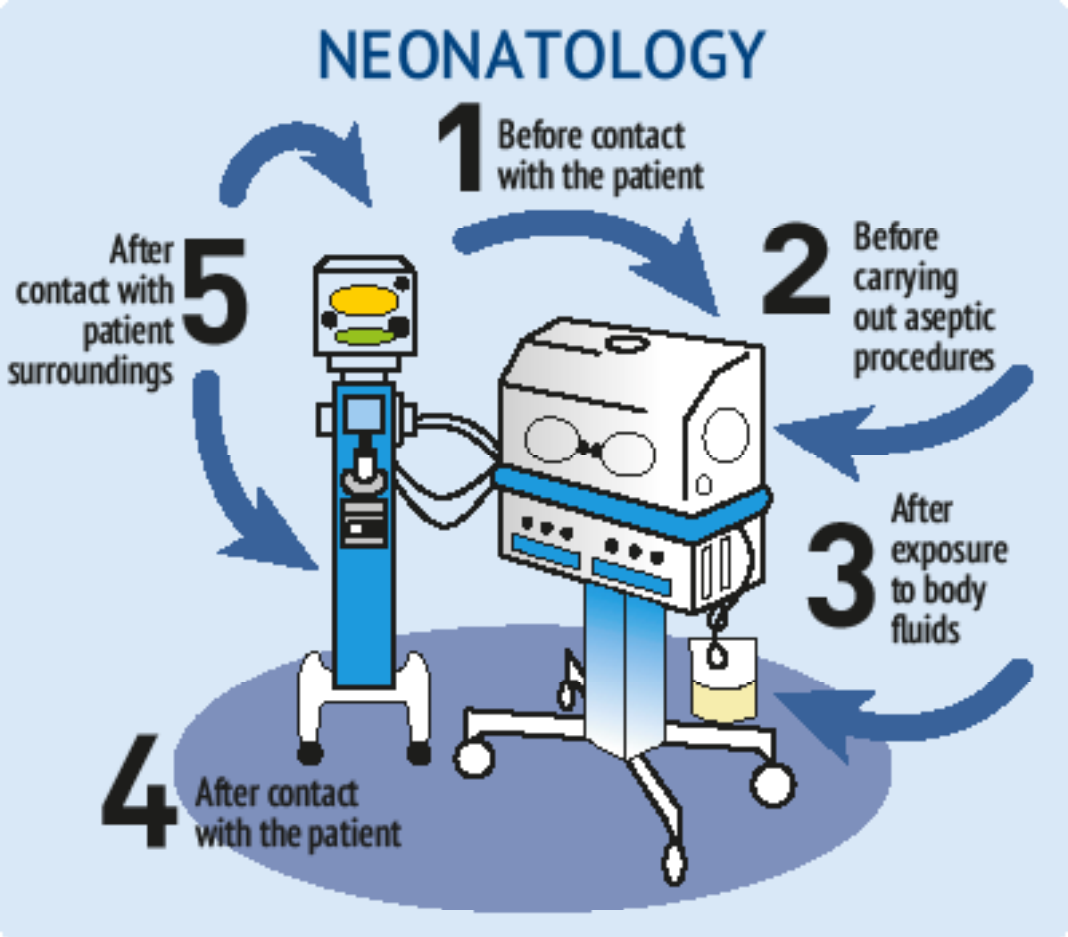


Figure 3: Five key moments for hand hygiene in a neonatal unit (Folder Neonatologia CAISM/UNICAMP Prevencao de Infeccao Associada a Cateter)

Precautions and isolation [28]

The appearance of new infectious syndromes, the emergence of multiresistant bacteria, and growing knowledge about the communicability of diseases common in hospitals have made it necessary to reevaluate the methods used for isolation in the hospital.

The recommendations for precautions and isolation used in the neonatal unit follow the same principles as those for the general population, while adding some special features. In this regard, it is important to recognize that a mother with an infection may be the source of cross-transmission to her child as well as to other inpatients or health professionals, including in low-risk areas such as rooming-in wards.

The following concepts are important for understanding and adhering to the standards for precautions and isolation.

Transmission of infections in the hospital environment [28]

For transmission of infection to occur, three elements must be present: a source of infection, a susceptible host, and a mode of transmission.

Source of infection

Patients, staff members, and, occasionally, parents and visitors can serve as sources of microorganisms. Inanimate objects in the hospital environment that become contaminated, including equipment and drugs, may also be sources of microorganisms.

Susceptible host

In the hospital environment, certain factors make patients more susceptible to microorganisms, including immunological deficiency from an underlying disease, use of chemotherapeutic agents and immunosuppressive drugs, breaks in natural defense barriers caused by surgical incisions or invasive procedures such as use of catheters and tubes, use of antimicrobial drugs, colonization by bacteria in the hospital environment, and nutritional aspects. In this regard, newborns, especially preterm and low birthweight newborns, are considered susceptible hosts for infection because they have immature immune systems, are frequently subjected to invasive procedures, and frequently have altered intestinal flora due to delays in beginning feeding and to use of antibiotics.

Modes of transmission

Microorganisms are transmitted in the hospital through several means, such as contact, droplets, air/aerosols, common vehicles, or vectors.

CONTACT: This is the most frequent and important mode of transmission of hospital infections. It occurs when professionals have not disinfected their hands (by washing or disinfection with alcohol solutions) or have not changed their gloves between one patient and another; through contact between patients, or through contaminated instruments.

DROPLETS: Although this is a form of contact, droplets are treated separately because of their specific characteristics. Droplets are produced during coughing, sneezing, aspiration of secretions, procedure (such as bronchoscopy), and even in normal conversation. When these particles are deposited in the conjunctiva, nasal mucous membrane, or mouth of the susceptible host, transmission of the agent takes place. The particles can travel 2 to 3 meters[24]. The infectious particles do not remain suspended in the air; transmission of the agent occurs directly through the droplets. Examples include meningitis, rubella, influenza, whooping cough, mumps, and respiratory viruses as such as influenza, parainfluenza, and adenovirus, among others.

AERIAL: Aerial transmission occurs when the microorganisms are in small particles (≤ 5 µm) suspended in the air, in evaporated droplets (releasing agents that remain suspended in the air for a long time), or in "smoke" particulates. Microorganisms carried in this form are disseminated by air currents and can be inhaled by susceptible hosts, even at great distances. Bacillary tuberculosis, chickenpox, and measles are examples.

COMMON VEHICLE: This occurs when microorganisms are transmitted through items such as food, water, drugs, or even equipment. Examples: hepatitis A resulting from a polluted water source; outbreaks of bloodstream infections linked with a contaminated lot of distilled water used in the dilution of drugs.

VECTORS: this occurs when vectors such as flies and mosquitoes, etc., transmit microorganisms. This mode of transmission is not considered important for the prevention of hospital-acquired infections. Example: dengue transmission within the hospital.

Types of Precautions:

I. STANDARD PRECAUTIONS

II. SPECIFIC PRECAUTIONS

C) FOR AERIAL TRANSMISSION
D) FOR TRANSMISSION BY DROPLETS
E) FOR TRANSMISSION BY CONTACT

Basic principles for isolation in hospitals [28]

Hand hygiene: This is the most important measure to prevent transmission of microorganisms from one patient to another. Follow all the guidelines contained in this chapter.

- **Use of gloves:** gloves should be put on immediately before the risk situation that indicates their use, and taken off when they are no longer necessary. They are used for three reasons:

a) to provide individual protection: this is mandatory for contact with blood and body fluids and for contact with mucous membranes and non-intact skin of all patients, as well as in venipuncture and other procedures for vascular access.
b) to reduce the possibility of contamination of the operative field, mucous membranes, or non-intact skin;
c) to reduce the possibility of transmission of microorganisms from one patient or fomite to another. Gloves should be changed between one patient and another, with hand hygiene in between.

THE USE OF GLOVES DOES NOT SUBSTITUTE FOR HANDWASHING.

FAILURE TO PRACTICE HAND HYGIENE AND FAILURE TO CHANGE GLOVES BETWEEN PATIENTS CAN DISSEMINATE MICROORGANISMS IN THE HEALTH SERVICES

Care with use of gloves: practical conduct

- Use gloves only when indicated.
- Use gloves before contacting blood, body fluids, mucous membrane, non-intact skin, and other potentially infectious materials (example: changing a diaper containing feces or urine).
  - Change gloves before touching another patient.
  - Change gloves also during contact with a single patient if the contact is changing from a contaminated site to a clean site.
  - Change gloves if they might be damaged.
  - When using gloves, never unnecessarily touch surfaces and materials such as telephones, handles, and doors.

- Observe correct glove removal technique to prevent contamination of the hands.

Accommodation of patients: a private room is important to prevent transmission by contact, droplets, and aerosols. Therefore, patients at risk for such transmissions should preferably be placed in a private room; exceptions should be discussed with the health professionals of the hospital Infection Control Committee (ICC), who will manage the possible grouping of cases.

In a neonatal hospitalization unit (ICU), a private room is essential for suspected or confirmed cases of infections transmitted through aerosols. For diseases whose transmission occurs via droplets and contact, incubators can be used instead of a private room, since the precautions for health professionals are well identified. For this reason, it is important to maintain a minimum distance between beds, which should be greater than 1 meter, with the specific goal of reducing opportunities for inadvertent sharing of materials between infected/colonized patients and other patients [24].

Rooms with **special ventilation** and negative pressure are recommended for patients who may be transmitting microorganisms by air. Antechambers for rooms used for aerial transmission precaution do not have proven effectiveness.

Transport: Patients who are carriers of highly communicable or epidemiologically significant microorganisms should leave their room only when it is essential for their treatment. Appropriate protection should be used for each patient, according to the likelihood of transmission: waterproof dressings should protect any secretions that can contaminate the environment, and patients with the potential to generate infectious particles should use masks. It should be stressed that the use of a mask is common for adult patients at risk of transmission through droplets or aerosols, but is not routine for newborns. In the latter case, appropriate precautions should be used by health professionals during transport and by staff members of the receiving site, who should be informed of the need for and type of precaution.

Mask, ocular protection, or facial protection: These should be used by health professionals when carrying out procedures that pose a risk of contamination of mucous membranes of the nose and mouth with blood or body fluids.

Aprons, leg covers, shoes, and shoe covers: These are used for individual protection in situations that pose a risk of contamination with blood and body fluids. When aprons are used in rooms with precautions for transmission by contact, they should be discarded within the room immediately after use. The apron should be changed before each contact with the patient.

Equipment and articles: Sharp materials, after use, should be transported or discarded carefully in order to prevent accidents and transfer of microorganisms to the environment or other patients. Used equipment should be cleaned and disinfected after use (stethoscopes, thermometers, sphygmomanometers, glucose testing equipment, etc.).

Clothes/laundry: The risk of microorganism transmission is negligible if clothes are handled, transported, and washed to avoid the transfer of microorganisms to patients, staff members, or the environment.

Plates, flatware, glasses, feeding bottles: The combination of heat and detergent is sufficient for decontamination of utensils; it is not necessary to separate those for isolated patients.

Routine and terminal cleaning: How to clean the equipment and environment surrounding patients in special precautionary conditions should be determined by the likelihood of contamination (procedure to be validated by the hospital ICC).

Standard precautions [28]

Standard precautions are those indicated for use **in contact with all patients**, regardless of risk factors or disease, whenever there may be risk of contact with blood and body fluids. These include correct hand hygiene and the use of gloves, aprons, masks, or facial protection to prevent contact between professionals and patients (material such as blood, body fluids, secretions, and excreta, but not sweat), and with non-intact skin and mucous membranes. This includes environmental precautions and prevention of accidents with biological material.

Patients with the diseases cited below require **only standard precautions**:

- AIDS;
- *Burkholderia cepacia* (infection or colonization) in patient with cystic fibrosis;
- Conjunctivitis, including gonococcal conjunctivitis in newborns;
- Encephalitides;
- Necrotizing enterocolitis;
- Infectious enterocolitis and gastroenteritis, including by *Salmonella* and *Shigella*;
- Hepatitis B and C;
- Recurrent mucocutaneous herpes simplex (skin, oral, genital);
- Impetigo;
- Infections of skin, surgical wound, and small or limited decubitus ulcers;
- Echovirus, poliovirus, and Coxsackie infections;
- Viral meningitis;
- Pericarditis, myocarditis;
- Primary or secondary syphilis with skin or mucous membrane lesions, including the congenital form;
- Extrapulmonary tuberculosis including scrofulosis and renal tuberculosis.

Precautions based on the mode of transmission [28]

Depending on the mode of transmission, specific precautions for aerosols, droplets, and contact are recommended for patients suspected or known to be infected or colonized by communicable pathogens of epidemiological importance.

In addition to being used singly, these precautions can be combined when the disease has more than one form of transmission: for example, precautions for contact and droplets in cases of respiratory viruses; precautions for contact and aerosols for chickenpox

IT IS ESSENTIAL TO REMEMBER THAT ALL THE SPECIFIC PRECAUTIONS SHOULD ALWAYS BE ACCOMPANIED BY THE STANDARD PRECAUTIONS.

Precautions for aerial transmission/aerosols [28, 31]

These should be used, together with STANDARD PRECAUTIONS, for patients with airborne diseases. A private room is recommended, and if possible, a room with special ventilation; the doors and windows should remain closed. If necessary use an N95 particulate respirator mask when entering the room.

This type of precaution is indicated in the following situations:

- **Pulmonary and laryngeal tuberculosis:** use of respirators with special filter for particulates (N95).
  In suspected cases, wait for results from smear microscopy: if the results are negative, precautions can be suspended.
  Maintain precautions until three negative microscopy samples have been collected on different days.
- **Measles:** the use of N95 particulate respirator masks is mandatory.
- **Chickenpox, disseminated herpes zoster, or localized herpes zoster in immunosuppressed patients.**

Professionals who are not immune to measles and chickenpox should use N95 particulate respirator masks when entering the room.

The use of gloves and aprons is indicated for all health professionals when entering the room in situations of direct contact with the patient.

These precautions should be maintained as long as there are active lesions.

Persons accompanying the patient can remain in the room and do not need to use masks as long as they are immune.

Management of special situations:

1. Susceptible hospitalized patients with a history of exposure to the herpes zoster virus should continue **aerial precautions** from the 8th day after exposure until the 21st day after the last exposure. Those exposed should receive immunoglobulin (VariZIG: varicella zoster immune globulin), maintaining precautions until the 28th day [31].
2. When the mother has chickenpox with clinical signs from 5 days before until 2 days after birth [31]:

- administer VariZIG to the newborn within 96 hours of life;
- place newborn in aerial isolation, separated from the mother;
- keep mother in aerial and contact isolation until the last vesicle is dry and crusted;
- professionals and nonimmune visitors: use N95 particulate respirator mask to enter the isolation area;
- hospital discharge as soon as possible if the clinical conditions permit;
- for other situations linked with maternal exposure to chickenpox, see Figure 4 below.

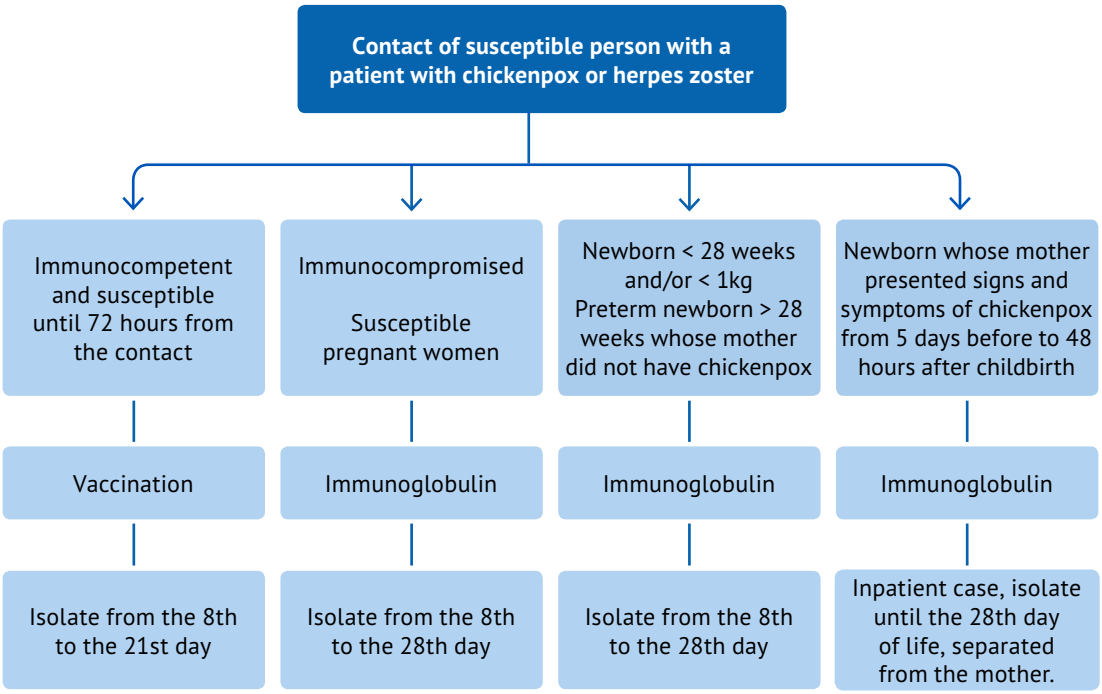


Figure 4: Behavior for mother exposed to chickenpox

3. Pregnant woman with bacillary tuberculosis diagnosed at the time of childbirth, uncontrolled by treatment [29,30].

Transport within the hospital environment should be with a common mask to prevent generation of aerosols.

- Private room, preferably with negative pressure in isolation for aerosols, during stay in the maternity unit.
- Newborn with the mother if clinical conditions permit.
- Avoiding close contact; use surgical mask to breast-feed, change diaper, and bathe.
- Initiate use of prophylactic isoniazid in newborn at 10 mg/kg/day.
- Professionals and visitors: use N95 particulate respirator mask to enter the isolation area.

During waiting periods in common areas for urgent care and during transport to the delivery room, a pregnant woman should be directed to use a common/surgical mask. In the delivery room, all professionals caring for the patient should use M95 particulate respiratory masks. Recovery of the client can be in the same environment. After childbirth there should be a terminal cleaning of the room.

After childbirth, the puerpera with symptoms of bacillary tuberculosis should be transported to a private room, using a common mask during transport. If the clinical conditions of the mother and child allow them to remain together, the mother should use a common mask when in close contact with the newborn, such as when changing diapers, bathing, and breast-feeding. In this case chemoprophylaxis with isoniazid for the newborn should be initiated at a dosage of 10 mg/kg/day. Do not administer BCG, but carry out PPD test within 3 months; if the PPD result is negative, suspend use of isoniazid and administer BCG. If the result of the PPD is positive, test for tuberculosis and carry out appropriate treatment. If the newborn is symptomatic at birth, investigate active tuberculosis with tuberculin test, chest x-ray, gastric lavage, and CSF test for the bacillus (Figure 5 [30]).

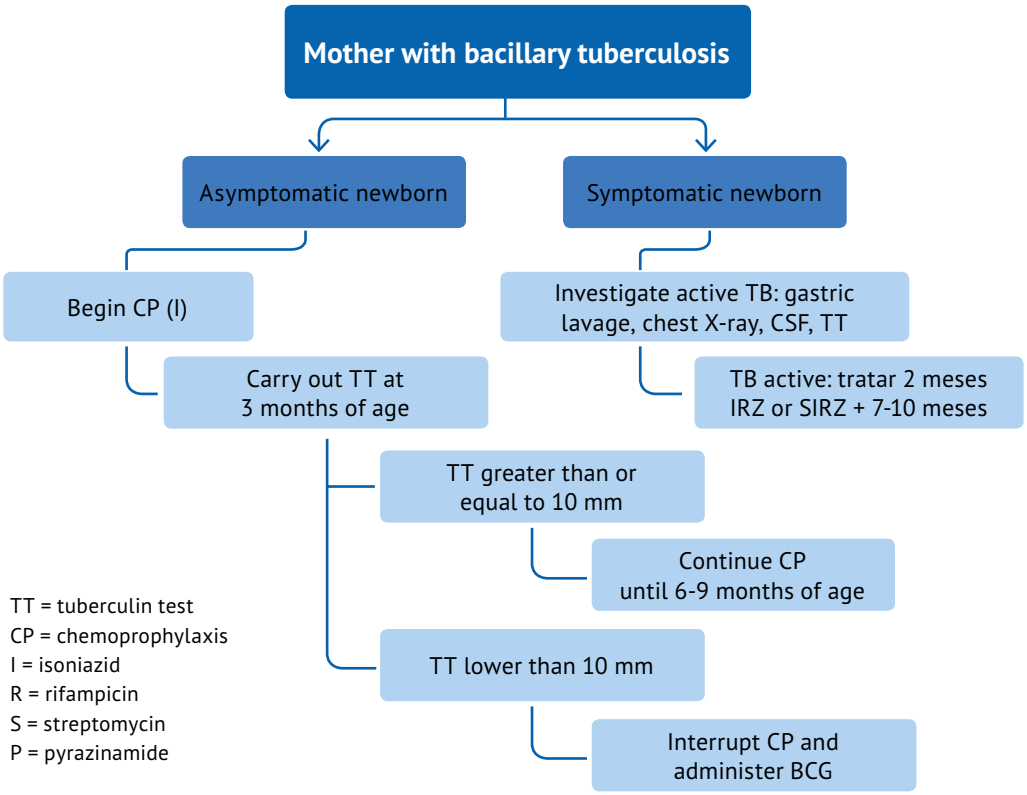


Figure 5: Management of infant of mother with an active case of bacillary tuberculosis [30]

For the prevention of aerial transmission, in addition to the use of N95 particulate respiratory masks by health professionals, rooms should be equipped with a special ventilation system. This should have negative pressure and filter or air venting to the exterior of the building, avoiding outgoing currents of air when the door is opened. During transport or movement in common areas of the hospital environment, patients with diseases transmitted through aerosols should be guided to use surgical masks to prevent the spread of disease.

The use of an N95 mask is not needed for health professionals who have confirmed immunity to chickenpox and measles. In this case, follow only standard precautions.

Precautions for droplet transmission

These are for patients known or suspected to have diseases transmitted through large particles (>5 µm). A common mask should be used when entering the room. To avoid dissemination in the environment, if accommodation is not possible in a private room, precautions for newborns can be implemented with incubators, with a distance of at least one meter between them.

Diseases for which droplet precautions are recommended:

- **Invasive disease with H. influenzae type B** (epiglottitis, meningitis, pneumonia): continue precautions for 24 hours after starting antibiotic therapy.
- **Invasive disease with meningococcus** (sepsis, meningitis, pneumonia): maintain precautions for 24 hours after starting antibiotic therapy.

- **Laryngeal diphtheria:** maintain precautions until after two negative cultures.
- **Whooping cough:** maintain precautions for 5 days after starting antibiotic therapy.
- **Mumps:** maintain precautions for 9 days after the onset of peritonitis.
- **Rubella:** maintain precautions for 7 days after onset of symptoms. For congenital rubella use contact precautions (see below).
- **Scarlatina:** maintain precautions for 24 hours after starting antibiotic therapy.
- **Influenza virus:** maintain precautions for 5 days or more after onset of symptoms (not defined for immunodeficient patients).

Note:

Health professionals should be guided by and follow droplet precautions (use mask) and should carry out hand hygiene when examining and caring for patients with signs and symptoms of respiratory infection.

Health professionals with symptoms of respiratory infection are advised to avoid direct contact with patients, especially high-risk patients such as newborns. If that is not possible, the professional should use a mask while providing care.

Precautions for contact transmission [28]

In addition to standard precautions, **contact precautions** are aimed at preventing the transmission of infectious agents, including epidemiologically important microorganisms spread by direct or indirect contact with the patient or the patient's environment. These precautions are used in cases of suspicion or confirmation of a disease easily transmitted through direct or indirect contact.

The use of gloves and apron is indispensable for contact with the patient, preferably in a private room. It is important to put on personal protective equipment (PPE) before entering the room and to take it off before leaving the patient's room in order to contain pathogens, especially those that may be involved in transmission through environmental pollution: for example, vancomycin-resistant enterococcus, norovirus, and other pathogens of the intestinal tract; respiratory syncytial virus.

In the neonatal unit, when a private room is not available, follow the hospital ICC guidelines for grouping patients with the same disease. In a room with several beds, when one or more cases need contact precautions, use an incubator with a visible sign saying "Contact Precautions", and maintain a minimum distance of one meter between beds to prevent inadvertent sharing of materials [23,24].

Indications for contact precautions [28]:

- **Severe mucocutaneous herpes simplex.**
- **Herpes simplex in neonates in contact with maternal disease:** for newborns born vaginally or by caesarean section, if the mother might have an active lesion and ruptured membranes more than 4-6 hours before birth.

- **Abscesses that are not contained,** with potential for extensive environmental pollution and risk of transmission.
- **Diarrhea.**
- **Congenital rubella:** up to 1 year of age.
- **Cutaneous diphtheria.**
- **Hepatitis A.**
- **Viral hemorrhagic fever (Ebola).**
- **Enteric infections with Shigella spp., rotavirus, and Clostridium difficile.**
- **Respiratory syncytial virus infection** in newborns, young infants, preschool children, and immunocompromised adults.
- **Multiresistant microorganisms:** MRSA, VRE, VISA/VRSA, ESBL enterobacteria, S. pneumoniae, and other bacteria of interest as defined by the local ICC.
- **Patients awaiting finding of surveillance culture for investigation of colonization by multiresistant bacteria** should receive empirical contact precautions until results of the culture are available for decision-making.

Table 1: Precautions recommended for the infections most prevalent in neonatology [28]

Disease	Type of precautions	Duration of precautions/observation
Acute viral conjunctivitis (hemorrhagic)	Contact	Duration of disease. Highly contagious infection. Adenovirus is the most common; enterovirus and coxsackie are also associated with community outbreaks.
Adenovirus	Contact	Duration of disease
Chlamydia pneumoniae	Standard	
Arbovirus disease (encephalitis, dengue, and yellow fever)	Standard	
B19 parvovirus: Chronic disease in immunosuppressed patients Transient aplastic crisis or red cell crisis	 Droplets Droplets	 Duration of disease 7 days
Bronchiolitis	Contact	Use of surgical mask following standard precautions
Candidiasis: all forms, including mucocutaneous	Standard	
Cellulitis: uncontained drainage	Contact	Duration of disease
Chickenpox	Aerosols + Contact	Until all lesions are crusted
Citomegalovirus: *Neonatal or immunosuppressed*	Standard	Avoid having pregnant women provide direct care to the patient
Clostridium difficile (Colitis associated with antibiotic)	Contact	Duration of hospitalization
Conjunctivitis: Bacterial, Gonococcal, and *Chlamydia trachomatis*	Standard	
Chlamydia trachomatis (conjunctivitis, pneumonia < 3 months).	Standard	
Dermatophytosis/ringworm/tinea	Standard	
Diphtheria: · Cutaneous · Pharyngeal	 Contact Droplets	 Treatments effective after +2 negative cultures with interval of 24 hours
Enterocolitis with *Clostridium difficile*	Contact	Duration of disease
Enterovirus (coxsackie and Echovirus)	Contact	Duration of disease
Epiglottitis (*Haemophilus influenzae* type b)	Droplets	Duration of disease
Erythema, infectious	Standard	
Exanthema, sudden	Standard	

Disease	Type of precautions	Duration of precautions/observation
Gastroenteritis *Campylobacter spp.*, cholera, cryptosporidiosis, enterohemorrhagic *E. coli* 0157:H7, giardiasis, adenovirus, rotavirus, salmonellosis, Shigellosis, vibrio parahaemolyticus, viral and *Yersinia enterocolitica*, norovirus	Contact	Duration of disease
Hepatitis A Virus	Contact	Duration of hospitalization
Hepatitis B Virus (HBsAg positive)	Standard	
Hepatitis C Virus and other hepatitis	Standard	
Herpes simplex: Neonatal	Contact	Even dry and crusted lesions
Impetigo	Contact	Until 24 hours of effective treatment
Influenza: a, b, c	Droplets	5 days or more in immunocompromised patients (at least for duration of disease)
Measles	Aerosols	Duration of disease
Meningococcemia	Droplets	Until 24 hours of effective treatment
Multiresistant bacteria, colonization/infection	Contact	Agents and duration of precaution are according to ICC criterion. Request evaluation.
Mumps	Droplets	9 days after onset of mumps
Parainfluenza	Contact	Duration of disease
Pediculosis	Contact	24 hours after the end of treatment
Pneumonia:		
Adenovirus	Contact + Droplets	Duration of disease
Chlamydia sp., Legionella ssp., S. aureus, fungal	Standard	
Meningococcal and mycoplasma (primary atypical pneumonia)	Droplets	
Other bacteria not listed, including Gram-negatives	Standard	
Pneumococcal (group a)	Droplet	Until 24 hours of effective treatment
H. influenza b	Droplets	Until 24 hours of effective treatment
Poliomyelitis	Contact	Duration of disease
Respiratory syncytial virus	Contact	Use of standard mask in accordance with the standard precautions. Evaluate antigen test before to dropping precautions (for patients with prolonged hospitalization).
Rubella:		
· Congenital	Contact	Until 1 year of age, maintain standard precautions if repeated negative oropharyngeal and urine tests after 3 months old.
· Other forms	Droplets	From beginning of rash for 7 days. Duration of disease for immunocompromised patients
Scabies	Contact	Therapy effective in 24 hours
Syphilis, congenital	Standard	

Disease	Type of precautions	Duration of precautions/observation
Toxoplasmosis	Standard	
Tuberculosis:		
Lung and laryngeal (suspected or confirmed)	Aerosols	
Mantoux test reaction (≥ 5 mm) without evidence of lung or laryngeal disease	Standard	Up to 3 negative microscopies + adequate treatment
Outside the lung, meningitis and other diseases with or without drainage	Standard	
Whooping cough	Droplets	From beginning of effective treatment for 5 days
Wound infection		
With secretion contained	Standard	
With secretion not contained	Contact	Duration of disease

Table 2: Indications for specific precautions for mother and newborn, based on status of exposure and identification of specific antibodies for chickenpox [24,31]

EXPOSURE/ANTIBODY	AEROSOL PRECAUTIONS: MOTHER/NEWBORN
+ Exposure/ + Antibody	
Mother with VZV antibody exposed to chickenpox does not have risk of developing the disease or transmitting infection.	Not necessary for mother or for newborn.
+ Exposure/ - Antibody	
=> Mother exposed to chickenpox 21 days or more before childbirth If there are no signs of chickenpox at the time of childbirth, it is presumed that the mother is not infected.	Not necessary for mother or for newborn.
+ Exposure/ - Antibody	
=> Mother exposed 6-21 days before childbirth and had not developed chickenpox by the time of childbirth. Mother may be in the incubation period and may be infected at and after childbirth.	The mother and newborn are potentially infected PRECAUTIONS FOR AEROSOLS
+ Exposure/ - Antibody	
=> Mother exposed to chickenpox 6 days before childbirth Mother will possibly not be infected before discharge.	There is no need for isolation unless the mother is still in the hospital more than 9 days after exposure. In a positive case, aerosol precautions should be maintained for the mother.
Mother in noncommunicable phase (presence of crusted lesions and no appearance of new vesicles in the last 72 hours)	Mother is considered uninfected. Newborn is considered potentially infected and should receive specific immune globulin (VariZIG), otherwise aerosol precautions should be maintained. The newborn may remain with the mother in both situations.

EXPOSURE/ANTIBODY	AEROSOL PRECAUTIONS: MOTHER/NEWBORN
Mother with active lesions at the time of childbirth	Infected mother = Precautions for contact and aerosols
a) Newborn with lesions at birth	Infected newborn = Precautions for contact + aerosols. Newborn may remain with the mother
b) Newborn without lesions at birth	Potentially infected newborn. Should receive specific immune globulin (VariZIG). Precautions for contact + aerosols until 28 days of life, if in hospital.

Control of multiresistant bacteria [23, 32]

- Testing for colonization or infection by multiresistant bacteria should be done, depending on the epidemiological situation of the neonatal unit and with guidance from the local ICC, especially in patients at greater risk, such as those with longer stays in the unit, use of mechanical ventilation, or subject to invasive procedures or prolonged use of antibiotics. Once the presence of multiresistant bacteria is detected, follow the guidelines for contact precautions.
- Testing for colonization by multiresistant bacteria (swab culture, whether rectal, umbilical, tracheal aspirate, or naso/oropharyngeal) can also be useful when newborns are admitted from other hospitals. In this case, newborns should be put on contact precautions until the culture results are available. If colonization or infection by multiresistant bacteria is ruled out, contact precautions can be suspended; if the presence of multiresistant bacteria is confirmed, contact precautions should be maintained.
- In neonatology, a private room is not essential for contact precautions. In practice, the incubator can be used to restrict the physical space of the newborn, and procedure gloves can be used. The use of long-sleeve aprons is indicated in situations where the professional has more direct contact with the child, for example, holding the child in the lap. Single-use aprons should be used for each health professional and each patient.
- Newborns colonized by multiresistant bacteria may be touched freely by the mother and placed in contact with the skin during the period of hospitalization, with only hand hygiene being required before and immediately after touching the newborn.
- In situations in which the mother is being treated for an infection or is colonized by multiresistant bacteria, as long as her skin is unbroken, contact with the newborn is not contraindicated, including skin-to-skin contact. In this situation, the mother should disinfect her hands before contact with the newborn, but gloves are not needed. In this case, the newborn is subject to contact precautions, so that if it is colonized by a multiresistant bacterium, there is reduced risk of transmission of this type of bacterium to other newborns on the hands of health professionals. Therefore, adherence to contact precautions is for health professionals, not for mothers, who only touch their own children.
- Guidelines for mothers colonized by multiresistant bacteria are similar to guidelines for other mothers, that is, routine body hygiene and disinfecting hands before touching the newborn. Use of gloves is not required for touching the newborn; the usual hospital gown allows skin-to-skin contact.
- In addition to strategies to reduce cross-transmission of multiresistant microorganisms, the rational use of antibiotics is crucial for control of multiresistant bacteria.

Rational Use of Antibiotics [23, 32, 33]

Precise indications for the use of antibiotics and adherence to the practices described below are of fundamental importance to prevent bacterial resistance [33].

- When infection is suspected, take two hemoculture samples at different sites: CSF culture (when not contraindicated) and urine culture (preferably by suprapubic puncture) before beginning the use of an antibiotic.
- Collect at least 1 ml of blood in each hemoculture sample to reduce the chance of false negatives.
- Whenever possible, opt for monotherapy based on the results from cultures and the antibiogram.
- Use of an antibiotic should be suspended immediately when the diagnosis of an infection is ruled out.
- The use of a prophylactic antibiotic is indicated only in contaminated or potentially contaminated surgeries, and in clean surgeries with placement of a prosthesis. An adequate tissue concentration should be present at the time of the procedure and 3-4 hours after the surgical incision. Thus, a single dose administered when inducing anesthesia is sufficient, except in lengthy surgical procedures or when there is heavy bleeding, in which case an additional dose of antibiotic is needed to maintain adequate blood levels.
- The empirical regimen for HAI treatment depends on the time of appearance of clinical symptoms (early or late), previous use of invasive procedures, knowledge of the flora, and the resistance standards of the hospital. The empirical regimens for treatment of early and late infections can be defined according to the guidance provided by the ICC of each hospital.

HAI prevention in neonatology units

Skin care

The skin is the body's first line of defense, acting as a barrier against infections.

In full-term newborns, the stratum corneum is formed by lamellar bilayers composed of hydrophobic lipids, mainly fatty acids, cholesterol, and ceramides (Figure 6). These lipids and proteins provide protection, creating a waterproof barrier and providing an acid and xerophytic environment that impedes the invasion of microorganisms [34].

The vernix caseosa appears at about the 20th week of gestation and is present in minimum quantities up to about the 24th week. Starting in the 24th week, its quantity increases, covering the newborn with a thick layer. As the term approaches, there is a decrease in the vernix, which accumulates in skinfolds and on the scalp. The vernix is composed mainly of water, proteins, and lipids [35].

In preterm newborns, the skin is an immature organ from the functional and anatomical standpoints. It has few layers of stratum corneum, with a limited number of fibers for fixation between layers and a low number of collagen and elastic fibers [36]. In other words, the preterm newborn has skin that is fine, thin, reddish, with visible and superficial veins when compared to the full-term newborn; cellular cohesion between epidermis and dermis is reduced and the cutaneous barrier is less effective. The most relevant consequences are transepidermal water loss, greater percutaneous absorption of chemicals, and easily induced cutaneous trauma [37,38].

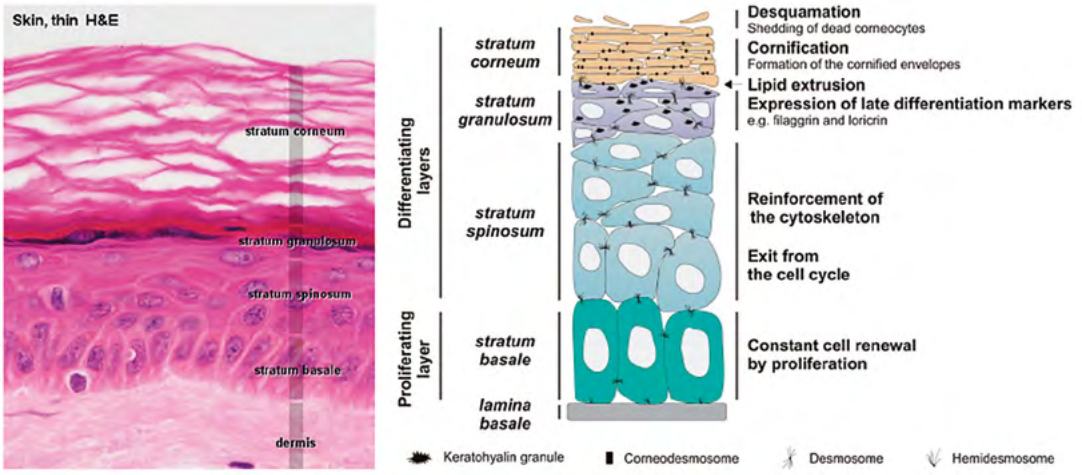


Figure 6: **Cornification** (Cell Biology Wiki. Available in [http://php.med.unsw.edu.au/cellbiology/index.php?title=Cell_Death_1]

The skin continues to develop until 12 months after birth. Hence, the skin of newborns, young infants, and other children is sensitive to excessive glandular secretions, dust mites, cumulative physiological secretions in the diaper area, and extreme atmospheric conditions[39]. In addition, in newborns the lipid content is lower due to low sebaceous gland activity[40] and the cutaneous surface has a pH with a neutral tendency, which significantly reduces defenses against excessive microbial proliferation, unlike the acid pH in adults (pH <5). The level of water is elevated, since the dermis of newborns has less mature collagen, with a greater concentration of proteoglycans.

Newborns do not present bacteria at birth. Aerobic flora appear in the first 24 hours and become quantitatively comparable to those of the adult within six weeks. *Staphylococcus epidermidis* is a coagulase-negative Staphylococcus that normally colonizes the skin and the mucous membranes of the human body, as part of normal microflora. However, when there is a rupture of the cutaneous surface by any type of trauma or by insertion of a medical device, Staphylococcus can penetrate the host, becoming pathogenic [35].

In addition to antimicrobial defense, the principal functions of the skin described in the literature are the reduction of transepidermal water loss, thermoregulation, protection against toxins of the external environment, and tactile function [41, 42].

Preterm newborns are at high risk of developing infections in the hospital, due to their physiological condition and the need for a wide range of procedures and devices such as venipuncture, temperature sensors, transcutaneous monitors, intravascular access, tubes, probes, and urine collectors. All these procedures and devices are conducive to skin injuries. In addition, injuries are more vulnerable to contamination by microorganisms present in the environment and in the skin of the preterm newborn itself. In addition to preserving cutaneous integrity, skin care can prevent toxicity from chemical products due to destruction of the protective lipid barrier [43,44]. In this regard, routine care for newborns should include the following:

- **Maintenance of environmental temperature and humidity**

  Thermal regulation, particularly in preterm infants, should be maintained with incubators. This equipment permits a neutral thermal environment so that the newborn maintains its normal internal temperature, with minimum oxygen and energy consumption.

- **Positioning**

  Positioning is an important strategy in the prevention of pressure ulcers. The team should have a clearly defined process and frequency for changing the decubitus position, including the use of supports such as cushions to relieve pressure on the patient's body, especially on the sites where bones are prominent. The sheet should be stretched smooth, avoiding folds in its surface. The use of hydrocolloid plaques can protect bony prominences from pressure injuries.

  In addition, positioning assists in thermal regulation by minimizing the transfer of heat from the body surface to the environment. The fetal position is particularly useful since it promotes reduction of the newborn's body surface and its contact with thermally neutral materials such as cotton fabrics [45].

- **Lubrication with emollient oils**

  Emollients have humectant properties (they attract water to the skin) and occlusive properties (they prevent water from evaporating). They lubricate and hydrate the skin, leaving a lipid film that protects the integrity of the stratum corneum and the cutaneous barrier. For this reason, the use of emollients prevents transepidermal water loss, restores the elasticity and homeostasis of the skin, prevents drying and cracking, and reduces the frequency of dermatitis. However, routine prophylactic use of emollients is controversial, since it can increase the risk of nosocomial infections by coagulase-negative Staphylococcus. Emollients should not be used in inflammatory and/or exudative dermatoses, nor in cutaneous skinfolds, because of their occlusive power [40]. The container of emollient should be for exclusive use for each individual newborn.

- **Use of cutaneous solutions for antisepsis**

  Although there is increased absorption of substances applied to the surface of newborn skin, the product indicated for bathing in the ICU is chlorhexidine, as it is effective in reducing colonization of the skin for 4-6 hours after bathing [46]. Although there is no evidence that chlorhexidine is toxic when absorbed by the skin, it should not be used in the middle ear, since it is toxic to the ear. Topical application of chlorhexidine at 0.5% in an aqueous solution is indicated to reduce colonization of the skin, an important risk factor for systemic infection, mainly by *Staphylococcus spp*., one of the principal agents causing sepsis [46]. The antiseptic should be applied twice at 10-second intervals, or once with exposure to the product for 30 seconds; the excess should be removed with sterile gauze soaked in sterile distilled water or physiological saline solution at 0.9% [46].

  Iodized substances should be avoided whenever possible, since they can result in a significant oversupply of iodine with consequent hypothyroidism.

- **Care in implementation of invasive procedures, such as venous or arterial punctures, and in affixing devices**
  - carry out gentle skin antisepsis, avoiding injuries to the skin;
  - avoid multiple punctures;
  - affix peripheral venous access with microporous adhesive tape. For fixation of central venous access, preferably use a transparent adhesive dressing that is anti-allergic, gas-permeable, and impermeable to external contaminants, facilitating continuous monitoring of the insertion site for the presence of phlogistic signs and infiltration.

  Also important is the appropriate fixation of devices used in newborns for cardiorespiratory monitoring and ventilation support

- the tracheal tube should be affixed securely* with elastic adhesive tape or microporous adhesive tape to avoid accidental extubation;
- the nasal prongs for CPAP should be affixed securely* to prevent injuries to the nasal septum.

* Note: fixation is considered secure when there is no traction or pressure of the tracheal tube or prong on the nasal septum or in the perioral region. Also make sure that the ventilator circuit does not pull on the tube because of its positioning. The technique of "H-shaped taping" is often used for the tracheal tube.

An option for fixation of the oximeter sensor and ocular protection of a newborn exposed to phototherapy is the use of Velcro strips. The site of fixation should be changed every four hours to prevent skin injury.

- **Removal of adhesive tapes used for fixation of devices and life support equipment**

For removal of adhesive tapes, cotton swabs soaked in mineral oil are recommended. The use of solvents such as benzine is contraindicated because of absorption and toxicity risk, as is the topical application of benzoin tincture, which increases the risk of skin injury in removal of adhesive tape [41].

- **Body hygiene routines**

Hygiene for newborns immediately after birth has the objective of removing maternal blood and fluids, minimizing exposure to the microorganisms present in these secretions[48]. Initially, the vernix caseosa should be wiped with a towel[40]. The World Health Organization (WHO) recommends that the first bath be given no earlier than six hours after childbirth, due to the risk of hypothermia during and after this procedure [49].

Bathing does not always produce beneficial results; it can trigger hypothermia and destabilize the vital signs of the preterm newborn. For an immersion bath, the child must be clinically stable, without any invasive devices[50]. In addition, the use of soaps can cause skin irritation and absorption of toxic substances [37], because of the chemical components used in soap formulation.

Skin pH is important for maintaining homeostasis of the cutaneous barrier. It influences the integrity and cohesion of the stratum corneum as well as its antimicrobial defense. Normal skin pH varies from 4 to 6, while the pH of the internal environment of the human body is from 7 to 9. This means that there is a gradient of 2 to 3 between the epidermis and the dermis, known as the "acid mantle," which functions as protection against invasive microorganisms. During bathing, the application of topical agents can affect this acid mantle, altering the skin pH of the newborn. Another consequence may be dissolution of surface fat from the epidermis, which influences conditions for hydration and leads to dryness and desquamation of the skin [40, 51].

The ideal cleaning agents are liquid, mild, soap-free, and fragrance-free, with neutral or slightly acid pH. These products are classified according to the surfactant used. They can also be formulated without a surfactant, as is the case for soaps based on synthetic detergents, called syndets, with pH <7, considered to be a good choice. Cleaning agents based on soaps are alkaline, with pH >10, and are more likely to irritate the skin. Most full-term newborns require a period of 1 hour to regenerate cutaneous pH after use of alkaline soap. In preterm newborns, return of the pH to the normal range takes longer [52,35].

Daily bath in the ICU

- This is unnecessary and contraindicated in preterm newborns.
- Disinfect the genital area only, with lukewarm water and neutral soap.
- In preterm newborns of less than 32 weeks' gestation or weighing less than 1,500 grams, use only lukewarm water applied with cotton balls or compresses.

Prevention of omphalitis

The umbilical cord of the newborn should be clamped and cut with sterilized scissors immediately after birth. Initially, the umbilical cord is gelatinous; it dries over time, becoming mummified around the 3rd or 4th day of life, and generally falls off the body between the 6th and 15th day (Figure 7). The presence of purulent secretion, with edema and hyperemia of the abdominal wall, particularly if it forms a triangle above the navel, indicates omphalitis, a high-risk infection for the child [53].

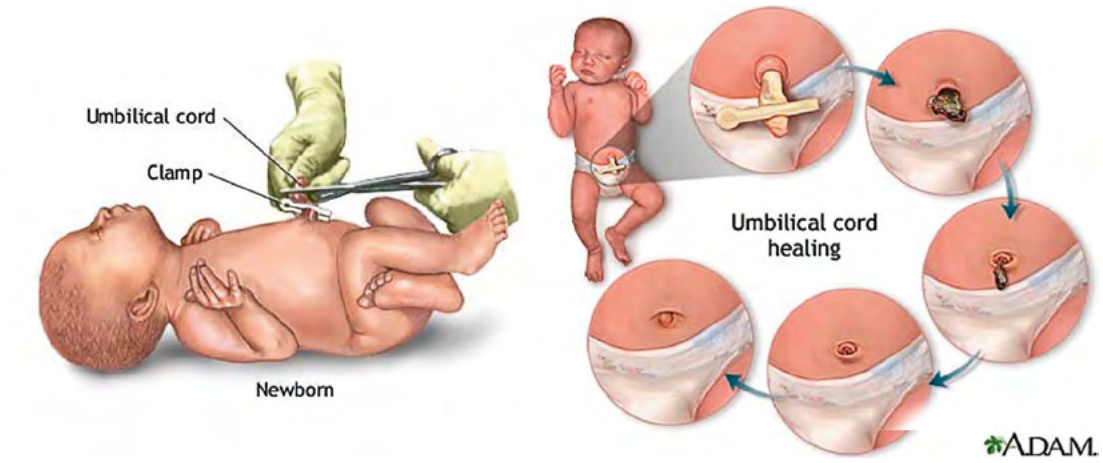


Figure 7: Procedure of clamping and cutting the umbilical cord and process of mummification of the umbilical stump (ADAM Images).

Hygiene of the umbilical region is an important factor in protection against infection. Keeping it clean and dry is recommended by WHO [53] and other international organizations [54,55]. This is because the use of antiseptics is still debated in the literature, with different products having different advantages and disadvantages. Studies comparing the use of antiseptics found chlorhexidine to be effective in reducing colonization and infection of the stump, but there are divergent findings regarding an increase in mummification time with use of this product [56]. Alcohol at 70% concentration can accelerate mummification when compared to other antiseptics, but it does not block colonization [52].

Several studies conducted in developing countries have demonstrated that the use of chlorhexidine in care of the umbilical cord has significant protective action in terms of preventing neonatal mortality, and is cost-effective. WHO has reviewed this evidence with a view to product recommendations [57].

Iodopovidone poses risks to newborns because of its high absorption[58]. However, when any of these antiseptics is compared to "dry care" or "natural care" procedures, studies demonstrate no significant differences between groups in terms of occurrence of omphalitis[53]. It is important to emphasize that whatever antiseptic is selected for cleaning the umbilical stump, it should be stored in a container for individual use.

A meta-analysis on the use of antiseptic in umbilical cord care for prevention of omphalitis in developing countries showed significant evidence of reduction of omphalitis (by 27% to 56%) and reduction of 23% in mortality (relative risk 0.77; confidence interval of 95% 0.63-0.94) [59].

Prevention of omphalitis = cleaning of the umbilical stump

- The stump should be kept clean and dry; this should be done once a day or more frequently, as necessary.
- Chlorhexidine at 0.5% concentration was shown to be effective in reducing colonization and infection of the stump, but it delays mummification.
- Alcohol accelerates mummification, but does not block colonization.

Important: whatever product is used, it should be stored in a container for individual use.

Prevention of conjunctivitis

From an epidemiological standpoint, conjunctivitis occurs when:

- purulent exudate is present in the conjunctiva or contiguous tissues (cornea, lachrymal glands, and other tissues);
- pain or hyperemia of the conjunctiva or periorbital region is accompanied by microscopy showing microorganisms in the exudate from the eye and presence of leukocytes; or a positive culture obtained from the conjunctiva or contiguous tissues (cornea, lachrymal glands, and other tissues); or a positive antigen test (for example, *Chlamydia trachomatis*, herpes simplex, adenovirus) in conjunctival exudate or scraping; or a positive virus culture.

The most serious type of conjunctivitis is caused by the *Neisseria gonorrhoeae* bacterium. A pregnant woman contaminated during childbirth with this type of bacterium can infect her newborn. Conjunctivitis caused by this bacterium manifests in the first days of life in its most severe form, with edema, hyperemia, irritation of the eyelids and conjunctivas, and intense purulent secretion. If not treated appropriately, this conjunctivitis can cause corneal ulcers and compromise the child's vision permanently.

Conjunctivitis caused by the *Chlamydia trachomatis* bacterium appears between the 5th and 14th day of life. The symptoms are the same as those of gonococcal ophthalmia, but much less severe, and silver nitrate eye drops are not as effective in this case. The herpes virus may also cause neonatal conjunctivitis. Care is very important, since ocular infection can spread to the brain and cause major damage.

To prevent conjunctivitis, the eyes of newborns should be cleaned with cotton or sterile gauze immediately after birth to remove secretions. Application of silver nitrate solution at 1%, within one hour after birth, serves to prevent gonococcal conjunctivitis in particular. The eyes should not be irrigated with saline solution or distilled water after application of the eye drops to avoid dilution of the product, but excess solution can be removed after one minute[60]. Although silver nitrate remains the principal method for prophylaxis, its use has been questioned because it does not offer complete protection against *Chlamydia*, currently the principal cause of neonatal conjunctivitis, and because of the frequent occurrence of chemical conjunctivitis. For this reason, other eye drops have been used, such as erythromycin, tetracycline, and PVP-I at 2.5% or 5%, with better reported results [60, 61].

In the first three days of life, redness may appear in reaction to silver nitrate eye drops used at birth. This irritation is normal and soon disappears.

Eye drops used for ophthalmological examination, or in providing care, can be another source of contamination and should be reserved for single use. Containers should be marked with the date of opening and expiration date of the ocular solution. Containers that come into accidental contact with ocular mucous membrane of the patient should be discarded and never used with other patients [62].

Critical patients, including newborns under sedation, are unable to close their eyelids or blink, thereby losing the principal mechanism for ocular protection; in addition, tear production can be reduced. These related factors can cause dry eye syndrome and exposure keratopathy. The eyes should be protected by closing the eyelids with eye drops and lubricant creams [61]. In addition, care should be taken to avoid splashes of airway secretions or tracheal secretion aspirates [60]. Hygiene is important to prevent infections that can affect vision.

During the physical exam, observe the presence of ocular secretion. When conjunctivitis is present, set up contact precautions or standard precautions, depending on the microorganism isolated. Bed linens should be changed daily to prevent retransmission.

Chemical conjunctivitis (e. g.: silver nitrate) and conjunctivitis from viral disease with systemic dissemination (e.g.: measles, chickenpox) should not be reported as hospital conjunctivitis [1,62].

Cleaning the eyes of newborns

- Once a day, e.g. at bath time.
- Before placing the newborn in the bathtub, wet a cotton wad in lukewarm water and wipe one eye from eyelid toward eyelashes.
- Use a new cotton wad to clean the other eye.
- Cotton swab sticks should not be used because of the risk of causing injuries with sudden movements.
- When bathing, take care to protect eyes from excreta and chemical products in the water.

Invasive procedures [23]

Invasive procedures are those that result in breaking the epithelial barrier or that contact mucous membranes. They include collection of samples, venous punctures, catheterization of umbilical vessels, and thorax drainage, among others.

Table 3: Standardization of antiseptic solutions and sequence suggested for use in invasive procedures in newborns [63]

Products and sequence of use by procedure	Alcohol at 70%	Chlorhexidine detergent (2% or 4%)	Chlorhexidine alcohol solution (0.5%)	Chlorhexidine aqueous solution (1%)	Physiological saline solution (0.9%)
Hand antisepsis before operative or risky invasive procedures*		1st			
Venous or arterial puncture	1st		or 1st		
Invasive vascular procedures **		1st	3rd		2nd
Preoperative skin antisepsis		1st	3rd		2nd
Hemoculture, CSF, urine culture by suprapubic puncture			1st		
Vesical probe		1st		3rd	2nd

* Examples of risky invasive procedures: thorax drainage, insertion of catheter for peritoneal dialysis, blood extraction or transfusion.

* Examples of invasive vascular procedures: insertion of umbilical venous or arterial catheter, peripherally inserted central catheter (PICC), and phlebotomy.

Note: PVP-I solution can be used as an antiseptic if chlorhexidine is not available. However, it should be avoided in neonatology since it is less tolerated by the skin of newborns and health professionals. In addition, the frequent use of PVP-I can lead to changes in thyroid hormone in newborns.

Collection of samples for testing

Follow standard precautions and use standard antiseptics:

- use aseptic technique;
- wash hands with chlorhexidine detergent solution;
- venous puncture, arterial or arterialized blood: use non-sterile procedure gloves and carry out skin antisepsis with alcohol at 70% or alcohol solution with chlorhexidine;
- collection of hemocultures, CSF, and urine samples by suprapubic puncture: use sterile procedure gloves and do skin antisepsis with chlorhexidine alcohol solution or PVP-I.

Vesical probe

- use aseptic technique;
- wash hands with chlorhexidine detergent solution and use sterile procedure gloves before the procedure;
- carry out antisepsis with aqueous chlorhexidine solution or PVP-I;
- in a prolonged probe, use a closed drainage system;
- carefully wash hands before and after handling urine collection devices.

Changing the probe and the collection system: There is no set time period. A change is recommended in the following situations:

- lockage or impaired operation of the system;
- breach of the closed system;
- change in the state of the urine, with the appearance of sediment;
- fungal urinary tract infection (UTI) during the use of the probe;
- sepsis without another focus or fever of undetermined origin, without another identified risk factor.

Surgical procedures

In surgical procedures carried out in the intensive care unit, follow the recommended aseptic technique for surgery:

- wash hands and forearms with chlorhexidine detergent solution at 2%-4% or PVP-I detergent;
- use complete surgical protective clothing with cap, mask, apron, and sterile gloves;
- use sterile operative field and sterilized instruments;
- carry out antisepsis of the operative field with chlorhexidine detergent at 2% to 4% or PVP-I, remove with physiological saline solution at 0.9%, and complement antisepsis with alcohol solution of chlorhexidine 0.5% or PVP-I tincture. In extremely preterm newborns, antisepsis may be accompanied by aqueous chlorhexidine solution at 1%, reducing risks of chemical burns.

For surgical procedures performed in the surgical center, carry out preoperative bath with chlorhexidine detergent, whenever possible.

Prophylactic antibiotic: when indicated, this should be administered when inducing anesthesia. The principal objective is to reduce the risk of infection of the surgical incision by reducing the number of pathogens present in the operative wound during surgery.

Peripheral venous access

In neonatology, a peripheral vein may be punctured for collection of samples, for infusion of parenteral solutions such as basal serum, or for administration of medication. Peripheral venous access requires good practices in the puncture and maintenance of the venous access. For these, follow the recommendations described below.

Puncture for peripheral venous access

- wash hands with chlorhexidine detergent solution;
- use non-sterile procedure gloves;
- carry out skin antisepsis with alcohol at 70% or chlorhexidine alcohol solution at 0.5%;
- avoid multiple punctures;
- for venous punctures for peripheral drip phleboclysis, give preference to polyurethane or silicone devices; avoid steel needles.

Care of peripheral venous access

- Fixation for peripheral venous access should be sterile, with surgical tape and gauze or transparent membrane, and should not be changed at preestablished intervals.
- The covering used for fixation of peripheral venous access should be changed immediately if there is suspicion of contamination or if the dressing becomes damp, loose, or soiled, or its integrity is otherwise compromised.
- Do not change the device used for peripheral drip phleboclysis if the insertion site is in good condition, with no signs of inflammation and good permeability of the venous access.
- Carry out antisepsis of the connections with alcohol at 70% or chlorhexidine alcohol solution before administration of medications or infusion of parenteral solutions.

Prevention of infection associated with central catheters [64, 65, 66]

To prevent infection associated with central catheters, all health professionals involved in this procedure must adhere to good practices for insertion and maintenance of the catheter.

One of the strategies for achieving this objective is to create a group of caregivers who are responsible for insertion of central catheters, with training of the team in maintenance and management of catheters and monitoring of adverse events associated with catheters, including infectious complications.

Precautions for insertion of central catheters

- Use maximum barrier precautions and aseptic technique as outlined above for catheterization of the umbilical vein or artery, peripheral insertion of a central catheter (PICC), or insertion of a central catheter for phlebotomy.
- In catheterization of the umbilical vein or artery, affix the catheter with surgical tape in a bridge shape and use daily application of chlorhexidine alcohol solution at 0.5% or PVP-I tincture.

Maintenance of the central venous catheter

- Care of the umbilical venous or arterial catheter includes good fixation of the catheter and cleaning of the insertion site with chlorhexidine alcohol solution at 0.5% three times

a day, or more often if necessary. Because of the high risk of bloodstream infection associated with this device, the umbilical venous catheter should be removed as soon as possible (maximum recommended time is seven days).

- The umbilical venous catheter should be replaced with a peripherally inserted central catheter (PICC) if necessary to maintain central venous access [66]. Similarly, because of the risk of mechanical and infectious complications, the umbilical arterial catheter should not be kept in place for more than five days.
- Remove and do not replace an umbilical venous or arterial catheter inserted in an emergency situation or if there are signs of thrombosis or infection associated with the device.
- The PICC or phlebotomy site should be covered with gauze at the time of insertion; afterward, a transparent film dressing is preferred. There is no recommended interval for changing a transparent film dressing, which should be changed only if blood is present or the transparent film becomes loose. The dressing should be applied with aseptic technique, using physiological saline solution and a chlorhexidine solution at 0.5%. If it is not possible to use a transparent dressing, a sterile gauze dressing is recommended, changing it every 48 hours, or as often as necessary.
- Disinfect the connections of the central or peripheral venous catheter with alcohol at 70% or chlorhexidine alcohol solution before administering medication or when changing the equipment.
- Use a dedicated line for infusion of parenteral nutrition.
- Equipment used for total parenteral nutrition should be changed every 24 hours.
- Equipment used for transfusion of blood products should be removed immediately after use.
- Equipment used for infusion of basal serum or PVC infusion bags, as well as adapter plugs or three-way valves, should be changed every 72 hours or more often, following the recommendations of the hospital ICC. If there is a break in aseptic handling technique or an accumulation of blood is seen in any of these devices, change immediately.
- Do not immerse the catheter or the catheter insertion site in water.
- Evaluate the conditions at the catheter insertion point daily and remove the device immediately if there are signs of local infiltration or phlogistic signs such as heat, redness, or purulent secretion.
- Evaluate the need for maintenance of the catheter daily and remove it as soon as clinical conditions permit.
- Obtaining a catheter tip culture is indicated only when the reason for removing the catheter was diagnosis or suspicion of a vascular catheter-associated infection. In this case, concomitant collection of hemocultures is suggested.

Prevention of pneumonia associated with mechanical ventilation [68, 69, 70]

Precautions in ventilation care

- Whenever possible, use a non-invasive ventilation method.
- Minimize whenever possible the duration of mechanical ventilation.
- Tracheal intubation should be done so as to cause the least possible trauma. The professional should use protective goggles, mask, and sterile procedure gloves.

- Avoid accidental extubation: necessary measures include adequate fixation of the tracheal tube and radiological examination after intubation so that personnel are aware of the position of the tube. The newborn should be kept calm through the use of pharmacological (analgesia/sedation) or non-pharmacological measures.

Monitoring of unplanned extubations and the use of measures to prevent these occurrences have been shown to be effective in reducing ventilator-associated pneumonia.

Precautions for mechanical ventilation equipment and accessories

- Use hand hygiene before and after touching respiratory devices.
- The humidifier reservoir should be filled with sterile water, using a closed system to replace water.
- Keep the ventilator circuit free of condensate. Ensure removal of condensate every 2 or 4 hours.
- Use procedure gloves to remove condensate from circuits and wash hands immediately.
- Condensed water in the circuits can be colonized by pathogenic bacteria and should be disposed of in a closed plastic bag and deposited in a covered hospital waste container or in a waste disposal unit. Use gloves to remove condensed water from the circuits. Carry out hand hygiene afterwards.
- Never return condensed water to the humidifier reservoir, and do not place wet towels near the patient's head.
- The humidifier reservoir should be changed at least as frequently as the respirator circuits, depending on the manufacturer instructions.
- Ventilator circuits should not be changed more than every 48 hours, since this has no impact on reducing hospital pneumonia. There is no recommendation for a maximum time for changing circuits; the current guidance is to change them only when they are visibly dirty or not functioning well.

Handling secretions

- Follow standard precautions and take care to avoid the spread of secretions in the hospital environment.
- Tracheal tube aspiration should be done only when necessary, with aseptic technique, using gloves and a sterile aspiration catheter that is discarded after use. Protect the eyes of the newborn during this procedure to prevent contamination of the eyes by pulmonary secretions, which can lead to conjunctivitis.
- Change the device for aspiration of secretions (a closed system) when it is dirty or not functioning well.
- Contents of the aspirator container should be go to waste disposal whenever possible, depending on the amount deposited.
- Change the aspirator container, as well as the latex extension tubing, at least every 24 hours.

Precautions for gastric probes and enteral feeding [71]

- Avoid gastric distention.
- Elevate head of bed 15 to 30 degrees to prevent gastric aspiration.
- The gastric probe should be changed every 48-72 hours or at longer intervals, depending on the routine of the service. It should be placed in the least traumatic way possible and with adequate fixation.

Use of antacid or histamine H2-receptor antagonist

- Consider neutralization of gastric acidity with the use of these drugs, since an increase in gastric pH favors bacterial gastric colonization by gram-negative bacilli, increasing the risk of pneumonia, especially in patients on mechanical ventilation.

Safety in the preparation and administration of parenteral medications and nutrition

Preparation of parenteral medications and solutions

One of the challenges relating to medications and other solutions in neonatology and pediatrics is the lack of pharmaceutical formulations appropriate for use in newborns, since most commercially available drugs have been developed and tested through clinical trials carried out with young adults [72].

Due to the absence of medical formulations specifically adapted for neonates and other children, most oral and intravenous drugs require dilution [72].

The administration of intravenous (IV) drugs in newborns and children requires drug dilution and, often, adjustment of dosages. IV drugs are perhaps the most studied because of the greater risk of adverse reactions, ranging from mild to fatal, that can occur, even immediately upon administration [72, 73].

- It is estimated that 15% of neonatal hospitalizations are associated with medication errors [73].
- The nursing team can intercept as many as 86% of medication errors related to prescription, transcription, and dispensing. However, only 2% of administration errors are intercepted[74].
- Some adverse effects of drugs on newborns can mimic a typical pattern for infections, characterized by apnea, peripheral perfusion disturbances, and electrolyte and acid-base imbalances, leading to unnecessary interventions [73]. Pharmacovigilance activities are important for detection of adverse reactions to drugs, assisting in the implementation of prevention measures.

Drugs need to be pure and free from physical and biological contaminants. To achieve this objective, it is necessary that safe practices be adopted at every stage, from the production of drugs all the way to their administration [75].

The administration of medication is a multidisciplinary process, with interrelated activities that involve [72,76].

- use of technology;
- quality control of drugs;
- quality control of equipment;
- technical preparation and responsibility of the professionals involved and institutional policies established for the drug sector.

In this context, the World Health Organization (WHO) and the Pan American Health Organization (PAHO) stress attention to drug safety, asking all health professionals to participate in continuous monitoring of the safety and efficacy of pharmaceutical products to make treatment with them safer and more effective [77,78,79].

Safety of medication administration in the health services depends on an array of actions that involve the entire medication cycle. This requires the participation of all professionals responsible for the different stages of the process, from drug selection to administration.

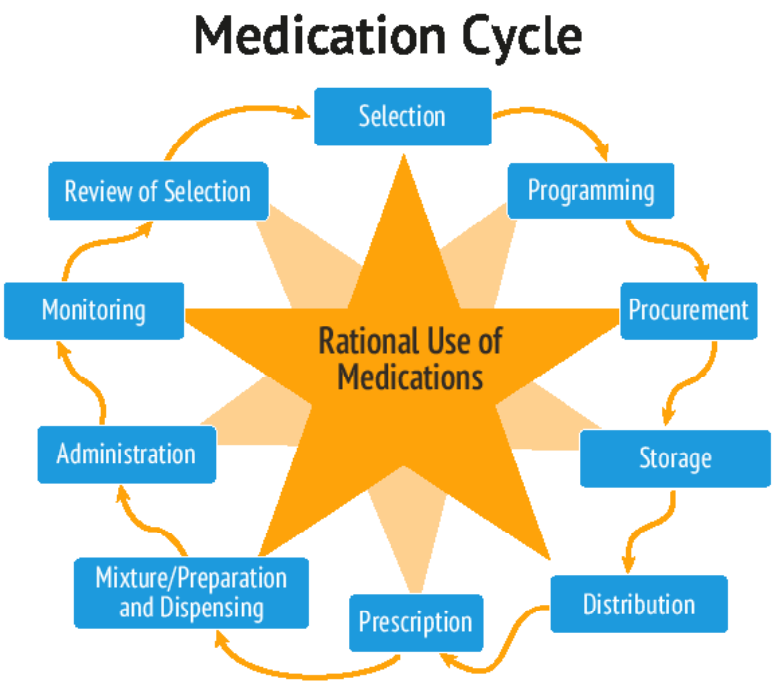


Figure 8: Medication cycle [80]

Selection of medications [80, 81]

Within the health services the process for the rational use of medications begins with selection of the drugs that will make up a hospital's therapeutic arsenal.

Drug selection should be based on the development of evidence-based clinical protocols for diagnosis and treatment of the most prevalent diseases, according to the profile of each hospital, giving consideration to principles of safety, efficacy, and effectiveness. This standardized list of drugs should be reviewed periodically with the participation of clinical personnel from various specialties and their representatives in the hospital's pharmacy and therapeutics committee.

In addition to drug standardization, safe administration also requires:

- Standardization of dosages and dosage intervals,
- Standardization of solutions for dilution appropriate to each type of drug,
- Standardization of dilution concentration for each drug,
- Standardization of infusion time.

Programming [80, 81]

Based on the standardization of drugs, the hospital's pharmacy and administrative team should have a drug **procurement program** to ensure timely supply of medicines. It is necessary to maintain a minimum stock of drugs to be used for treatment of events that are rare but serious, and which require treatment to be initiated immediately. The purchase of larger stocks should be considered for drugs used daily, based on the profile of patients being treated.

Certain standardized drugs that are rarely used do not need to be kept in stock and can be acquired after they are prescribed if the treatment scheduled allows this. In this case, it is important to have organized logistics for timely procurement. In short, drug standardization should consider not only the frequency of use but also an evaluation of the drugs that are most commonly used to treat the diseases that correspond to each specific health service.

Mixture/preparation and dispensing [82]

When one or more sterile products are added to a liquid IV to be administered, the resulting combination is known as a mixed IV [82]. To ensure sterility, absence of pyrogens, and integrity of the solution, specific precautions are needed when preparing parenteral solutions, both in small and large volumes.

Drug preparation is critical in this process, given the possible errors (wrong drug, incorrect dosage, incorrect dilution, problems with conservation of the product, and contamination at the time of preparation, etc.).

Drug mixture/preparation can be done in the pharmacy service, with single doses dispensed for administration to the patient on a schedule. This can also be done by the nursing team, which can receive the medication and the appropriate solution for dilution; such preparation is usually done at the nursing station.

The nursing team is directly involved in the following steps:

- requisition and verification of the medication dispensed by the pharmacy;
- storage of the medication at the nursing station;
- preparation, with utmost care to prevent contamination in reconstitution, dilution, and administration of the drug;
- administration of the drug (the last protective barrier against errors that may have occurred at any other stage of the process);
- monitoring the patient's response to the administered drug;
- checking on the prescription and notation of actions carried out and of any complications.

Prescribing medication is an important step often associated with medication error, through mistakes in calculation, inadequate dilution, or misinterpretation of instructions. The nursing team is directly involved because nurses implement the prescription by administering the medication and share responsibility under the nursing code of ethics.

Therefore, like pharmacists, nursing professionals who have any doubt about a prescription or identify any problem should alert the prescribing physician to prevent possible errors in drug preparation and administration.

Dosing and administration of parenteral solutions [75,93.]

A parenteral solution is defined as an injectable, sterile, and apyrogenic solution, of large or small volume, appropriate for parenteral administration.

A large-volume parenteral (LVP) solution is packaged in a single-dose container with capacity of 100 ml or more. A small-volume parenteral (SVP) solution comes in a container with less than 100 ml capacity.

Parenteral solutions should be prepared and administered by qualified professionals and in sufficient quantity for the intended use [83].

Physical infrastructure [75]

Because of the complexity and inherent risks in procedures for preparation of parenteral solutions, particularly when other drugs are added, there should be an area used exclusively for this purpose.

The best safety conditions for preparation of parenteral solutions can be obtained with correct use of a laminar flow hood, ensuring the absence of microbiological, physical, or chemical contamination. If a laminar flow hood is not available, parenteral solutions should be prepared in areas reserved for this purpose, adhering to the most rigid aseptic standards [72].

The areas and facilities for preparation and administration of parenteral solutions should be orderly to prevent the risk of contamination or of adding incorrect components to the prescription, and to ensure the proper sequence of operations [83].

These areas should have washrooms and sinks in sufficient number, with taps that can be turned off without using the hands, with soap, antiseptic, and hand-drying materials.

Access to the area for preparation of parenteral solutions should be restricted to the professionals directly involved.

Preparation areas should be protected against dust, insects, rodents, and other animals.

Dosing and administration of medication [75, 84]

To ensure safety in the preparation and administration of parenteral solutions, it is essential to adhere to best practices established in technical standards. That allows for maintenance of the drugs' identity, compatibility, stability, sterility, safety, and traceability.

For safe use of parenteral solutions, minimum requirements must be followed in both preparation and administration to prevent microbiological, physical, and chemical contamination and to guard against drug interactions and incompatibilities.

The responsibility for preparation of parenteral solutions can be assigned to an individual or to several professionals jointly, depending on the standards of professional practice of each country.

Individual functions and responsibilities should be formally described and should be understood by all personnel involved in the process.

- Every professional involved should know the basic principles for preparation and administration of parenteral solutions. Written procedures should exist and should be available to guide the preparation of parenteral solutions in the health services.
- The professional involved in preparation and administration of parenteral solutions should receive initial and ongoing training to develop and continuously upgrade these skills.
- Training should follow an established program that is adapted to the needs of the service, with required record-keeping.
- Training programs should include the concept of quality, instructions on hygiene and health, and operational aspects of transmission of diseases and work safety.
- The professional should be trained in personal hygiene practices, especially hand hygiene.
- The professional should wear a uniform and maintain standards for cleanliness and hygiene.
- The professional is not permitted to smoke, drink, or keep plants, food, beverages, or drugs for personal use in the preparation and administration area. Staff members should be evaluated in accordance with each country's program for medical control of occupational health.

It is the responsibility of the health services to establish written procedures for preparation of parenteral solutions, with instructions for dosages, dilution, or the addition of other drugs.

Preparation of parenteral solutions should follow the prescription, preceded by careful evaluation by the pharmacist of physical-chemical compatibility and drug interactions that may occur between components.

If the pharmaceutical evaluation suggests that the prescription should be modified, this should be discussed with the person responsible, who should be the one to make any such change.

Products used in preparation of parenteral solutions should be carefully compared to the medical prescription, and inspected for physical integrity, coloration, presence of particles or foreign bodies, and expiration date.

Any changes that may prevent use of the product should be communicated in writing to the sector managers and the competent health authority. When preparing and administering parenteral solutions, it is important to follow the ICC's recommendations with respect to disinfecting the general area and surfaces in particular; hand hygiene; use of personal protective equipment; and disinfection of ampules, containers, drug preparation areas, and connections for infusion lines. Drugs should be prepared immediately before administration, unless the manufacturer recommends otherwise.

Needles, catheters, winged infusion sets, syringes, and other equipment and accessories (filters, covers, etc.) used in the preparation of parenteral solutions should be used only once and then discarded in an appropriate container.

When opening and handling ampules and glass containers, recommendations designed specifically to prevent accidents with these articles should be followed.

In large-volume parenteral solutions, equipment should be correctly labeled with at least the following information: full name of the patient, bed/registry, product name, qualitative and quantitative description of the components added to the solution, volume and rate of infusion, administration route, date and time of preparation, and identification of the professional who prepared the solution.

For small-volume parenteral solutions, labels should correctly identify, at a minimum: full name of the patient, room/bed, name of the drugs, dosage, schedule, administration route, and identification of the professional who prepared the solution.

Equipment with a penetrating tip should be used to ensure a connection that prevents leakage of solution or the entry of air.

Administration of medications and parenteral solutions [72,75,76]

Medication administration is one of the most important activities and is frequently carried out by nursing staff. The term "administration" is defined by Phillips[87] as being the process of releasing drugs into various parts of the body.

Understanding the nature of a drug and the risk involved in its administration allows nursing professionals to administer a prescribed therapy safely. This competence is closely linked with ongoing training in theories of professional practice for everyone involved in this process.

The health services should have an organizational structure and sufficient competent personnel to ensure quality in the administration of parenteral solutions.

Every procedure related to the administration of parenteral solutions should be carried out according to written operational instructions.

When infusion pumps are necessary, they should be used by duly trained professionals.

The health services should ensure the availability of a sufficient number of infusion pumps that are calibrated and regularly maintained by skilled professionals.

Infusion pumps should be certified or registered by the competent organization in each country. They should be periodically cleaned and disinfected according to standards set by the ICC. Before use, infusion pumps should be carefully checked to verify their cleanliness and operational condition. Calibration and maintenance of the infusion pumps should be recorded and the documentation should be easily accessible.

Large-volume parenteral solutions should be administered in a closed system. Central venous access and peripheral insertion, whether central or not, should be carried out according to procedures established in coordination with the Infection Control Committee in the health services.

Parenteral solutions should be inspected before administration to verify their identity, integrity of packaging, coloration, presence of foreign bodies, and expiration date. Intravenous administration of parenteral solutions should only be carried out after confirming the permeability of the access route, adhering rigorously to the time established for infusion.

Before administering any medication, confirm that all the information related to the procedure is correct, in accordance with the following 9-point checklist [86]:

- correct patient (use two forms of identification for every patient);
- correct medication (check the medication against the prescription and confirm the label three times);
- correct dosage;
- correct method;
- correct time;
- medication compatibility;
- proper guidance provided to the patient, or the patient's legal representative;
- the right to decline the drug (patient or legal representative);
- correct record keeping.

Make sure that all this information is documented correctly. Incomplete information should be clarified before administration of the drug.

To increase the safety of the process, the drug should be double-checked by two nursing professionals before administration.

During the infusion, if any abnormality is noted, interrupt administration of the parenteral solution and immediately report the occurrence to the professional responsible for the sector, who will determine what action is needed. This incident should be registered in a notebook kept for this purpose.

When parenteral solutions are ready for administration, they should be transported from the preparation site to where the patient with utmost care to maintain their physical-chemical and microbiological integrity.

When the access route is interrupted, administration of the same parenteral solution should only be restarted if physical-chemical and microbiological integrity is maintained.

The container with the parenteral solution and the infusion equipment should be protected from direct exposure to sunlight and from sources of heat.

Signs and symptoms of complications should be communicated to the responsible physician and noted in both the notebook and the registry.

It is the nurse's responsibility to ensure that all events and data referring to patients and their treatment are registered correctly. This ensures that necessary information will be available for evaluation of the patient's condition, the effectiveness of treatment, and tracking in the case of adverse events.

After administration of the parenteral solution, the professional should dispose of the used material in accordance with the waste management plan of the health services and the standards set by the institution's Infection Control Committee.

Parenteral nutrition [67]

Parenteral nutrition is a solution or emulsion composed basically of carbohydrates, amino acids, lipids, vitamins and minerals. It is sterile and apyrogenic, packed in a glass or plastic container. It is intended for intravenous administration in patients, who may or may not be malnourished, in the context of hospital, outpatient, or home care, aiming at the synthesis or maintenance of tissues, organs, or systems [67].

Parenteral nutrition is used very frequently in neonatal ICUs in the care of preterm or sick newborns who do not tolerate enteral feeding, in order to partially or completely provide the nutrition required for adequate growth [83, 88].

Parenteral nutrition in neonatology is individualized for each newborn, according to the infant's nutritional needs, gestational age, time of life, clinical and hemodynamic picture, and laboratory profile[88].

Routes of administration [88]

In selecting the administration route, consider the clinical picture, the duration of parenteral nutrition, nutritional needs, difficulties of venous access, concentration of nutrients, and osmotic concentration of the solution.

Central venous access is recommended when the patient needs a high supply of nutrients, mainly in cases of hydric restriction and/or glucose concentration higher than 12%, osmotic concentration higher than 900 mOsm/L, prolonged duration of parenteral access, and difficulty of establishing venous access [88, 89].

Regardless of the administration route, it is advisable to maintain an exclusive route for administration of parenteral nutrition. If there is a need to administer blood products or other medications as well, a separate venous access should be used [67, 88, 89].

The purpose is to prevent the risk of contamination and incompatibility of parenteral nutrition with other solutions.

Standards for the preparation of parenteral nutrition

Health institutions should have a pharmaceutical professional who is responsible for the preparation of parenteral nutrition [67]. However, if such a professional is not available, another qualified professional should assume the duty. The preparation of the mixture of components for parenteral nutrition should be done so as to ensure that it is appropriate for the intended use and to avoid exposing the patient to risks from lack of safety, quality, and efficacy.

Quality assurance is the responsibility of the professionals who make up the interdisciplinary nutritional support team, consisting of specialized physicians, pharmacists, nutritionists, and nurses. This requires involvement and effort by each professional in the different phases of the process: prescription, preparation, dispensing, and administration [67]. The role of each professional on the team in this process is described in detail in the "Latin American Consensus on Parenteral Nutrition", a document drafted in 2008 by a group of specialists in this field, representing several countries of Latin America [89].

To achieve consistent quality, it is important to have a quality management system that is designed and implemented correctly. All aspects of this system should be documented, and its effectiveness should be evaluated periodically [83].

Physical infrastructure for parenteral nutrition [67, 90]

Ideally, the pharmacy where parenteral nutrition is prepared should be appropriately located, planned, and constructed to ensure the quality of the preparations, with at least the following [75]:

- preparation area;
- anteroom;
- room for cleaning and hygiene of pharmaceuticals and related products;
- preparation wing;
- changing rooms;
- storage area;
- dispensing area.

The areas and facilities should be appropriate and sufficient for the purpose, with all the needed equipment and materials organized in a rational way to prevent risks of contamination and mixing of components and to ensure the proper sequencing of operations. The site should have smooth internal surfaces (floors, walls, and ceiling), with no cracks that are resistant to cleaning. These surfaces should not shed particles and should be easily washable.

In areas for preparation, cleaning, and hygiene, avoid drains to reduce the chance of infestation by insects or rodents. Other areas of the pharmacy used for preparation of parenteral nutrition should have closed siphon drains.

The surroundings should be clean and disinfected according to detailed written procedures.

Lighting and ventilation should be sufficient so that temperature and humidity do not lead to deterioration of the drugs and related products or impair the precision and functioning of equipment.

Changing rooms, washrooms, and restrooms should be easy to access and sufficient for the number of staff members, and restrooms should not have any direct communication with the preparation and storage areas.

Break rooms and cafeteria should be separate from the other areas.

The room used for preparation of parenteral nutrition should be separate and used exclusively for this purpose. It should be equipped with air filters that trap particles and microorganisms at the recommended level (ISO class 5, grades A or B, previously known as class 100)[91] with unidirectional flow in the room (ISO class 7, grade C, previously class 10,000), and with positive pressure. The preparation room for parenteral nutrition should have an area of 5 m^2 with a unidirectional flow booth, formerly called a laminar flow hood [92].

Preparation of parenteral nutrition [93]

The preparation of parenteral nutrition, which involves pharmaceutical review of prescription, handling, quality control, conservation, and transport, requires that a pharmacist[75] or other high-level professional have responsibility for and direct supervision over the process.

Since some classes of products, such as parenteral nutrition, cannot be sterilized at the end of the process, the alternative way to address the hazards of microbial contamination is to prepare parenteral nutrition using an aseptic process.

An aseptic process starts with sterile inputs and aims to prevent contamination of the sterile components by viable microorganisms. In an aseptic process, the environment where the parenteral nutrition is prepared should meet cleanroom classification standards and the air quality should be ensured by appropriate equipment. The aseptic technique should be validated, the process monitored, and the personnel trained and properly equipped [94] :

- Preparation of parenteral nutrition should be carried out with aseptic technique, following written and validated procedures to ensure physical-chemical compatibility, sterility, apyrogenicity, and absence of particles, as well as the composition and dosage prescribed. This requires adherence to best practices in the preparation of parenteral nutrition.
- Preparation of parenteral nutrition should be done within an ISO class 5 [91] area and involves measurement, transfer, and mixture of the component solutions. All the steps – opening the ampule, cleaning the rubber stoppers on the vials, insertion of the sterile needle and syringe into the vial, and transfer of liquids for the final packaging of parenteral nutrition – should be done with aseptic technique.
- The personnel who prepare parenteral nutrition should be well trained in the relevant theory and practice, they should also have knowledge about cleanrooms [91].

- In the preparation of the room, all surfaces including walls and floors should be cleaned with sterile material that does not release particles.
- Entry into the preparation area should be exclusively through the anteroom. The professional should have carried out the correct handwashing with antiseptic and should be appropriately garbed.
- Personnel involved in preparation should be appropriately trained, educated, and authorized to proceed correctly and should document the following activities during aseptic preparation:
  - antisepsis of the hands for meticulous elimination of skin microorganisms using a tensioactive solution associated with a wide-spectrum germicide with residual effect, such as chlorhexidine detergent solution at 2%-4%.
  - for protective equipment, use coveralls with a hood and boots, made of material that does not release particles, non-woven fabric, and dust-free sterile gloves.
- Preparation of parenteral nutrition should follow best practices for sterile products.
- Use non-woven compresses (do not use materials that release particles) soaked in sterile alcohol at 70% for cleaning of small surfaces and for opening ampules.
- For small volumes use a sterilizing filter (0.22 µm).

Note: If the institution does not have the physical structure and/or sufficient human resources to install a parenteral nutrition service on its premises, this service can be provided by an outside company that meets all the legal requirements for such services.

Conservation [67, 93]

Immediately after preparation and throughout any transport of parenteral nutrition, it should be kept (at 2º C to 8º C) in a refrigerator used exclusively for drugs and with hygienic conditions, except in cases of immediate administration, ensuring that it is physically and chemically stable and free from contamination [67, 93].

Transport

Parental nutrition should be transported in thermally insulated coolers used exclusively for this purpose, in previously established hygienic conditions, and under the supervision of the pharmacist responsible for preparation. The product must be maintained at a temperature of 2 ºC to 20 ºC for the duration of transfer from the production area to the final destination, which should not exceed 12 hours. In addition, parenteral nutrition bags should be protected against external environmental conditions and direct sunlight [75].

Upon receiving a parenteral nutrition bag, check for:

- Integrity of packaging
- Presence of particles
- Precipitation

- Color change
- Phase separation
- Labeling
- Expiration date

The label must include all the information below:

- Name of the patient
- Number of the bed and hospital registry
- Date and time of preparation
- Composition
- Osmotic concentration
- Total volume
- Infusion rate
- Access route
- Expiration date
- Sequential control number
- Conservation and transport temperature
- Professional responsible

Before use, maintain the parenteral nutrition in the following conditions:

- temperature: 2 °C to 8 °C;
- refrigerator used exclusively for drugs;
- clean refrigerator (cleaned regularly, as determined by the ICC);

Remove from the refrigerator in advance of use, allowing enough time for the product to reach an appropriate temperature.

Care in the installation and administration of parenteral nutrition

- responsible staff member: nurse;
- observe aseptic principles;
- evaluate and secure the parenteral nutrition equipment;
- evaluate and carry out the administration of parenteral nutrition;
- ensure that the catheter insertion site is cleaned and redressed.

The installation and administration of parenteral nutrition is the responsibility of the nursing team, using the hygienic and aseptic conditions needed to maintain the quality of parenteral nutrition.

Setup for parenteral nutrition equipment [67, 75, 93]

- Set aside a clean physical area for the installation of equipment for parenteral nutrition bags.
- Disinfect hands thoroughly before beginning to place the bags for administration.

- Use complete protective clothing with cap, mask, apron, and sterile gloves.
- Clean the bag with alcohol at 70%, especially in the area closest to the site of installation of the equipment.
- Remove the protective cap from the intermediary tubing of the bag.
- Support the bag on a stand, maintaining it in the horizontal position in order to provide better support for the bag.
- Press to break the internal membrane and put it in place.

Administration of parenteral nutrition to the patient [67, 75, 93]

- Evaluate the conditions of the catheter (positioning, perfusion, and insertion site).
- Use appropriate personal protective equipment.
- Perform asepsis of the hands and of the site where the catheter connects to the equipment for the parenteral nutrition bag.
- Fill the device with parenteral nutrition to an appropriate level.
- Program the infusion pump according to the prescription.
- Monitor the infusion periodically.

Precautions during infusion [67, 75, 93]

- Ensure maintenance of the administration route.
- Make sure to infuse the prescribed volume, monitoring the correct operation of the infusion pumps.
- Ensure that no other prescribed drug and/or nutrient is infused by the same administration route as the parenteral nutrition, unless formal authorization is provided by the multidisciplinary nutritional team or physician.

Maintenance of the catheter [67]

The catheter for infusion of parenteral nutrition should have a dedicated line not used for any other purpose. It should be changed every 24 hours to ensure:

- Greater longevity of the catheter.
- Less risk of contamination.
- Stability of the nutrients.

A continuous drip should be ensured to maintain adequate flow of the solution.

Quality control for preparation of parenteral nutrition [67, 75, 89]

Following these guidelines helps technicians and pharmacists prepare sterile quality products.

Microbiological analysis: sterility of solutions should be verified by laboratory tests to ensure the validity of the aseptic process. Nationally and/or internationally recognized standards of interpretation and test frequencies should be followed [93].

Personnel involved in preparation should be requalified annually to test their aseptic practices.

Air quality conformity: recommended tests [91, 93,95].

- rate and uniformity of air flow;
- integrity of the absolute filters;
- water-tightness of the absolute filters;
- electronic particulate count;
- viable microorganism count.

Control of the end product [67, 93]

Preparation should be evaluated based on the existence, adaptation, and implementation of standardized written procedures.

Samples of all batches of parenteral nutrition solutions should be conserved under refrigeration (2 °C to 8 °C) for microbiological laboratory testing and control.

Samples for microbiological laboratory testing should be statistically representative of one preparation session with *n* (number of parenteral nutrition bags prepared) + 1, collected randomly at the beginning and end of the preparation process.

The control samples of all parenteral nutrition bags prepared should be conserved under refrigeration (2 °C to 8 °C) until 7 days after their expiration date.

NOTE: For purposes of microbiological testing, only parenteral nutrition solutions in their intact original packaging or samples from these are valid.

When ready for use, parenteral nutrition should be checked as follows:

- visual inspection of 100% of the samples to ensure physical integrity of the packaging and absence of particles, precipitation, and phase separation;
- verification of the accuracy of information on the label;
- sterility test of one sample representative of the parenteral nutrition bags produced in one work session, to confirm that it is sterile.

Transport [67, 93]

Parental nutrition should be transported in thermally insulated coolers used exclusively for this purpose, in previously established conditions, under the supervision of the professional responsible for preparation. The product should be maintained at a temperature of 2 °C to 20 °C for the duration of transport, which should not exceed 12 hours, and should be protected from the elements and from direct sunlight.

Validation of transport [67]

Parenteral nutrition should be transported by a company authorized for health surveillance; this is critical for maintenance of product quality. Temperature variations and exposure to direct sunlight may degrade the physical-chemical stability of the product. Therefore, transport should be under controlled conditions and at temperatures between 2 °C and 20 °C, with a maximum duration of 12 hours.

Transport should be validated and standardized with fixed quantities of reusable ice packs for a given number of parenteral nutrition bags, in thermal packaging.

Milk preparation unit

Milk preparation units are hospital units for the preparation, hygiene, and distribution of milk formulas and milk substitutes for consumption by newborns and other patients in the pediatrics unit. These activities are carried out under the most rigorous aseptic techniques to provide infants with an appropriate diet and the lowest risk of contamination [96]. Precautions during the preparation of this kind of nutrition should be rigorous, since the target population, in addition to having greater susceptibility to foodborne diseases, may be immunologically weakened [97].

In neonatal care units and intensive care units (ICUs), the use of milk formulas is reserved for situations in which breast milk cannot be obtained exclusively from the mother herself or from a breast milk bank and, exceptionally, for situations in which breast milk is contraindicated due to the clinical condition of a newborn or young infant.

Considering the vulnerability of hospital patients, quality control to ensure the safety of the products supplied by the milk preparation unit is of fundamental importance.

Quality control of raw material

Although milk formula manufacturers have improved their processes, there is still concern about contamination of the product during manufacture, since the technology currently in use seems not to be capable of commercially producing sterile powder or eliminating the possibility of contamination. For example, there are reports of outbreaks of infection in newborns linked with contamination of the raw material by *Enterobacter sakazakii* [98].

E. sakazakii has caused disease in all age groups, with specific risk to children <1 year; those at greatest risk are newborns, especially preterm, low-birthweight, or immunocompromised newborns. Children of mothers who are HIV-positive are also at risk because they specifically require formula and can be more susceptible to infection [99].

This bacterium has been found more frequently than Salmonella during the manufacturing process, becoming a potential source of contamination after being subjected to heat. Low levels of contamination by *E. sakazakii* in powder preparations for nursing infants become a risk factor due to the potential for multiplication during preparation and storage, before consumption of the reconstituted powder [100].

Improper storage practices for reconstituted powdered milk formula can promote rapid growth of *Enterobacter sakazakii*. In accordance with the basic principles of risk control, "due to the exponential nature of bacterial growth [...] after 6 hours at 25°C, the relative risk increases thirtyfold and after 10 hours at 25°C, the relative risk increases 30,000-fold compared to the baseline. Risk reduction can be achieved by ensuring rapid cooling and storage below 10°C if not for immediate use; and minimizing the length of time between reconstitution and consumption" [100]. The basic risk control principles demonstrated in preliminary risk assessment for *E. sakazakii* would also apply to other species of enteric bacteria.

With respect to raw material, the Codex specification for Salmonella is the absence of microorganisms in 60 samples of 25 g each; however, the Codex does not contain specific criteria for *E. sakazakii* [100].

Quality standards for preparation of milk formulas in milk preparation units [101]

Quality control for a milk preparation service should include all the critical steps in the work process needed to ensure a safe product that maintains the nourishing properties of the formula with the lowest possible risk of contamination.

This should include monitoring every step in the process, including selection, procurement, and storage of the raw material; personal hygiene of the professional who prepares the formula; environmental hygiene; preparation of the equipment and utensils used in mixing and dilution; temperature control, sterilization, cooling, refrigeration, and warming of the formula. With regard to sanitary conditions, good manufacturing practices for producers and manufacturers of food are fully applicable, and they should serve as guidelines for preparation of milk formulas in preparation units. Adherence to these practices should be monitored through supervision, training, and regular evaluation of workers [99].

For this purpose, the hazard analysis and critical control points (HACCP) method is an important tool for ensuring food quality[100]. Its use is fundamental for establishments where food preparation needs rigorous hygienic conditions, as is the case for milk preparation units, where enteral diets and special milk formulas and nutritional supplements are prepared.

Finally, to evaluate the effectiveness of practices used to prepare food that is microbiologically safe, a routine should be established for microbiological analysis of test samples [103, 104].

Table 4: Microbiological conformity standards for prepared milk formulas

Microbiological test	Milk formulas	Enteral formulas
Bacteria count (on plates incubated at 37o C for 48 hours)	Less than 100/ml	
Total coliform count	Absence in 1 ml	Absence in 1 ml
Mold and yeast counts	Less than 10/ml	Absence in 1 ml
Bacillus cereus count	Less than 100/ml	Absence in 1 ml
S. aureus count	Absence in 1 ml	
Clostridium, sulfite-reducing at 44o C	Absence in 1 ml	
Salmonella count	Absence in 25 ml	Absence in 25 ml

Physical facilities for milk preparation units

These facilities should meet at least the minimum health standards in force in each country. In general, the physical structure should be conducive to adherence with best practices in the preparation of milk formulas.

Many countries have their own regulations on the minimum dimensions for milk preparation units. One example is the Brazilian regulation[92] that requires health facilities that provide pediatric and/or obstetric care also to have a milk preparation unit. According to this legislation, the milk preparation unit for a health facility with up to 15 pediatric beds should be at least 15.0 m^2, with clear separation between "dirty" and "clean" areas, and independent access to the "clean" area through a separate changing room. In the case of institutions with more than 15 pediatric beds, this minimum requirement should be adjusted.

Tabele 5: Minimum size requirements for a milk preparation unit [92]

Milk preparation unit	Minimum dimension
Area for receiving, cleaning, and decontamination of feeding bottles and other utensils	8.0 m^2
Area for sterilization or high-level disinfection of feeding bottles	4.0 m^2
Area for preparation and packaging of milk and non-milk formulas	7.0 m^2
Area for storage and distribution of milk and non-milk formulas	5.0 m^2
Area for final sterilization *A double-door autoclave can be used for final sterilization (heat sterilization), using the door in the clean area*	1.0 m^2

Support areas are also recommended, such as an administrative room, a storage area for cleaning material, and a restroom with a dressing area for staff. These areas must be separate from those used for preparation, packaging, and storage.

These areas should be set up to avoid cross-circulation flows of staff members and food; preferably, rooms should be divided with a half-glass wall partition to allow supervision of the procedures [105, 106].

> Preparation must be done in an area separate from the area for reception and cleaning and it requires protective clothing.

Between the areas for reception, cleaning, and sanitizing of inputs and the areas for preparation, there should be an area for donning protective clothing. This serves as a "barrier area" to prevent contamination by cross-flow from different activities.

In hospitals that have an open system for milk preparation activities and preparation of enteral diets, the areas for reception, cleaning, and sanitizing of inputs can be shared [107]. However, milk and non-milk formulas should be prepared in a separate space from where enteral nutrition is prepared. When it is not possible to have two different environments for preparation of enteral diets and milk formulas, fresh food should be disinfected in the pre-preparation area and formula preparation and enteral nutrition activities should be carried out at different times, after cleaning the area and all equipment and utensils. Whenever possible, equipment and utensils for the two activities should be kept separate [107].

In institutions that have human milk banks, the milk preparation team can prepare portions, package, and dispense pasteurized breast milk, as long as this is done in the milk preparation unit with a separate preparation process and under specific handling conditions, following current legislation [108].

The walls should be constructed with chemical-resistant materials and should have hard, smooth surfaces with rounded corners to allow for regular cleaning and disinfection [92, 108].

The milk preparation area should have a filtered air conditioning or air recycling system that keeps temperatures below 25 °C, as well as an exhaust system for steams and vapors (autoclaves) [92, 108]. The use of fans is prohibited in the areas for food pre-preparation and preparation; the same guidance applies to milk preparation areas [109].

The components of climate control equipment should receive proper cleaning and maintenance. Climate control components should undergo regular cleaning and maintenance and filters should be changed in accordance with the specific regulations [110].

There should be uniform lighting, without direct sunlight on work surfaces, and with white artificial light to prevent discoloration of food and high temperatures [110].

Heat treatment and sterilization of formulas

According to data from the United States Food and Drug Administration (FDA), loss of nutrients was observed when infant formulas were reconstituted using boiling water.

Although heating milk formula in an autoclave provides greater microbiological safety for the diluted dosages, it also has the disadvantage of nutrient loss.

Heat treatment in an autoclave, when recommended by the manufacturer, makes use of moist heat at a temperature of 110 °C for 10 minutes, followed by cooling to 21 °C for 2 hours, followed by refrigeration at 4 °C for 4 hours. This thermal treatment can eliminate heat-resistant bacteria, but does not eliminate bacterial spores; it is typically a method for thermal disinfection of infant formulas but not for sterilization. Milk formulas treated by this process should preferably be consumed within 12 hours, and in all cases within 24 hours. This treatment process should not alter the color of the formula [106].

To prevent product contamination, some health services have established a routine for preparing, dividing up, and distributing milk formulas with the most aseptic technique possible, using HACCP as a dynamic quality control tool, mainly in the preparation of special formulas and for preterm newborns, thereby avoiding the need for thermal treatment in an autoclave.

The recommendations below suggest how to organize the work flow in the milk preparation unit.

Organization of the work flow in the milk preparation unit [103]

Milk formula preparation practices vary depending on the hospital and on the availability of trained personnel and appropriate facilities. Whatever facilities are available, two elements are crucial for the safe preparation of milk formulas [99]:

- availability of potable water (sterilized);
- aseptic conditions.

The work process for milk preparation units, including all standards and routines, should be formalized in protocols drafted by the milk preparation team, approved by the appropriate technical personnel, and validated by the hospital ICC. These protocols should cover selection, procurement, and storage of raw materials, preparation of the work area, cleaning techniques, necessary materials and products, protective clothing for the person handling the materials, and the preparation, division, storage, and distribution of milk formulas.

The technician responsible for the milk preparation unit is usually a nutritionist attached to the hospital's nutrition and dietetics service.

All professionals assigned to work in the milk preparation unit should be thoroughly trained before beginning their activities. To ensure a safe product, professionals must have detailed knowledge of the work process and should receive regular revaluation and retraining.

Human resources: Staff members of the milk preparation unit usually report to the hospital nutrition and dietetics service. They undergo pre-employment and periodic medical evaluations

based on their country's occupational health standards for health care providers. They must follow rigorous body hygiene practices including a daily bath, clean hair protected by a cap during work activities, short nails with no nail polish, brushed teeth, unperfumed deodorant, and no jewelry [112].

In addition to regular health examinations, professionals should receive guidance on how to detect illnesses that pose risks of contamination of milk formulas, especially signs and symptoms of gastrointestinal infection (vomiting and/or diarrhea), respiratory infection, and skin injuries, whether infectious or not [112].

Uniform: The health professional's uniform should be well maintained and clean, and it should only be worn in the work environment. Shoes should be closed, clean, and in good repair.

Protective clothing: In the anteroom before entering the production area, the staff member, already in uniform, should put on a disposable cap and mask, thoroughly wash hands and forearms, and put on a clean apron. In services that opt for aseptic preparation technique, the professional should put on an apron and sterile gloves immediately before beginning preparation of the formula.

Hand hygiene: Use rigorous hygiene with hands and forearms, with water and soap or antiseptic detergent (chlorhexidine at 2%, for example) at the beginning of activities and between one procedure and another; in this case, alcohol gel can replace hand washing when the hands do not appear soiled, as long as appropriate techniques are used.

Sterile latex gloves: These are indicated for preparation of milk formulas ready for consumption, even for those that have already undergone heat treatment and those that do not require heat treatment. Remember that using gloves does not remove the need for hand hygiene, which should be carried out by the professional immediately before putting on gloves and after taking them off.

During the preparation of formulas, if there is a problem with glove-use technique, they should be removed immediately. Hands should be disinfected before putting on a new pair of gloves.

Rubber gloves for cleaning and handling of chemical products: These should be used exclusively to protect the professional in the areas of the milk preparation unit used for cleaning and washing of containers, feeding bottles, accessories, equipment, and utensils, and for general cleaning and collection of refuse.

Control of raw materials

Raw materials should be of known origin, containing product registration as well as packaging and labeling that meets the legal requirements of the country where it is being marketed. This should include information referring to the formulation, date of manufacture, and expiration date [99, 102].

Raw materials are normally refrigerated at 4 °C or at room temperature up to a maximum of 26 °C, always following the manufacturer's instructions.

Reconstitution of milk formulas [94, 100, 102]

Milk formulas that are reconstituted by adding water should undergo rigorous hygienic control during preparation to prevent contamination. This requires adherence to the following precaution:

> Water to be used for dilution of formulas should be boiled for 15 minutes or heat-treated in an autoclave at 121 °C for 10 minutes.

Milk formulas that will not undergo thermal treatment (final autoclave) should be diluted with water at a temperature of 70 °C, following aseptic technique in preparation and dosing.

This strategy of using water above 70 °C has the objective of very rapidly inactivating microorganisms. However, there is substantial diversity in the thermal resistance of different strains of microorganisms. This suggests that the use of relatively mild thermal treatments is a potential risk reduction strategy for reducing or eliminating *E. sakazakii* in reconstituted powdered infant formula [98].

Sequence for implementation of the procedures [100, 102]

1. Calculate the quantity to be prepared: Based the medical prescriptions for the day, calculate the volume to be prepared of each type of milk formula and separate out the raw material needed.
2. Room preparation: Workers should put on uniform, cap, and mask and wash hands and forearms before beginning to prepare the room according to the technique previously described.
3. Proceed with disinfection of milk formula packaging with alcohol at 70%.
4. Disinfect the counter to be used for preparation of formulas and up to 70 cm of the wall, using alcohol at 70%, or work in a food-preparation room with germicidal action, if one is when available.
5. Keep previously cleaned equipment and utensils and sterilizing agents near the site where the formula is to be prepared.
6. Repeat hand hygiene, put on apron and sterile gloves, and begin reconstitution of the formulas.
7. Reconstitute the formulas, adhering rigorously to recommended dilution standards, weighing and measuring with precision balances and a sterile container with visible graduation in ml.
8. Dilute milk formulas that will not undergo thermal treatment, using water at 70 °C.
9. After preparing each type of milk formula, prepare dosages using duly sterilized beakers with covers, and affix labels with the following information: type of milk formula and dilution, volume, date and time of preparation.
10. After preparation, milk formula can be packed in cruets for immediate consumption or stored at 4 °C for consumption within 12 hours.
11. When thermal treatment is used, use an autoclave at 100 °C (when recommended by the manufacturer; in this case, there should be no change in coloration), followed by

cooling to 21 °C. Use forced cooling (immersion of cruets in water, ice and alcohol for 10 minutes) or a fast cooling technique with equipment designed for such a procedure. After cooling, immediately store the formulas under refrigeration at 4 °C.

12. Keep a control sample for each batch of formula in the refrigerator under the same conditions as the formulas being used. Send these samples for culture at the end of the period of validity or according to the schedule established by the local ICC.

13. When the activities are completed, clean the utensils and equipment used, as well as a general cleaning, according to the routine established and validated by the local ICC.

Precautions in the administration of milk formulas, pumped breast milk, or pasteurized breast milk [98]

- Milk formula, pumped breast milk, and pasteurized breast milk for a neonatal unit should be transported under refrigeration. These products should also be kept refrigerated until they are to be used.
- Formulas kept under refrigeration at 4 °C can be offered for consumption at room temperature and/or warmed in water at a maximum temperature of 40 °C.
- For babies who can breast-feed, suck, and breathe, milk formula or pasteurized breast milk should be warmed rapidly, immediately before consumption; if not consumed, it should not be reheated.
- Unused formula remaining in the container should be disposed of after a specified time.
- For preterm or ill infants who cannot properly suck or swallow, feeding should be by nasogastric or orogastric tube or gastrostomy. In this case, check periodically for gastric residuals.
- Preparations can be provided continuously or intermittently through an infusion pump or drip with a volume appropriate for the child's tolerance. The tolerated volume is determined by gastrointestinal motility. In this case, there is no need to warm the formula to be infused.
- When pumping a continuous infusion of milk formula into the gastrointestinal tract, it is necessary to control the amount of time a given volume is administered through the syringe and monitor the homogeneity of the preparation inside the syringe.
- The system for infusing milk formula or breast milk should be managed with the same precautions as for parenteral nutrition systems.
- Clean the gastric probe with sterile solutions after each feeding to reduce microbial contamination and formation of biofilms.

HAI Prevention in Rooming-in Arrangements

Rooming-in is a type of hospital accommodation for a mother and a newborn who is in good clinical condition [113, 114]. It has the advantage of allowing for closeness and interaction between the newborn and the mother, father, and other family members. Allowing the infant to remain with the mother full-time favors mother-child bonding, permits breast-feeding on demand, and provides an opportunity for the mother to learn to care for the newborn and to begin to familiarize herself with her infant's behavior [115].

Newborns admitted for rooming-in seldom need invasive procedures, which reduces the risk of infection in this population. For this reason, infectious complications resulting from provision of care should be infrequent.

Infections acquired during rooming-in can manifest during the hospital stay or after hospital discharge (Table 6).

Unlike the situation with newborns rooming in nurseries, colonization of the skin, oral cavity, and intestinal tract of newborns in rooming-in situations is influenced especially by maternal flora and partially by flora from health professionals who participate in care of the newborn [24, 115]. As a result of colonization, infections may emerge, the most common being impetigo, conjunctivitis, omphalitis, and possibly viral infections. The source of contamination for the newborn can be parents, family members, visitors, or health professionals who take part in caring for the newborn during rooming-in [62].

Table 6: Type of infection and incubation period [64]

TYPE OF INFECTION	INCUBATION PERIOD
· Gastroenterite,	Up to 3 days
· Sepsis · Conjunctivitis · Impetigo · Omphalitis · Other skin infections · Urinary tract Infection	Up to 7 days

Chemical Conjunctivitis

This is a complication resulting from silver nitrate eye drops used at birth for the prevention of gonococcal conjunctivitis. Chemical conjunctivitis is characterized by palpebral edema, and can be accompanied by conjunctival hyperemia and yellowish secretion. Usually it appears on the first day of life, with benign evolution and spontaneous regression on the second or third day of life [116].

Omphalitis

Omphalitis continues to be a health problem, especially in developing countries where unsafe birth practices may still exist, such as clamping the umbilical cord with non-sterile material and poor adherence to best practices for hygiene of the umbilical stump [116].

Omphalitis is characterized by the presence of erythema and purulent drainage from the umbilical stump, or presence of erythema and/or serous drainage from the navel, along with a positive culture of the material drained or collected by fine-needle aspiration; or a positive hemoculture.

The necrotic tissue of the umbilical cord provides an excellent environment for bacterial growth. The umbilical stump is rapidly colonized by bacteria from the maternal genital tract and the environment, the most common infectious agents being *Staphylococcus aureus, Escherichia coli, Klebsiella spp., Pseudomonas aeruginosa*, and *Streptococcus pyogenes* [117, 118]. The proximity of umbilical vessels favors the dissemination of these microorganisms to the bloodstream. Omphalitis can remain a localized infection, or it can extend to the abdominal wall, peritoneum, umbilical or portal veins, and liver [118].

Neonatal impetigo

Impetigo is an infection of the skin by Group A beta-hemolytic Streptococcus (*Streptococcus pyogenes*), *Staphylococcus aureus*, and less frequently by other Streptococci of groups B, C, and G.

In the neonatal period, impetigo is usually caused by *Staphylococcus aureus* and occurs in the first two weeks of life.

The clinical picture of impetigo in the neonatal period is characterized by the presence of pustules and flaccid blisters that appear mainly around the navel, in the diaper area, and in folds of the neck and axilla. Lesions begin as vesicles that turned into blisters with initially clear yellow content; healing occurs without scars. The blisters rupture rapidly and leave a red moist surface, later forming a crust. Bullous impetigo, such as staphylococcal scalded skin syndrome, represents a form of cutaneous response to the extracellular toxins produced by *S. aureus* phagotype II. This exotoxin acts by detaching the granular layer of the epidermis through its direct effect on the desmosomes (exfoliative toxins)[28, 118, 119]. In the hospital environment, health professionals who are colonized by *Staphylococcus aureus* or who have skin lesions can be a source of infection for newborns, with reported outbreaks from this cause [119].

Treatment of impetigo in its mildest forms involves general measures such as daily cleaning with water and soap along with an antiseptic such as chlorhexidine at 2%, or topical antibiotics such as mupirocin and fusidic acid [119]. When multiple lesions are present, the preference is for systemic treatment with first-generation oral cephalosporins (cephalexin and cefadroxil). In the more serious cases, the prescribed treatment is with an endovenous antibiotic, for example, oxacillin [119, 120].

Transient neonatal pustular melanosis is sometimes confused with impetigo, but it is not caused by infection. In contrast to impetigo, this type of skin lesion is present from birth. It involves the face and trunk with small, flaccid, and superficial pustules that rupture easily and form a crust and scales, leaving residual hyperpigmented brownish patches [119].

Among the measures to prevent infection during rooming-in and after hospital discharge of newborns considered normal, the most important are adherence to hand hygiene, care of the newborn's skin, hygiene of the umbilical stump, and hygiene precautions to prevent viral respiratory tract infections.

Hand hygiene in rooming-in

Since rooming-in takes place in a hospital unit considered at low risk for infection, hand may be kept clean with water and liquid soap or by rubbing the hands together with alcohol gel when they are not visibly soiled.

Health professionals, parents, siblings, and family members should adhere to hand hygiene standards, with emphasis on five moments detailed in guidelines from the World Health Organization [27,121].

Hand hygiene is required:

- before providing care for the newborn, such as examinations, checking vital signs, changing clothing, or positioning in the bed, and before breast-feeding;
- after providing care for the newborn;
- before carrying out invasive procedures such as collecting blood for a blood glucose test strip or for newborn screening (heel prick test), etc.;
- after changing the diaper or any contact with biological material from the newborn;
- after touching the space around the newborn's bed.

For more details on hand hygiene, see the chapter on this topic in this document.

In case of contact with any biological materials of the newborn, follow standard precautions.

> Parents and family members should receive instruction on hand hygiene routines and providing other hygienic care to the newborn after hospital discharge.

Skin care

Proper daily cleaning of the child's skin is essential to eliminate potentially irritating substances such as feces, urine, nasal secretions, saliva, dirt, and microorganisms [122].

For daily cleaning of urine, it is sufficient to use only lukewarm water and cotton for skin hygiene in the diaper area. The use of soap numerous times a day increases the chances of contact dermatitis. For cleaning of feces, neutral soaps are recommended [122].

Premoistened wipes, although practical and pleasant smelling, are not recommended for routine use because of the risk of removing the lipid film of the skin and because the soap they contain is not removed by rinsing, instead remaining in continuous contact with the skin and causing irritation [123, 124].

The frequency of bathing normal newborns varies by country and is influenced by individual, social, and cultural factors. Bathing with soap is a common and traditional hygiene procedure that is not justified by evidence. Daily baths with soap should be avoided and mild soaps (neutral or slightly acid pH[51]) should be used. Baths of 5-10 minutes are recommended, in lukewarm water at a temperature of 37° to 37.5 °C. The bathtub should to be filled sufficiently to cover the infant's body up shoulder height. The child should be held securely to prevent drowning [123]. Shampoos are not needed when the hair is short, fine, and fragile[125].

To prevent contact dermatitis caused by irritant substances in the diaper area, avoid excessive moisture in the area. Diapers soiled with urine should be changed frequently, depending on their absorptive capacity. Diapers with feces should be changed immediately[123]. Protective creams or lotions that are thick and adherent, based on zinc oxide, titanium dioxide, and starch, or creams with dexpanthenol, are not indicated for routine use in children with normal skin, but are useful for those with damaged skin because they help block contact between feces and lesions[123,125].

Even so, use of such creams can frequently be omitted if hygiene is maintained and diapers are changed frequently [125]. To remove creams, use baby oil; removal with water is difficult and can cause further damage. In addition, avoid removing the product every time the diaper is changed in order not to irritate the skin. The use of irritating powders, oils, soaps, and creams aggravates the clinical picture [123]. With increases of temperature and local moisture, there is frequently secondary infection by *Candida albicans* or by bacteria such as *Bacillus faecalis, Proteus, Pseudomonas, Staphylococcus,* and *Streptococcus*. Yeast infections should be considered, tested, and treated when a dermatitis lasts more than three days [123].

In hygiene for newborns and other children, avoid products that contain perfumes and dyes, because of the risk of contact dermatitis. Also avoid additives that simulate the colors and appetizing aromas of fruit and sweets, because of the risk of poisoning if the product is ingested [124]. The use of powders such as talcum, clay, and starch is not recommended for newborns because of the risk of accidental inhalation causing irritation, pneumonitis, and the formation of granulomas and lung fibrosis [53]. Another precaution is to keep the nails of newborns clean and short to prevent scratches to the body and face.

Care of the navel

The umbilical stump should remain dry and clean for rapid cicatrization and reduction of infection. It should be cleaned at least two or three times a day, using an antiseptic such as alcohol at 70% or chlorhexidine alcohol solution at 0.5%. When cleaning, lift the umbilical stump using gauze and clean thoroughly at the base of the umbilical stump with a cotton swab, either dry or moistened with antiseptic [52, 53, 56, 59].

The umbilical stump should be monitored daily, with attention to the presence of secretions at the base of the stump or erythema of the skin around the umbilicus [52]. If there is excessive secretion or bleeding, clean the stump every time the diaper is changed.

Oral hygiene

Oral hygiene care should begin at birth, using gauze or cloth moistened with water that has been boiled or filtered. Clean the entire mouth, including gums, inner cheeks, and tongue, to remove milk residues [126].

Oral candidiasis is one of the most common mycotic infections of the buccal cavity, with increased susceptibility during the neonatal period, due mainly to the immaturity of defense mechanisms and the lack of a balanced oral microbiome [127].

Feeding bottles and pacifiers are risk factors when they are not well disinfected.

Table 7: Buccal care in children with spontaneous breathing and oral feeding: breast-feeding and artificial feeding with feeding bottle or cup (adapted table) [128]

STAGES	RATIONALE	SPECIAL CONSIDERATIONS
Wash hands, use PPE (gloves, mask, cap).	Reduces transmission of microorganisms and body secretions.	In the case of allergy to latex, use silicone gloves.
Elevate the head (± 30 °C) and incline it slightly to one side.	Minimizes the risk of aspiration of oral secretions and/or used solutions.	Have aspiration equipment ready in case it is needed.
Disinfect the buccal cavity: · soak the sterile gauze with water or a chosen solution (without excess); · gently wipe the bottom of the mouth, mucous membranes, and tongue (from back to front).	Good oral hygiene reduces the risk of microbial colonization associated with immunosuppression and/or hospitalization.	Non-alcohol solutions help control microbial flora without drying the mucous membranes, for example: chlorhexidine gluconate (0.12%).
Hydrate lips with water-soluble gel, massaging them.	Reduces drying of the tissue.	Lip fissures are entry portals for microorganisms.

Prevention of viral respiratory infection during rooming-in and after hospital discharge [118, 129, 130]

To reduce transmission of respiratory viruses during rooming-in and after hospital discharge, provide guidance to health professionals and family members on the following precautions:

- health professionals: disinfect hands before and after contact with patients.
- isolate patients hospitalized with suspicion of respiratory infection, with precautions that include:
  - hand washing before and after contact with patients and their personal items;
  - use of gloves and apron for contact with patients;
  - use of mask and protective goggles when there is a possibility of direct contact with secretions and aerosolized particles, for example, during aspiration of airways.
- disinfect surfaces exposed to bodily secretions: clean with water and soap, followed by alcohol at 70% or other products, according to the standards of the local ICC;
- whenever possible, do not allow health professionals with respiratory tract infections to provide care to newborns;
- prohibit the entry of visitors with respiratory tract infections;
- inform family members about the importance of correct hand hygiene.

At hospital discharge [131]

- Caretakers for patients who are part of risk groups, including newborns, should take care to:
  - avoid exposing the patient to crowds of people;
  - avoid passive exposure to smoke from parents and other family members;
  - limit contact between newborns and infected people as much as possible.
- If parents present signs of flu or a cold:
  - increase personal hygiene precautions, including hand hygiene;
  - put a mask or a handkerchief over the mouth and nose while caring for newborns;
  - try to maintain a distance of at least one meter between the parents' bed and the newborn's cradle;
  - disinfect spaces close to the newborn's bed where its personal items are kept.
- Provide guidance on vaccination against influenza in children from 6 months to 2 years of age, according to the national immunization program of each country.
- One possible strategy for protecting newborns up to 6 months old is to vaccinate the child's parents and caretakers against influenza. Another way of protecting newborns is to vaccinate pregnant women, since studies demonstrate some protection for the fetus while the woman is pregnant, as well as for some months after a child's birth.

Personal hygiene for mothers

After childbirth, as soon as they are steady on their feet, mothers can take full baths, including washing their hair. This should be done daily, with special care to keep the genital region clean. In the first days after childbirth, it is normal to have vaginal bleeding, which will decrease over time. Use sanitary pads and change them every 4 hours or more often if necessary. The use of tampons for menstrual flow is safer after healing of genital region (2 to 3 weeks after the childbirth) [132].

When birth has been by caesarean section, care for the surgical incision is to wash it with water and soap and dry with a clean towel. It is normal to have some discharge from the scar, but if the region shows redness, increased pain, and pus, it should be examined by the doctor, since the scar may be infected. Breasts also require hygiene, but no special care; water and soap during the bath is sufficient. It is not necessary to wash the breasts before each breast-feeding [133].

Mothers should maintain the hygiene noted below during hospitalization and after hospital discharge:

- bathe every day, or more frequently if necessary;
- keep up oral hygiene, brushing her teeth after meals and at bedtime;
- avoid soaps and deodorants with strong smells, and avoid use of perfumes;
- there is no need to wash the breasts before putting the newborn to the breast to nurse; just disinfect the hands;
- disinfect the hands before contact with the newborn and before touching the newborn's personal items, especially those that may go in the mouth, such as nipples and feeding bottles;
- disinfect the hands before preparation of milk formulas or other food for children;
- if the mother has a cold, she should use a handkerchief over the mouth and nose when coughing or sneezing, and wash her hands afterward.

Guidance for hospital discharge

At the time of hospital discharge, the newborn's mother, family members, and caretakers should be given recommendations for promoting normal, safe growth and development and for preventing infections.

The guidelines below should be adapted to the clinical particularities of each newborn. These recommendations pertain specifically to infection prevention and should be included in a set of more comprehensive recommendations.

Oral hygiene

Guidance

- wash hands;
- moisten a cloth or gauze in filtered or boiled water;
- with rotating motions, clean the mucous membranes, gums, and tongue;
- wipe the lips gently.

Buccal care in children with spontaneous breathing and oral feeding: breast-feeding and artificial feeding by feeding bottle or cup (adapted table) [126]

- See Table 7

Cleaning the umbilical stump

The main precautions for the umbilical stump concern hygiene. The umbilical stump of the newborn does not have nerve endings and therefore does not hurt during cleaning. If newborns cry during this care, it is due to the discomfort of the situation, not pain.

- Wash hands well before cleaning the umbilical stump.
- Use a cotton swab moistened with alcohol at 70% or chlorhexidine alcohol solution at 2% to clean the umbilical stump.
- Remember that the part of the stump that enters the abdomen should be kept clean. Hence, cleaning should start there.
- Never pull on the umbilical stump. Let it fall off by itself.
- Position the diaper below the navel to prevent contamination of the stump by urine and feces. Let the stump air to prevent infections.
- Newborns can have daily baths without any special protection for the umbilical stump. The infant can be washed with water and neutral soap, following by a good drying.
- After the bath, dry the stump gently and follow the steps above.
- Cleaning of the umbilical stump should continue for at least 10 days after the cord has detached, since the tissue is still in the cicatrization phase. A small amount of occasional bleeding is normal.
- Do not use swaddling bands or any other article that impedes ventilation of the region. The use of substances such as foot powder, rope tobacco, chicken feathers, cobwebs, coffee grounds, ashes, and animal feces is to be strictly avoided because of the high risk of transmission of neonatal tetanus[134], known as the " seventh day disease".

Nasal hygiene

When the nostrils are obstructed, the passage of air becomes noisy, and difficult breathing can interfere with breast-feeding and sleep.

Guidance

- Inject 1 ml of physiological saline solution with a syringe in each nostril, before breast-feeding or whenever necessary.
- Make circular movements in the nostrils.

Observations

- Physiological saline solution, after opening, can be stored for 7 days in the refrigerator. Do not put chilled solution in the nose, but allow it to reach room temperature before use.
- The syringe, after use, can be washed with water and soap and used for 7 days.

Hygiene after bowel movements

Guidance

- Remove excess feces with the disposable diaper.
- Take the baby to water for a cleaning, removing all feces, or use a cloth diaper moistened with lukewarm water to clean, avoiding friction. When cleaning infant girls, it is important to wipe from the vagina toward the anus rather than the reverse (to prevent urinary infection).
- Dry thoroughly and put on a clean diaper. Use cornstarch but avoid talcum powders, which can cause allergies.

Observations

- Avoid the use of premoistened wipes, which can cause allergic reactions in the child.
- It may sometimes happen that the baby urinates or defecates while the diaper is being changed. In this case the mother should allow the baby to finish and should not react negatively. A negative reaction can frighten, inhibit, and even traumatize the baby.
- In boys: Lift the skin from the end of the penis gently and clean with a circular motion. Do not use force that can bruise the region.
- In girls: gently separate the labia majora to remove waste from feces and urine that has accumulated; always clean from front to back.

Bath

- Choose a location for the bath without drafts, during the warmest part of the day.
- Have all necessary items ready in advance and close at hand: towel, soap, clothes, diaper, blanket.
- Bathe daily or more than once a day, if necessary (if the newborn is restless, crying, hot, feverish...).
- Do not use alcohol in bath water; it dries the skin and irritates the mucous membranes.
- Do not use lotions, perfumes, talcum powder, or ointments.
- Dry skinfolds thoroughly.
- Use appropriate clothing for the temperature. Do not restrict the arms or legs, since babies like and need to move.
- The baby may feel insecure and cry. Talk to the infant, since the bath is a moment of interaction between mother and child and should be pleasant for both.

Procedure

- Put the water in the bathtub, testing the temperature with the forearm.
- If the infant has urinated or defecated, clean the child before the bath.
- Place the infant in the bathtub and begin washing, moving from the head to the feet.
- First wash the face, using only water. Wash the area of the eyes gently (from the inner corner to the outer corner), and dry with a towel.
- Using the middle fingers and thumb of your hand, cover the infant's ears, and with the other hand moisten the head, washing it with shampoo or soap. Rinse and dry.

- Place the baby gently in the bathtub, always holding the child.
- Rotate the baby and support it with your arm while you wash its back.
- For the **female genital area**, cleaning should be from the vagina toward the anus.

Washing of clothes

Guidance

- Wash the infant's clothes separately, rather than together with adult clothing.
- Use coconut oil soap or other neutral soap with less acid; do not use bleaches, powdered soaps, softeners with perfume, or bleach solutions (these products have chemicals that contact the baby's skin, causing allergies).
- After washing, rinse thoroughly so that there is no residue from the cleaning agent on the fabric.
- Hang to dry in the sun (if possible) and iron (to eliminate microorganisms).

Dermatitis or rash

These are skin irritations caused by prolonged contact with urine and feces. To avoid them, the diaper should be changed as often as needed. It is important to clean the baby with water and neutral soap after bowel movements, and to keep the diaper region dry.

Guidance

- Change diaper frequently.
- Wash the region with neutral soap.
- Keep the skin clean and dry, especially in folds and grooves.
- After washing, dry the area well and powder with dry cornstarch in the affected region.
- Leave the site exposed to the sun, in a daily sunbath.
- Evaluate with the physician the need for other products. Do not use any product without medical advice.
- If using cloth diapers, wash well with neutral soap, and rinse several times.
- Avoid: rubbing the skin during cleaning, using premoistened wipes, and using soap powder and softeners.

Precautions in administration of pumped breast milk, milk formula, and drugs by gastric tube, enteral tube, or gastrostomy

In clinical situations where the child has difficulty nursing or some physical limitation that contraindicates oral feeding, breast milk or formula can be supplied through a gastric tube, an enteral tube, or a gastrostomy. In this case, the mother and/or caretaker should receive the guidance below at the time of hospital discharge.

Administration of milk by gastric tube, enteral tube, or gastrostomy:

- prepare the volume of pumped breast milk or milk formula prescribed by the physician;
- put milk in the feeding container;
- connect the administration set to the container, with a closed tab;
- open the tab and replace the air in the administration set with milk, closing the tab so as not to let milk escape;
- connect the end of the administration set to the tube;
- open the tab and let the milk drip until it is finished;
- close the tab and disconnect the administration set;
- close the tube.

Observations

- Allow the proper interval of time between feedings.
- Take care that milk does not flow too fast

Washing the container and the administration set

- Wash with water and soap;
- rinse well;
- flush with hot water and allow to dry, then put in a covered container until the next feeding.
- ***THE CONTAINER IS GOOD FOR 5 DAYS***
- ***THE ADMINISTRATION SET IS GOOD FOR 3 DAYS***

Preparation of artificial milk

Guidance

- Wash hands.
- Boil filtered water (after it begins to boil, wait 15 minutes), and then allow to cool to room temperature.
- Use the quantity of water corresponding to the quantity of feed desired; for every 30 ml of water add one level measure of milk powder.
- Shake the feeding bottle until the powder is totally dissolved.
- Milk should be prepared at the time of each feeding.

Medication

Put drops of medication in the syringe connected to the tube and give medication according to the instructions received before discharge.

Observations

- Change the tube attachment after a bath or when it comes loose from the skin.
- If the tube comes out, do not replace it at home. Wash the tube and take it with the baby to the nearest health center.
- Follow up with outpatients on return visits, based on the guidance given before discharge.

Environmental precautions

Cleaning in the unit

The literature has demonstrated that the hospital environment is an indirect source of infection. Surfaces, particularly around the bed, help to transmit epidemiologically important microorganisms such as vancomycin-resistant enterococcus, oxacillin-resistant *S. aureus*, carbapenem-resistant enterobacteriaceae, and viruses [135, 136]. However, the degree to which such contamination contributes to the development of infections is still being debated [136]. The following factors favor environmental contamination [137]:

- moist or wet surfaces, which facilitate the proliferation of gram-negative bacteria and fungi and the formation of biofilms;
- dusty surfaces, which facilitate the proliferation of gram-positive bacteria and mycobacteria;
- loss of integrity of surface coatings;
- failure to immediately remove organic matter;
- improper cleaning techniques;
- incorrect use of disinfectant.

Surfaces, including walls, ceiling, floor, furniture, medical equipment, and other articles in the health services should be cleaned regularly to provide a suitable environment and prevent potentially contaminated objects from acting as sources of HAI [137].

The presence of body fluids, secretions, dust, and moisture favor dissemination and proliferation of bacteria. The unit should undergo rigorous cleaning, using correct techniques.

Cleaning is the removal of dirt from an article or surface, reducing its microbial load. Disinfection is the process applied to an article or surface to eliminate microorganisms, except for spores[135,138]. Methods for disinfection of the environment are usually chemical [139]. The disinfectants most often used are chlorinated solutions and alcohol. Products based on quaternary ammonium may also be used [138, 140].

Criteria for selection of a disinfectant

There is no ideal disinfectant; the one selected should meet the greatest number of requirements for the desired purpose. A good disinfectant is one that, in the same concentration and over the same period, eliminates bacteria, virus, fungi, protozoa, and parasites. Ideally, a disinfectant should [135]:

- be germicidal;
- be low-cost and economical (good cost-benefit ratio);
- be nontoxic to humans and animals, not irritating the skin and mucous membranes;
- be stable in contact with organic matter, pH, or light;
- be soluble in water;
- not add odor to objects;
- have lasting effectiveness;
- be easy to apply;
- have penetrating power and rapid action;
- not be corrosive;
- be biodegradable.

Effectiveness of disinfectants

The effectiveness of chemical disinfectants depends on several factors, such as [138]:

- concentration or dilution of the product: Follow the manufacturer's recommendations on how to apply and the quantity to use;
- time of action or exposure: Follow the manufacturer's recommendations;
- temperature: High temperature accelerates the process of disinfection, but it is also necessary to follow the manufacturer's recommendations on the need for heating of water and activation of the product;
- presence of organic matter: Most disinfectants become inactive or display reduced activity in the presence of organic matter. Prior removal of dirt improves their effectiveness;
- material to be disinfected: The more porous the material, the less effective the disinfectant;
- sensitivity and quantity of microorganisms present in the material or environment to be disinfected;
- users' level of health education.

Quaternary ammonium solution

Different formulations of quaternary ammonium are called "generations". The fifth generation of quaternary ammonium offers the most effective compounds developed to date. The latest generation is the seventh; it is a low-level disinfectant and is only indicated for surface disinfection[141].

Advantages: low toxicity.

Disadvantages: gauze and cotton fibers can affect its action, and it is not a strong disinfectant.

Products based on quaternary ammonium are indicated for cleaning and disinfection of the environment, furniture, and equipment close to the patient, since they do not damage materials such as respirator screens, cardiac monitor screens, and acrylics [140]. Compatibility of equipment with cleaning products should always be verified with the equipment manufacturer. Use of quaternary ammonium products is currently contraindicated for disinfection of medical instruments or articles, synthetic rubbers, cement, and aluminum [140]. Do not use a disinfectant that contains alcohol, abrasives, or sodium hypochlorite on acrylic and polyurethane parts so as not to damage the material. Adequate personal protective equipment should be used due to the risk of skin irritation.

Given the role of the hospital environment in the spread of microorganisms, it is essential to establish cleaning routines in the health services that give special attention to the space around beds, including equipment and stands [137,139]. Health services must have routine procedures in written form, validated by the ICC, specifying the team responsible for each task, the frequency of cleaning, the products to be used, and the cleaning techniques. In addition to having written procedures, it is essential to train the team and supervise their performance [137].

The following recommendations––on cleaning the environment, equipment, and materials, as well as the required frequency––should be adapted to local needs based on the epidemiological situation.

Cleaning the environment [139, 140]

- Floor and walls should be cleaned with water and soap. Walls should be cleaned at least once a week, or more frequently if needed.
- Sodium hypochlorite at 1% should be used on surfaces (floor, walls) for disinfection of areas with spilled blood or secretions. Another option is organic chlorine. Blood or organic matter should be removed with absorbent tissues or cloth before the application of chlorine to the surface.
- Sodium hypochlorite at 0.1% can be used on surfaces (floor and walls) during outbreaks or when a large number of patients are in isolation.
- Surfaces around the bed (e.g. stands and tables) should be cleaned three times a day or according to the guidance from the hospital ICC, using water, soap, and alcohol at 70% or quaternary ammonium.

Incubators and cribs

These should be cleaned daily with water and liquid soap, without disinfectant if occupied by a newborn [141].

Terminal cleaning should be done with disinfectant after a hospital discharge, transfer, or death of a newborn, or weekly in case of the incubator for a newborn who remains in the hospital. Terminal cleaning of this equipment should be done at an appropriate site, reserved for this purpose, according to the following recommendations:

- before beginning the cleaning, remove all removable parts of the incubator (mattress, tray, rubber plug, metallic shafts and tubes, etc.).
- evaluate the condition of the air filter, changing it when required according to the manufacturer's instructions. For the filter and oxygen cell, follow the maintenance recommendations from the manufacturer.
- follow the manufacturer's recommendations on disinfection or sterilization of the water reservoir.
- regularly confirm the integrity of the mattress in an incubator or a heated crib.

Incubators or heated cribs should always be changed between patients. Likewise, the incubator should be changed when there is visible dirtiness or every seven days when clinical conditions permit [50]. It should be stressed that the routine weekly changing of incubators for the same patient, despite being a frequent practice, is not validated by studies. Therefore, routine changes for the same patient should be preceded by risk-benefit assessment, especially in unstable newborns.

Articles for common use

Medical articles such as stethoscopes, thermometers, and non-invasive blood pressure cuffs should be reserved for individual use. When individual use is not possible, disinfect the article between patients [141]. Even in the case of individual use, maintain a daily disinfection routine (at least once every morning, afternoon, and night).

Bathtubs used for bathing clinically stable newborns should be cleaned before and after the procedure [50], using water and soap, followed by disinfection with alcohol at 70% or another disinfectant recommended by the bathtub manufacturer and validated by the local ICC.

Toys should also have a well-defined routine for cleaning and disinfection. Give preference to toys that can be cleaned with water and soap, followed by disinfection with alcohol at 70% or another compatible product. Do not use toys that can accumulate water inside. Avoid leaving toys in incubators, especially for newborns with invasive devices [50].

Articles for individual use

Pacifiers

Physicians sometimes prescribe the use of pacifiers to calm newborns or as a stimulus for nursing in newborns receiving enteral feeding with a gastric tube. When a pacifier is indicated, it should be for individual use and should be changed every 24 hours, or more often

if necessary. When the pacifier is not being used, it should be kept in a sterilized covered container in the incubator drawer or crib cabinet. Avoid leaving it with the newborn, due to the increased risk of proliferation of bacteria and fungi [50].

Pacifiers belonging to the hospital should receive cleaning and high-level disinfection or sterilization in an autoclave.

Feeding bottles, nipples, and cups for milk

Like pacifiers, feeding bottles, nipples, and cups should be for individual use, with cleaning and disinfection or sterilization after use [50].

Other materials

Materials for ventilation assistance are classified as critical when they contact lesions in mucous membranes, or semi-critical when the contact is with intact mucous membranes or body fluids. These materials therefore need sterilization and high-level disinfection, respectively, depending on their use. For heat-sensitive items, there is the option of sterilization at low temperature, as with ethylene oxide, or chemical sterilization with disinfectant products. Disinfection can be carried out with thermal disinfection or with chemical products such as sodium hypochlorite.

It is important to emphasize that the use of chemical agents for sterilization or disinfection should strictly follow the manufacturer's recommendations regarding dilution and how long the product remains active for the desired purpose.

Table 8: Recommendations for cleaning and disinfection of articles for common and individual use in neonatology [141].

Article	Use		Frequency of cleaning or exchange	Process for cleaning/ disinfection/sterilization
Incubators and cribs	Individual	Concurrent cleaning	Daily	Daily with water and liquid soap; do not use disinfectant with the newborn in the incubator or crib
		Terminal cleaning	Between patients Same patient: visible dirtiness or every 7 days (see paragraph above)	Solution based on quaternary ammonium or another disinfectant recommended by the manufacturer and validated by the ICC
Stethoscopes	Individual or common		Before and after use	Disinfection with alcohol at 70%
Thermometers	Individual or common		Before and after use	Disinfection with alcohol at 70%
Bathtubs	Individual or common		Before and after use	Water and soap followed by disinfection with alcohol at 70%
Non-invasive pressure sleeves	Individual or common		Visible dirtiness or every 7 days	Wash with water and soap
Toys	Individual or common		Visible dirtiness or every 7 days	Water and soap followed by disinfection with alcohol at 70%
Pacifiers	Individual		Between patients or same patient every 24 hours	Cleaning and high-level disinfection or sterilization in an autoclave
Feeding bottles, nipples, and cups for milk	Individual		At each use	Cleaning and high-level disinfection or sterilization in an autoclave

In neonatology units, in addition to the concern for cleaning of the environment and equipment, steps should be taken to reduce noises and bright lights. In addition, individualized care, with minimum handling, allows newborns to rest when clinical conditions permit. Accordingly, attention should be paid to the architecture of the unit, including selection of the raw materials to be used in its construction, as well as equipment and furniture. The top priority is to work on improving the team's performance in order to create an environment conducive to the well-being of newborns, parents, family members, and the health team itself [140]. Such improvements in the neonatal unit reduce stress for newborns and for health professionals, with an impact on the quality of care provided and the quality of work life.

Flowers or plants are not recommended for decoration of the neonatal unit. Washable decorative strips or wall paints are an option for decoration [139].

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