Paediatric Infectious Diarrhoea in resource limited setting

MINGHA AFRICA ONLUS

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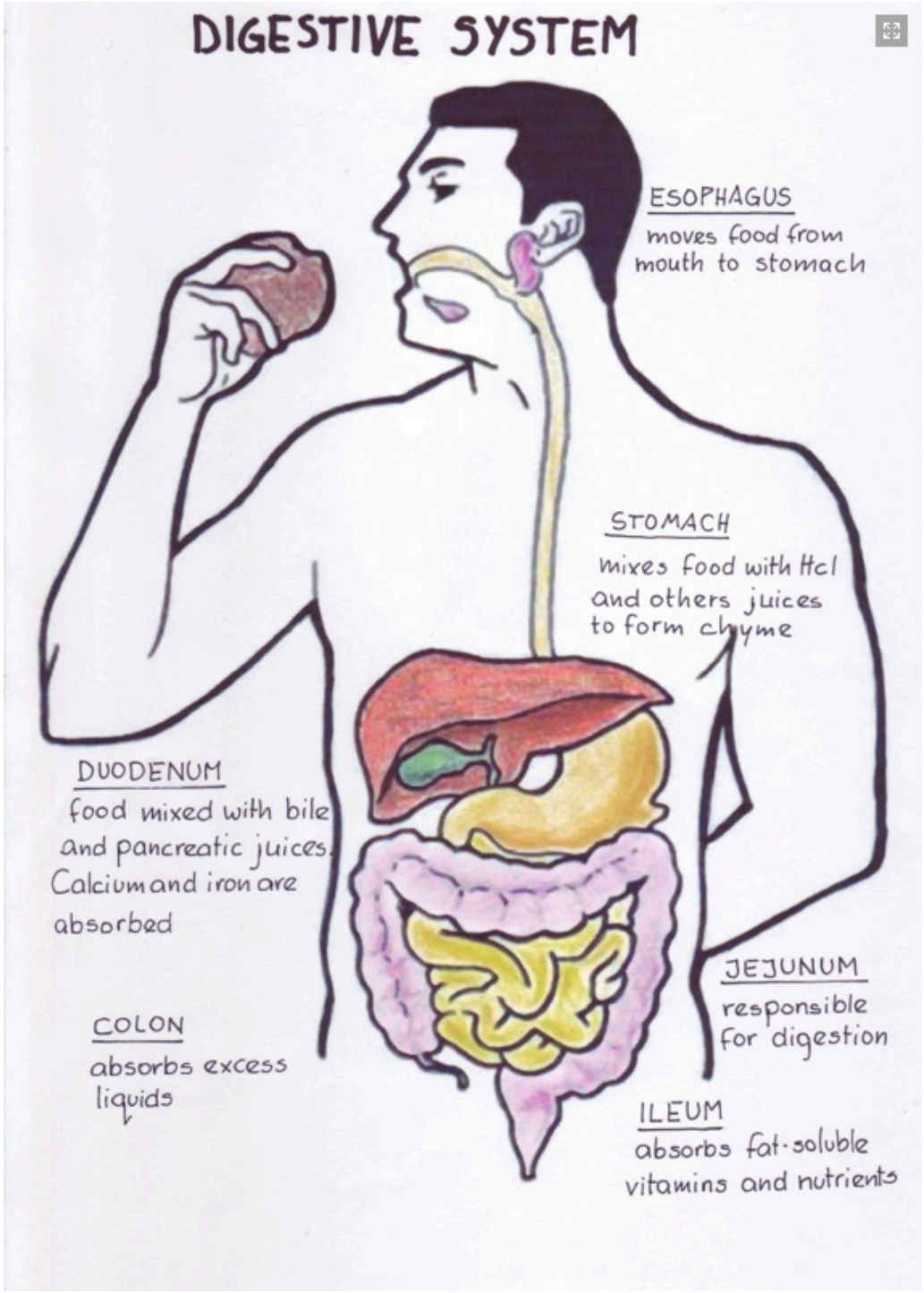

DIGESTIVE SYSTEM
ESOPHAGUS
moves food from mouth to stomach
STOMACH
mixes food with Hcl and others juices to form chyme
DUODENUM
food mixed with bile and pancreatic juices. Calcium and iron are absorbed
JEJUNUM
responsible for digestion
COLON
absorbs excess liquids
ILEUM
absorbs fat-soluble vitamins and nutrients

Classification (1)

On the basis of clinical and epidemiologic parameters, episodes of diarrhea are classified into three categories

-**Acute diarrhea** is defined as the presence of three or more loose, watery stools within a 24-hour period.

- **Dysentery**, often termed bloody diarrhea, indicates the presence of visible blood and mucous in diarrheal stools.

- **Persistent diarrhea** is defined as episodes lasting more than 14 days

Classification (2)

The diarrhea can be also distinguished as:

- **watery**: due to etiologic agent not able to cause enterocyte damage, but to act producing some toxins able to induce cellular hypersecretion of fluids in the intestinal lumen

- **inflammatory**: due to etiologic agent able to penetrate the intestinal mucosa or producing citotoxic agents; in these cases the stools contain also mucous, leukocytes, sometimes red blood cells

- **dysenteric**: due to causative agent able to induce mucosal intestinal damage; in these cases the stool contain always mucous and red blood cells

Etiology

Diarrhea is caused by a mix of bacterial, viral, and parasitic pathogens.

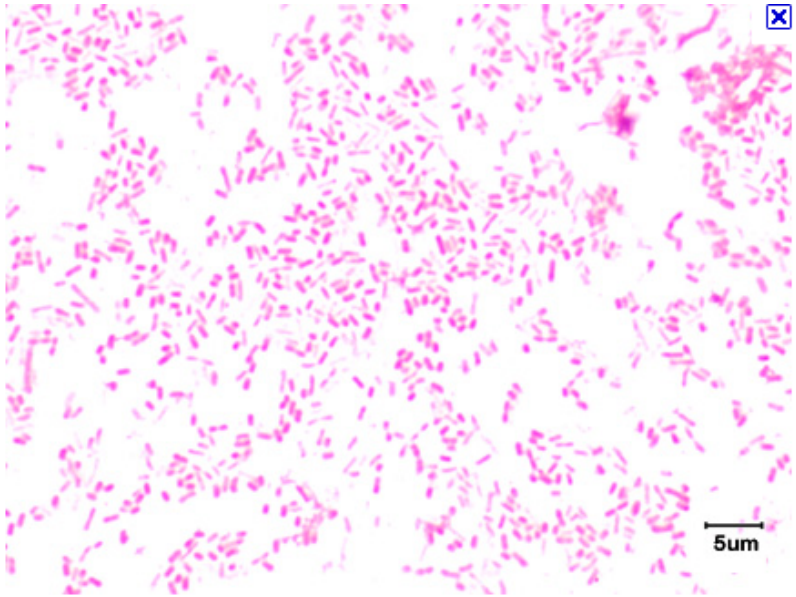
In developing countries with poor hygiene and sanitation, enteric bacteria and parasites are more prevalent, and these agents typically peak during the “summer months or dry seasons”.

Most prevalent infectious agents responsible of diarrhea

Agents	%
Rotavirus	20%
E. Coli	11%
Campylobacter	7%
Shigella	5%

Worth noting is that certain enteric pathogens cause mild or asymptomatic infections and that the duration of asymptomatic carriage, particularly in young children, may be prolonged.

Escherichia Coli



Escherichia coli (Gram neg) colonizes the infant gastrointestinal tract within hours of birth.

Although most E. coli strains are harmless or even beneficial to their human hosts, several highly adapted clones are capable of causing diarrheal disease.

Escherichia Coli

Five classes of diarrheagenic E. coli have been defined, but only specialized diagnostic tests can distinguish the pathogenic strains from normal flora.

✓ **Enterotoxigenic E. coli (ETEC)** strains are a frequent cause of acute **secretory diarrhea** among children

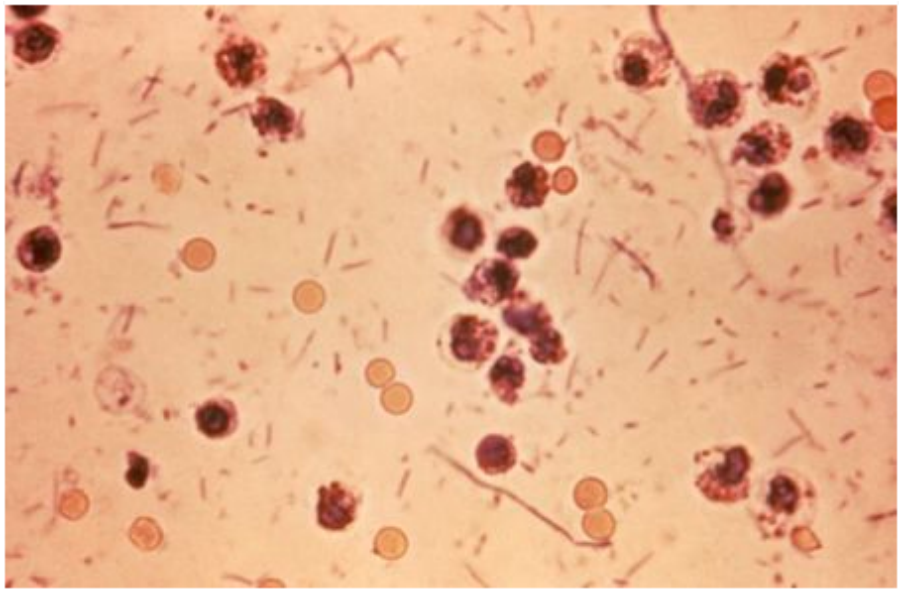
✓ **Enteropathogenic E. coli (EPEC)** strains cause acute (not only) **secretory diarrhea**, predominantly in children <2 years old (especially if < 6 months old)

✓ **Enteroinvasive E. coli (EIEC)** strains cause **bloody mucoid diarrhea**. Watery diarrhea also is seen, and fever is a common finding.

✓ **Enterohemorrhagic E. coli (EHEC)** strains also cause **bloody diarrhea**, and severe hemorrhagic colitis and the hemolytic uremic syndrome are seen in 6-8% of infections.

✓ **Enteroaggregative E. coli (EAggEC)** the mechanism by which they act remains poorly understood. They are associated with **watery diarrhea** in young children have been reported as a cause of persistent diarrhea in HIV-children

Shigella



Shigella is estimated to cause more than 160 million **dysenteric diarrhea** annually in developing countries, primarily in children.

Shigella infections are relatively more common findings in toddlers and older children than in infants.

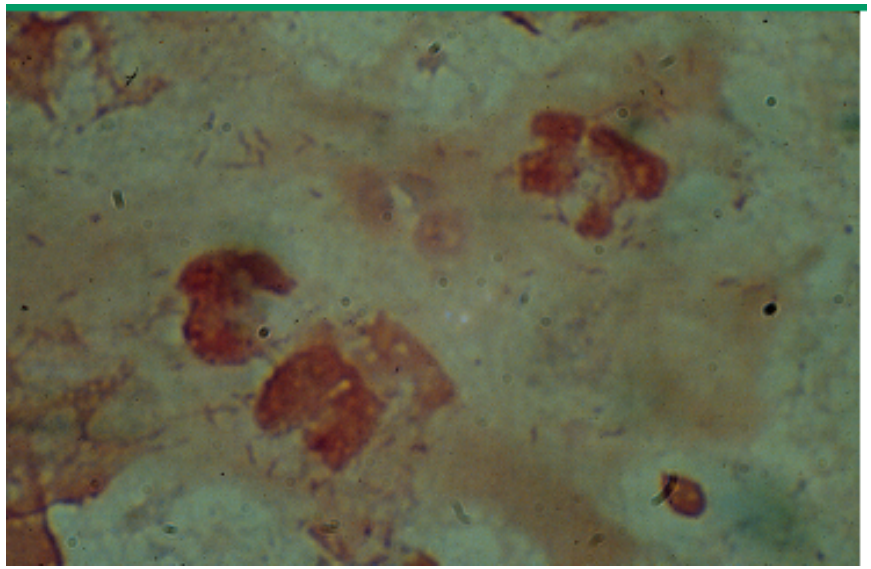
There is four recognized subgroups of **Shigella**

- *S. flexneri*, which is more likely to cause dysenteric symptoms and more persistent illness, is the most common subgroup in developing countries, with S. sonnei being the next most common.

- ***S. sonnei*** is the subgroup that causes the mildest illness and is seen most commonly in developed countries.

- The other two subgroups (***Shigella boydii*** and ***Shigella dysenteriae***) comprise < 5% of isolates in most studies but are noteworthy for their association with more severe disease. In particular, S. dysenteriae type 1 (Sd1), which produces the same Shiga-toxin as does EHEC, has caused devastating epidemics of bloody diarrhea, with reported case-fatality rates approaching 10 percent in Asia, Africa, and Central America.

Campylobacter



Gram stain of stool (x1000) can, in some cases, show Campylobacter jejuni, which are small, faint Gram negative curved rods which may be gull-winged in shape. This finding may provide presumptive evidence of Campylobacter infection prior to the results of stool culture.

Campylobacter is one of the most frequently isolated bacteria (Gram neg) from the stools of infants and children in developing countries. It is associated with **watery diarrhea and on occasion dysentery**, with peak isolation rates found in children 2 years of age and younger.

Poultry is an important source of Campylobacter infections in developed countries, and the presence of an animal in the cooking area is a risk factor for acquiring campylobacteriosis in developing countries.

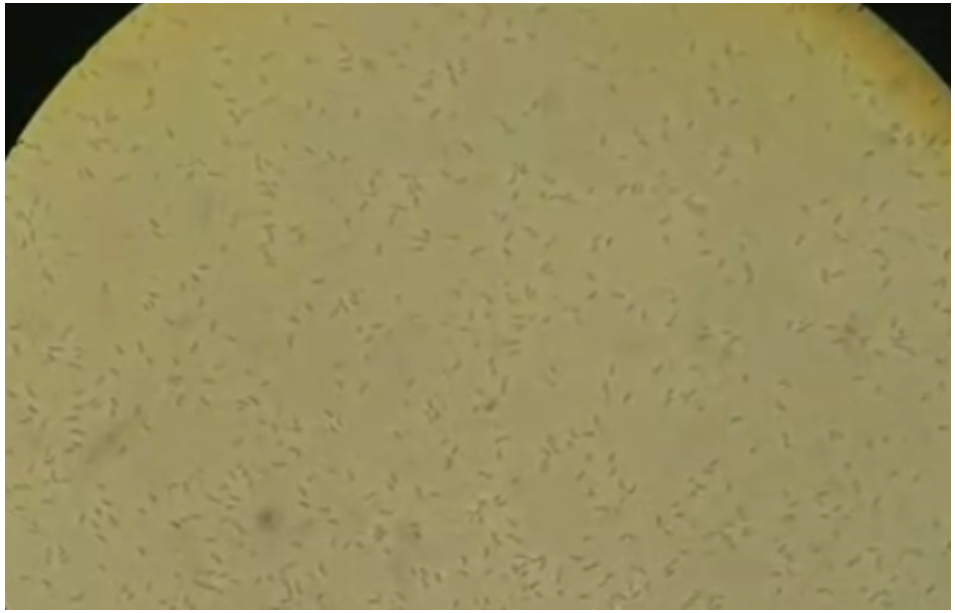
Guillain-Barré syndrome, an autoimmune disorder of the peripheral nervous system that can lead to complete paralysis, is a rare complication of infection with Campylobacter.

Vibrio Cholerae

Many species of Vibrio cause diarrhea in developing countries, but the causes of epidemic cholera, ***V. cholerae*** serogroups O1 and O139, are of special importance.

No illness produces depletion of volume as rapidly and as severely as does cholera; in the absence of prompt and adequate rehydration, hypovolemic shock and death can occur within 12 to 18 hours after onset of the first symptom.

Stools are watery, colorless, and flecked with mucus. Vomiting is a common finding, but fever is a rare event.



Life-threatening electrolyte imbalances must be avoided by using appropriate solutions for rehydration. Children with cholera are especially prone to the development of hypoglycemia, which can lead to convulsions and death.

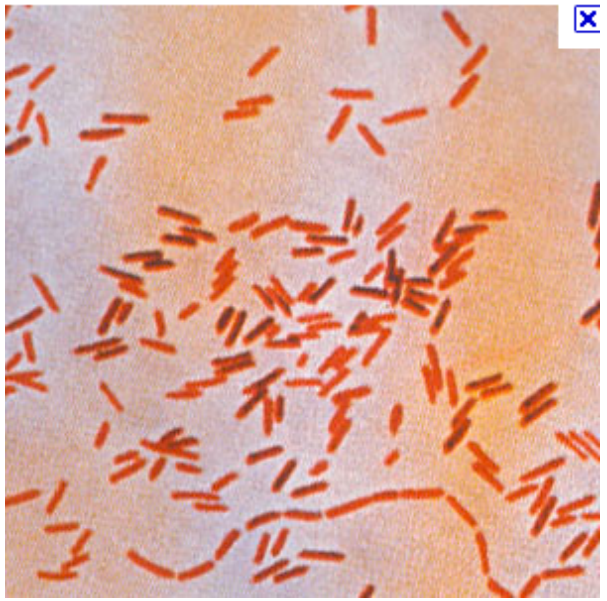
Because of the potential for epidemic spread, confirmed or suspected cases of cholera (including severe dehydrating diarrheal illness in patients < 5 years) should be reported promptly to public health authorities.

Salmonella

More than 2000 serotypes of Salmonella (Gram neg) exist, all of which are pathogenic for humans.

Infants and the elderly appear to be at greatest risk, but all age groups are susceptible to salmonellosis.

Animals are the major reservoir for Salmonellae, and different serotypes predominate among reptiles, fowl, and mammals.



The acute onset of nausea, vomiting, and diarrhea that may be watery with mucous characterize most cases of Salmonella gastroenteritis.

Fever occurs in approximately 70% of affected children.

Bacteremia occurs in 1 to 5% of patients, most frequently in infants.

Enteric fever (21 million cases/year with 600,000 deaths/year), which classically is associated with Salmonella serotype Typhi (typhoid fever) or serotype Paratyphi A, B, or C, also is seen rarely with non-Typhi serotypes.

The only reservoir for S. typhi is the infected human.

Typhoid fever is identified most frequently among school-age children but also presents in a milder form in children 2 years of age and younger.

In children, the disease not uncommonly presents with diarrhea, with or without blood, but it is characterized by fever lasting 3 or more weeks.

Complications of typhoid fever include intestinal hemorrhage and perforation, myocarditis, meningitis, pneumonia, and shock

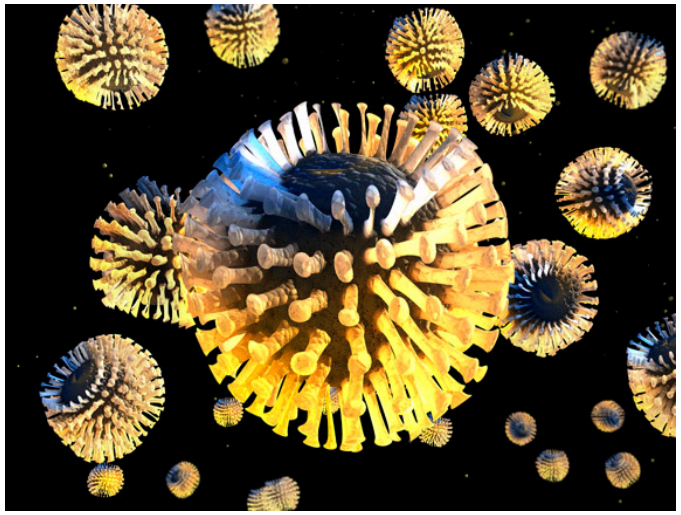
Rotavirus

Rotavirus is the leading cause of severe, dehydrating gastroenteritis among children, accounting for one-third of all hospitalizations for diarrhea and an estimated 500,000 deaths worldwide each year.

Nearly all children in both industrialized and developing countries are infected with rotavirus by the time they are 3 to 5 years of age.

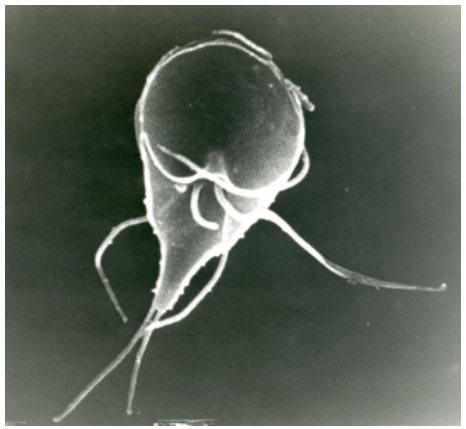
Neonatal infections are common occurrence but often are asymptomatic. The incidence of clinical illness peaks in children between 4 and 23 months of age.

Children often are infected with rotavirus multiple times, and each infection confers progressively greater immunity. Therefore, severe disease occurs most commonly in young children with first or second infections.

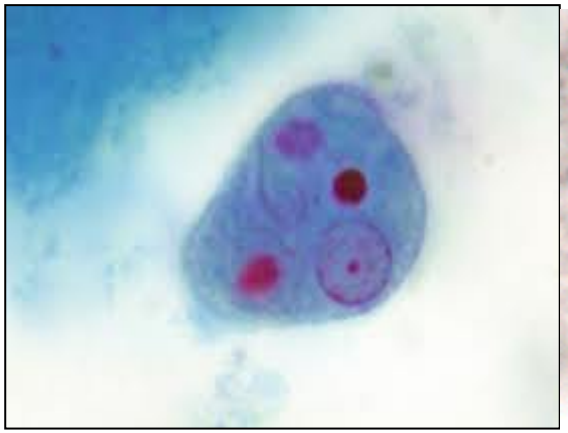


Parasites

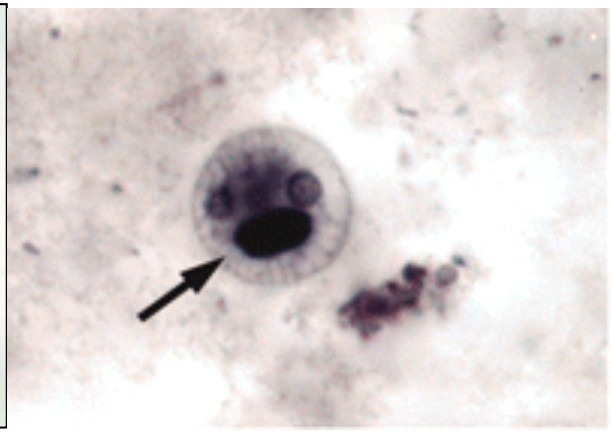
Parasitic agents accounting for a relatively small proportion of infectious diarrhoea cases. ***Giardia lamblia*** and ***Entamoeba histolytica*** are the parasites that most commonly cause acute diarrheal illness in children. The prevalence of G. lamblia can be as high as 20 to 30 percent in developing regions. All the seven existent species of *Entamoeba* living commensally in the human intestine with the exception of *E. histolytica* that is able (not all sub-species) to invade the intestinal tissues. The cyst of *Entamoeba* are the resistance form of the parasite.



Giardia lamblia



E. Histolytica
Trophozoite



E. Histolytica
Cyst

The reservoir are the infected humans

Transmission

✓ **Bacterial diarrhoea:**

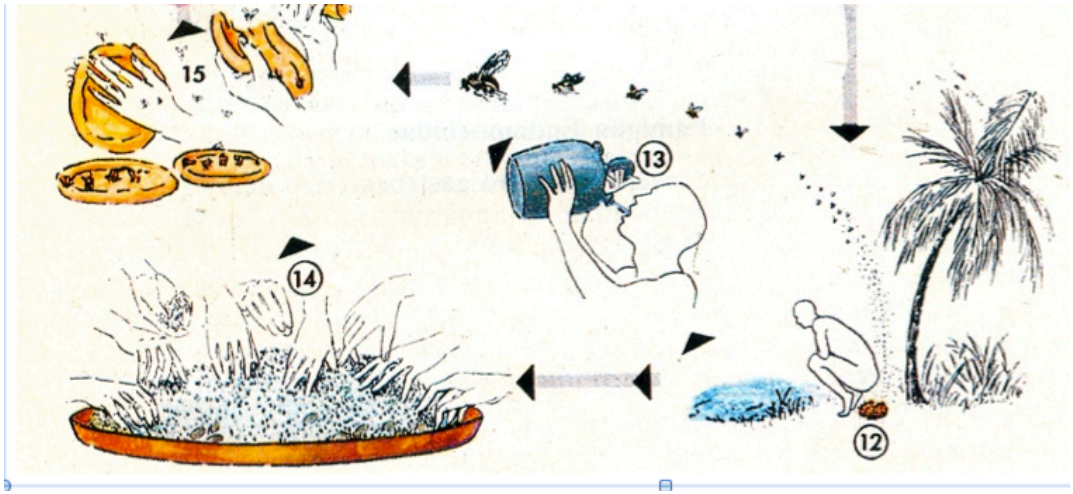
The transmission follow the oro-faecal way through direct inter-human transmission or contaminated food or drink

✓ **Viral diarrhoea**:

inter-human transmission through oro-faecal way

✓ **Parasitic diarrhoea**

The transmission follow oro-faecal way through direct inter-human mechanism or food or drink contaminated by human faeces (the man is the only reservoir of the infection). The contamination of the food can be mediated by flies.



Clinical aspects

Acute diarrhea usually manifests as an increase in the frequency or volume of stool.

Fever is a common occurrence and usually is associated with **invasive pathogens.**

Bloody stools are present in diarrhea caused by **invasive pathogens** and those that release cytotoxins; the presence of bloody stools in the absence of fecal leukocytes should raise the consideration of EHEC infection.

Most viral agents and bacteria that release enterotoxins usually do not cause bloody diarrhea.

Vomiting is observed more frequently in **viral diarrhea** and illness caused by ingestion of preformed bacterial toxins.

Despite these clues, determining the causative agent of diarrhea in an individual patient based on clinical grounds alone usually is difficult.

Clinical aspect of bacterial Diarrhea

Causative Agent	Mechanism of action	Incubation	Food	Fever	Vomit	Diarrhea
Salmonelle	Mucosal invasion (small and large intestin)	12-48 h	Cattle meat, poultry, eggs, milk, shellfish, vegetable	+	+	++ (inflammatory)
Shigelle	Mucosal invasion of colon and toxin production	6 h – 5 gg	Drinks and uncooked food Possible inter-human contagion	+/-	-	++ (dysenteric)
Vibrio cholerae O1	toxin production	1-5 gg	Water and uncooked food	-	+	+++ (watery)
Enteroinvasive *E. Coli* (EIEC)	Mucosal invasion of colon	10-18 h	Mostly interhuman contagion	+	-	++ (dysenteric)
Enterohemorragic *E. Coli* (EHEC)	Mucosal invasion of colon and toxin production	1-3 gg	Cattle meat	-	+	++ (dysenteric)
Enterotoxigenic *E. coli* (ETEC)	Adhesion and toxin production	10-72 h	Drinks and uncooked food	-	+	++ (watery)
enteropathogenic (EPEC) and Enteroaggregative (EAggEC) *E. coli*	Adhesion and probable toxin production	9-12 h	Mostly interhuman contagion	+	+	++ (watery)
Cl. Botulinum	Toxin production	18-36 h	Food conserve (vegetables, fruits, fish)	-	rare	rare
Campylobacter	Invasione mucosa	2-7 gg	Meat, poultry, milk	++	+/-	++ (inflammatory)
Yersinia enterocolica	Invasione mucosa, produzione di tossina	2-11 gg	Milk, meat, vegetables	++	++	+ (inflammatory)

Clinical aspects of viral gastroenteritis

The incubation period is 24-72 hours

The beginning of the disease is sudden with
- nausea,
- vomiting,
- diarrhoea,
- abdominal pain,
- sometimes moderate fever

The stool have a yellow-like colour without mucous or blood.

The diarrhoea stops generally in 2-4 days

The dehydration is the major enemy

Clinical aspects of Parasitic infections

***Giardia lamblia* infection**

The presence and the quality of symptomes depend from parasitic charge and duration of the infection. There is no fever.

The **acute *G. lamblia* infection** is often asymptomatic. If symptoms are present, they are:

- Diarrhoea
- Meteoric abdomen
- Anorexia (loss of appetite)
- Abdominal pain
- Nausea, sometimes vomit

The acute infection is not associated with immunisation of the patient

The **chronic and massive *G. lamblia* infection** can be accompanied by, especially in children, impairement of mental and physical development, malabsorbtion of lipids, lactose, vitamins A and B12

Clinical aspects of Parasitic infections

***E. histolytica* infection**

90% of cyst-carriers of *E. histolytica* are asymptomatic

The **acute *E. histolytica* infection** (incubation 2-6 weeks) is without fever and is characterized by:
- Bloody and inflammatory diarrhoea (5-15 episodes/day)
- Abdominal pain
- Asthenia
- Malaise

The acute infection is not associated with immunisation of the patient

Repeated *E. histolytica* infections can cause alteration of the physiological intestinal peristalsis secondary to the cicatrisations of the intestinal wall. It follows a chronic colitis post-amoebic with crisis of abdominal pain (followed by diarrhoeal episode), alternation of diarrhoeic stools or constipation, anorexia.

Complications (**hepatic abscess**, rarely cerebral or pulmonary abscess) with:
- Intermittent fever with chills
- Right hypocondral dolour and dolourability
- Nausea and vomit
- Diarrhoea (1/3 of the cases)
- rarely icters

Diagnosis

- Clinical history (beginning, symptoms, nutrition, hygiene, other sick familial members, etc.)

- Microscopic stool examination (direct exam that must be done quickly after the availability of the stool sample) helpful also for bacterial diarrhoea, but especially for parasitic infections

- Widal agglutination test (for excluding typhi or paratyphi serotype of salmonella)

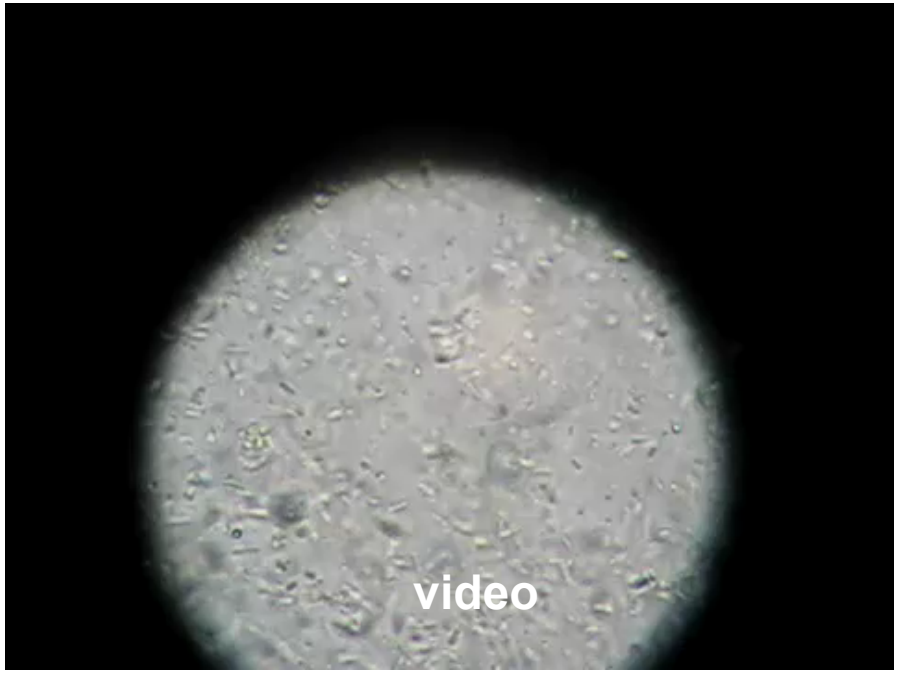
Antibody against Antigen O:
They are present in the acute phase of the disease and they remain for few months

Antibody against Antigen H:
They can remain also for years after the disease

Diagnosis

Microscopic stool exam:

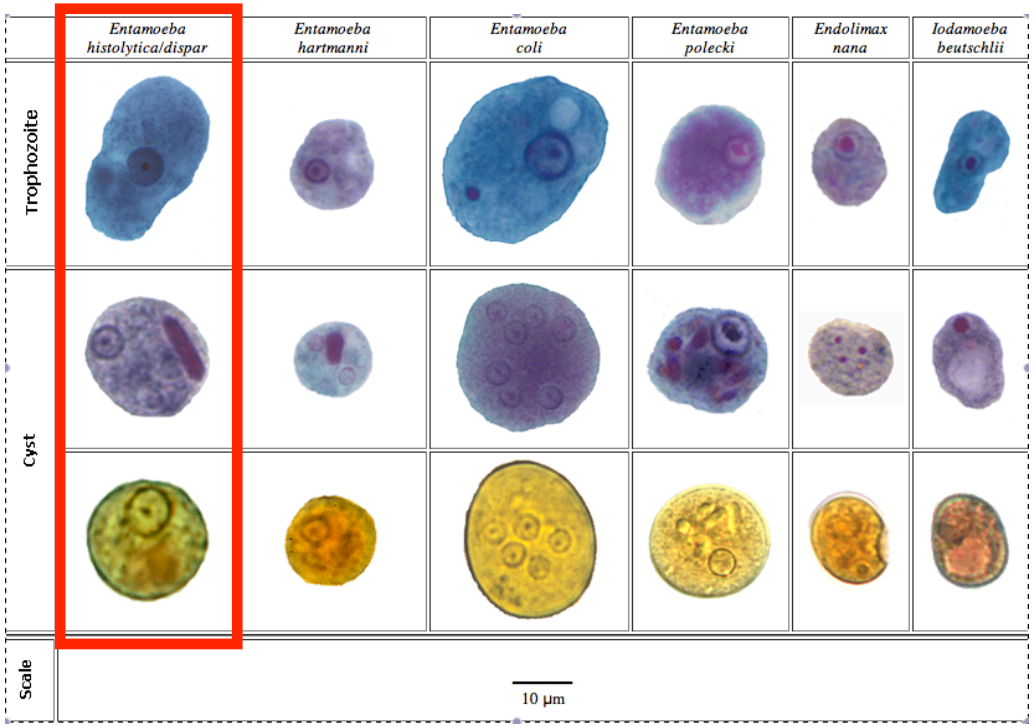
Giardia lamblia



Diagnosis

Microscopic stool exam: *Entamoeba*

Stool exam (direct examination with Lugol's colouration)



E. histolytica cysts are found generally in formed stools, instead trophozoite are founded usually in diarrhoeic stools

Management

Effective prevention of mortality and management of morbidity associated with diarrheal illnesses among children is dependent on making a timely and accurate assessment of the **status of hydration**, followed by promptly instituting **appropriate treatment**.

All children presenting with acute diarrhoea should be evaluated promptly for features of dehydration to ascertain information about the severity of illness and the need for rapid initiation of therapy

Indicator	Normal/No Dehydration	Some Dehydration (≥2 of these signs)	Severe Dehydration (≥2 of these signs)
Sensorium	Normal	Restless or irritable	Abnormally sleepy or lethargic
Sunken eyes*	No	Yes	Yes
Drinking	Normal	Drinks eagerly	Drinking poorly or not at all
Skin pinch†	Normal (immediate)	Slowly (<2 seconds)	Very Slowly (>2 seconds)

*Assessment of sunken eyes should be done both objectively and by asking the mother/ caregiver, as she is more familiar with the child.
†Skin should be pinched longitudinally (eg, thoracoinguinal direction) between the thumb and forefinger, held for 1 to 2 seconds, then released by opening the finger and thumb.

Rehydration Therapy

Severe dehydration is a medical emergency, and intravenous rehydration therapy should be instituted immediately.

Lactated ringer solution, normal saline, or a similar solution should be administered at a **rate of 30 mL/kg of body weight for 1st hour** (after 70 ml/kg in 3-5 hours) until pulse, perfusion, and mental status return to normal. As soon as the child's condition is stable and the mental status is normal, therapy can be changed to the oral route.

For children with mild to **moderate dehydration**, oral rehydration therapy (**ORT**) should be initiated with ORS, administered at a rate of **75 mL/kg of body weight per hour** over a period of 4 hours. ORS contains a mixture of glucose, sodium, potassium, and chloride in a bicarbonate base.

For children who are unable to tolerate ORS through the oral route, nasogastric (NG) feeding can be used to administer ORS. NG feeding is particularly beneficial in patients who have persistent vomiting with oral administration

ACUTE PHASE - REHYDRATION

Initial 4-6 hours

Dehydration Status†	None	Some	Severe
Hydrating Solution	ORS	ORS	Ringer's Lactate
Rate of Administration			
≤10 kg (~ age ≤1 yr)	See maintenance	75 ml/kg/hr X 4 hrs. (total 200-600 ml)	30 ml/kg 1st hour, 70 ml/kg next 5 hours
>10 kg (~ages 2-4)	See maintenance	75 ml/kg/hr X 4 hrs. (total 600-900 ml)	30 ml/kg 1st 30 min., 70 ml/kg next 2.5 hours
Mode of Administration	Oral	Oral	Intravenous (IV)

After fluid replacement

MAINTENANCE PHASE – REPLACEMENT OF LOSSES

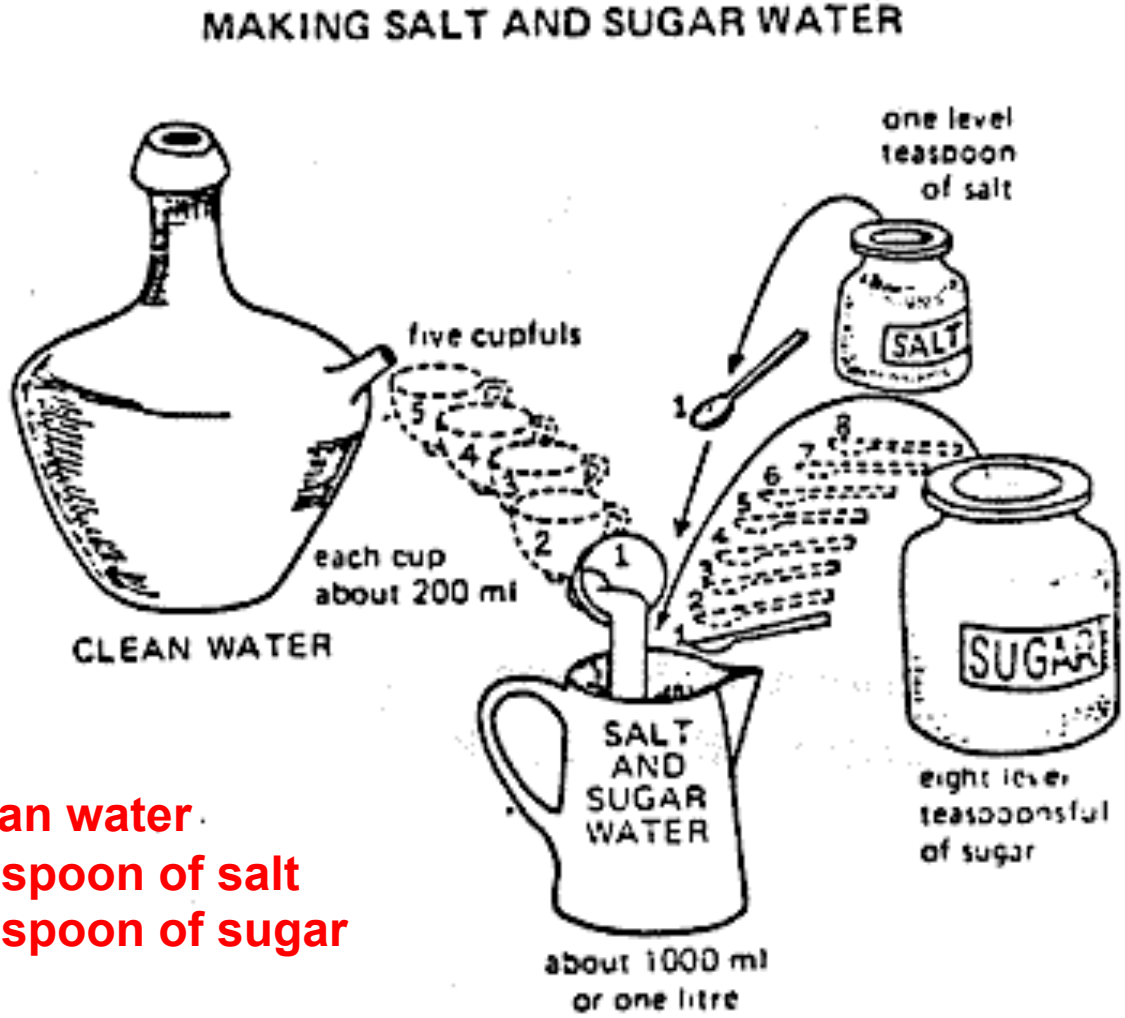
Until diarrhea stops

Hydrating Solution	----------ORS-
Rate of Administration	
<2 years of age	----------50-100 ml/loose stool----------
≥2 years of age	----------100-200 ml/loose stool----------
Nutrition‡	
Infants	----------Continue breastfeeding----------
≥ 6 months	----------Age-appropriate diet ad libitum----------

To be taken orally-
Infants - over a 24 hour period
Children - over an 8 to 24 hour period, according to age or as otherwise directed under medical supervision.

Oral Rehydration Salt

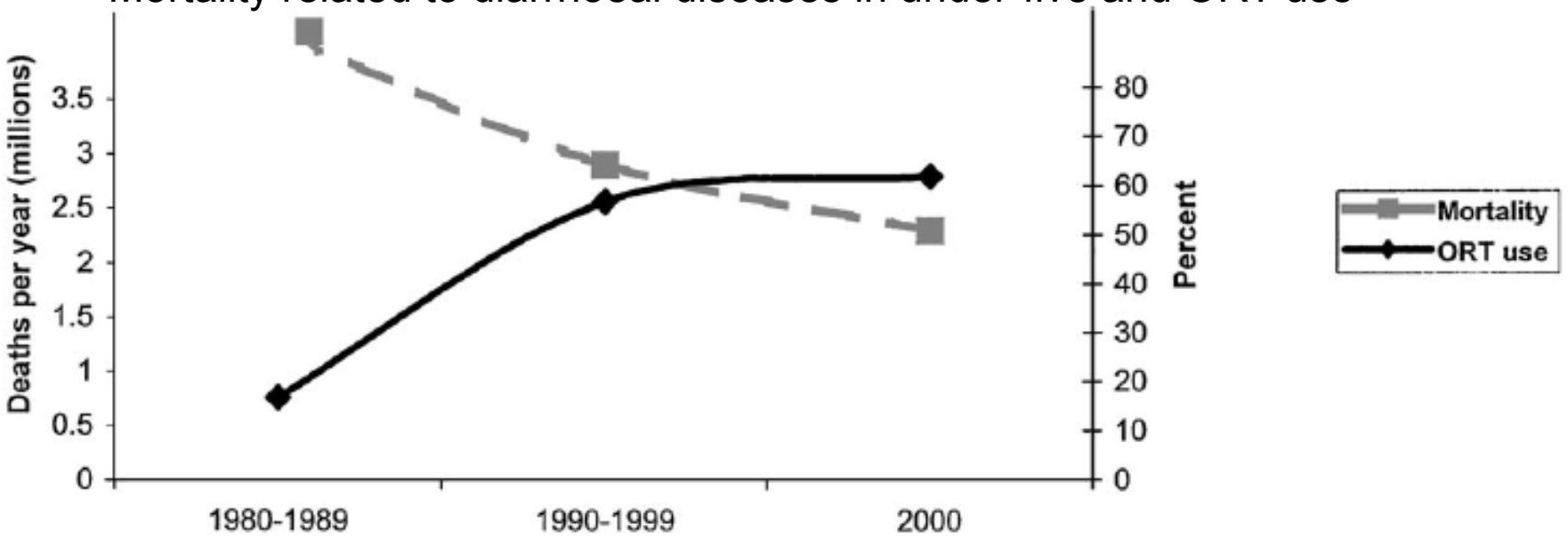
Home-made ORS



1 liter of clean water
+ 1 level teaspoon of salt
+ 8 level teaspoon of sugar

Both the incidence and risk of mortality from diarrheal diseases are greatest among children younger than 1 year of age, and thereafter rates decline incrementally

Mortality related to diarrhoeal diseases in under-five and ORT use



Although the rate of mortality from diarrhea has declined substantially, morbidity from diarrhea has remained relatively constant during the past two decades, with each child under 5 years of age experiencing an average of three episodes (range: 2.8 to 6.3) annually

Dietary Therapy

Age-appropriate intake of nutrients, including breastfeeding for infants and nutrient-dense solid food intake for children, should be maintained.

The importance of sufficient caloric intake should be emphasized to offset weight loss from illness and as a fundamental facilitator for proper growth and development.

Efforts should be made to educate the mother or caregiver on early recognition of dehydration, appropriate ORS and therapy, and energy intake.

Exclusive breastfeeding should be recommended for infants younger than 6 months old, and identification of locally available foods that will support nutrient and caloric needs of older children may be useful.

Antimicrobial therapy

Antimicrobial agents usually are not recommended for the routine treatment of acute diarrheal illness

Possible causative agent	Antimirobial	Duration
Cholera	TMP/SMX (Bactrim) 4-6 mg/kg of TMP every 12 h Doxycicline (only for > 8 ys old) 1-2 mg/kg every 6h	3-5 days
Shigella, E. coli	Ciprofloxacin 10-15 mg/kg every 12 h TMP/SMX (Bactrim) 4-6 mg/kg of TMP every 12 h	5-7 days
Salmonella	Ciprofloxacin 10-15 mg/kg every 12 h Ampicillin 50 mg/kg every 6 h Chloramphenicol 12.5-25 mg/kg every 6 h TMP/SMX (Bactrim) 4-6 mg/kg of TMP every 12 h	10-14 days
Campylobacter*	Erythomicin 10 mg/g every 6 h	7 days
Giardia lamblia	Metronidazole 7,5 mg/kg every 6 h	5-7 days
E. histolytica	Metronidazole 7,5 mg/kg every 6 h	10-14 days

*more frequent in immunedepressed patients

Micronutrient Supplementation

Supplementation with **zinc** has been shown to be efficacious as an adjunct therapy for acute and persistent diarrheal episodes in children in developing countries.

Results of a recent meta-analysis that reviewed seven trials for acute diarrhoea concluded that **treatment with zinc shortens the duration and lessens the severity of illness**. Administration of zinc supplements to children suffering from persistent diarrhoea is recommended by the WHO, and randomized trials have demonstrated its utility in reducing mortality rates up to 75% (range: 19 to 63%) among children with persistent diarrheal illness

Research on vitamin A supplementation is less consistent and generally does not support the use of vitamin A supplementation for reducing morbidity associated with acute diarrhea

Prevention

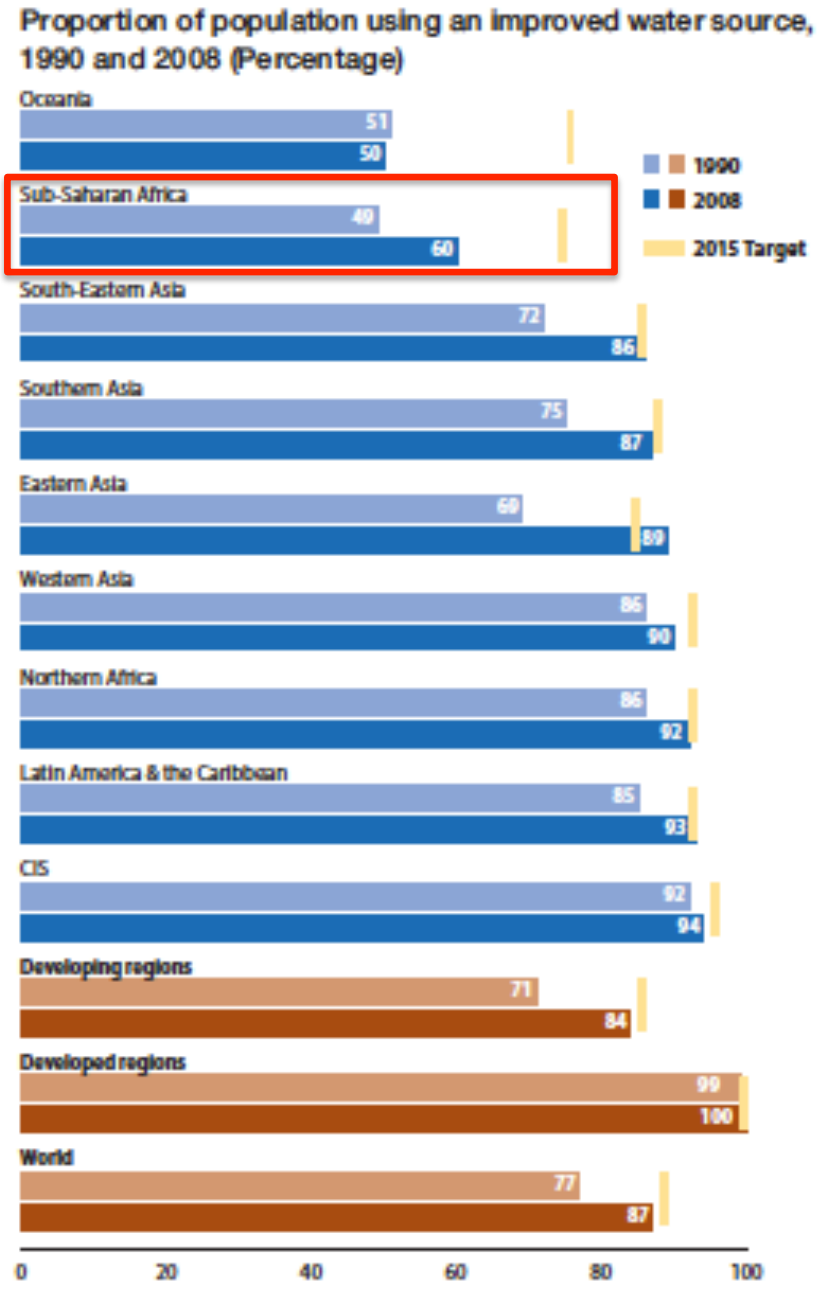
Improved food safety

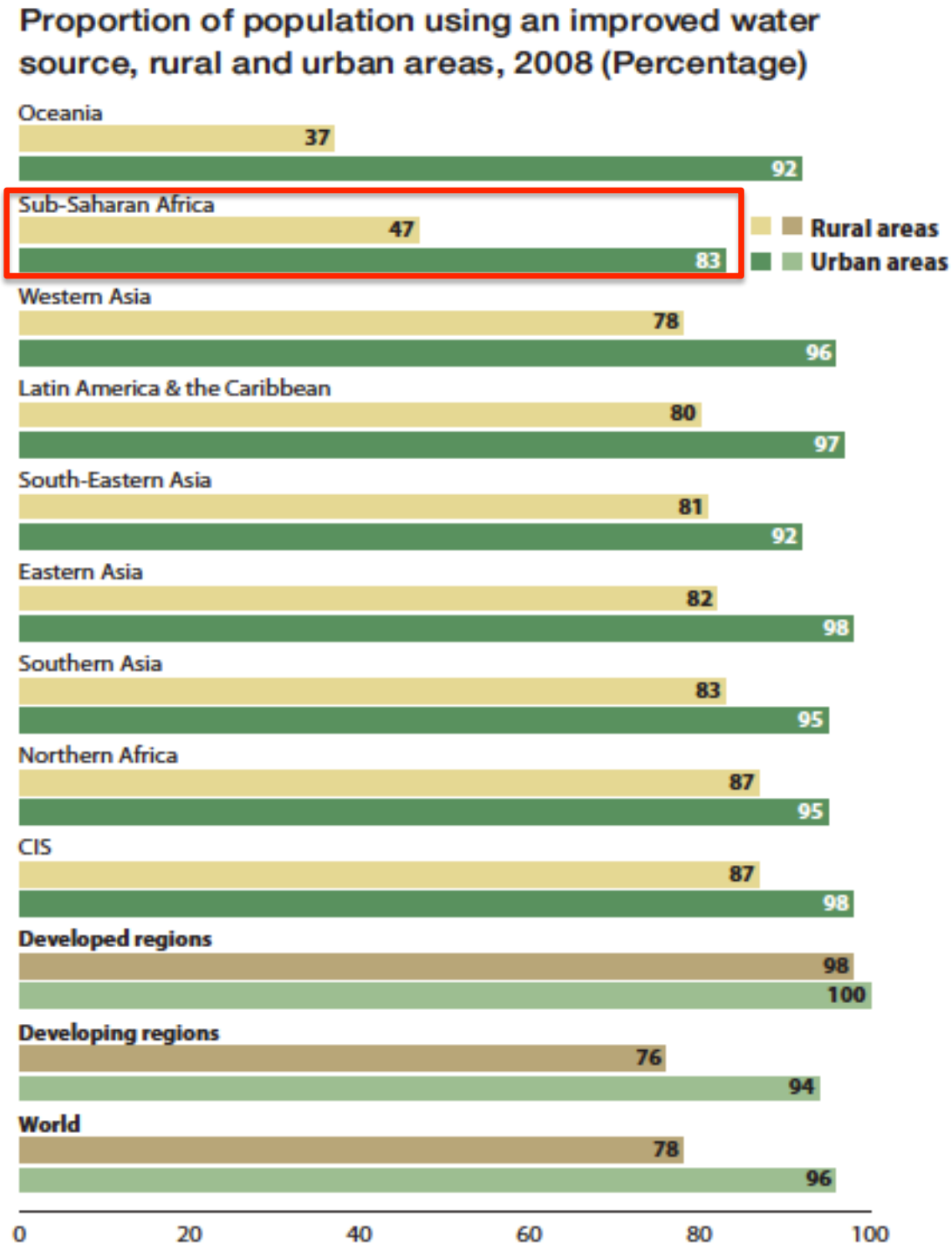
Proper food preparation and handling

Infectious human or animal wastes and contaminated water should not be used to fertilize or irrigate fruits and vegetables, especially those grown close to the soil and eaten raw.

Thorough cooking eliminates most pathogens from foods; however, poor hygiene and improper storage can lead to recontamination multiplication of bacteria. As a result, thoroughly reheating cooked foods before serving them is important.

Safe Water access

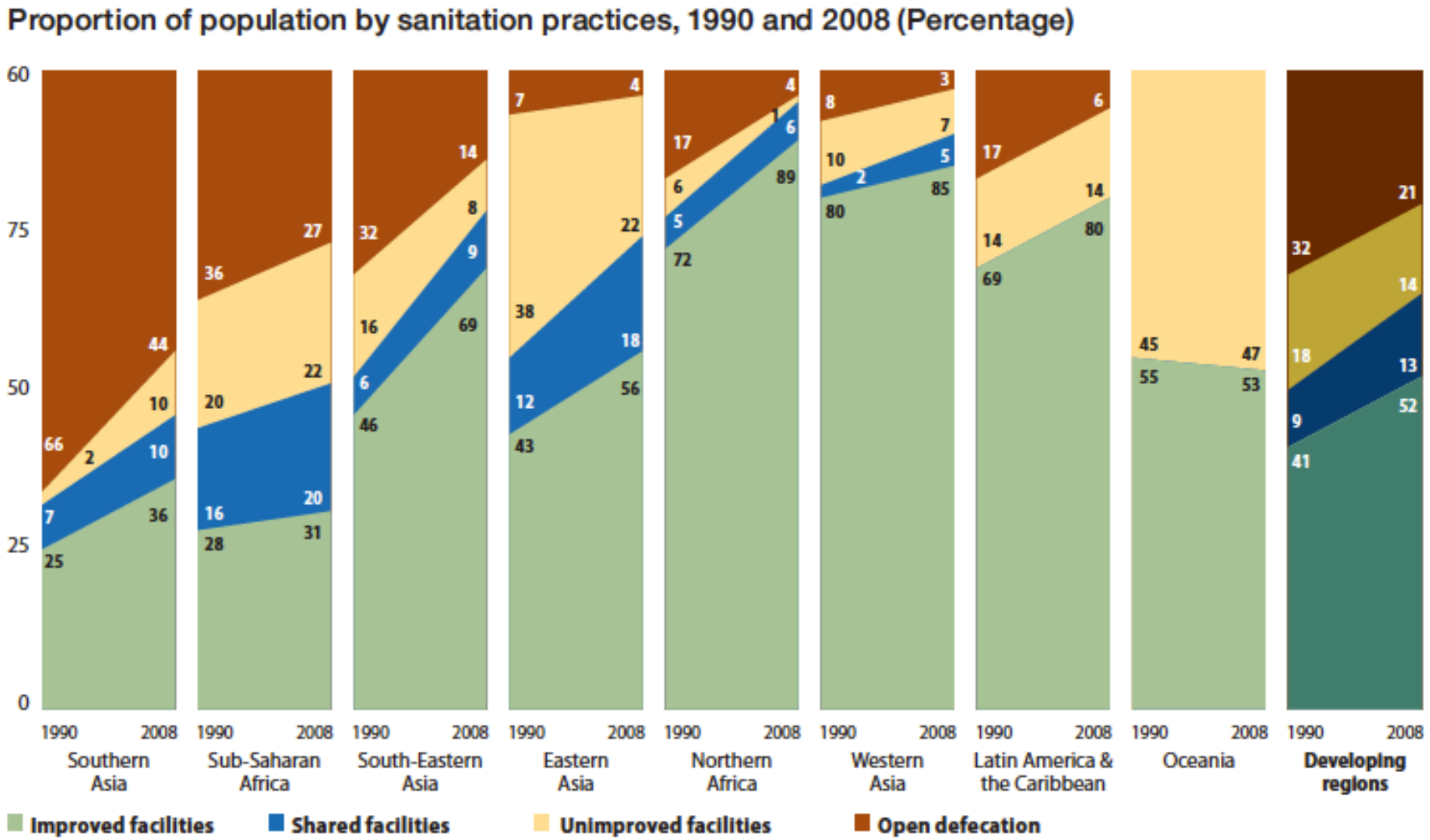




Improved Sanitation

The median reduction in the incidence of diarrhoeal diseases resulting from improvements in sanitation has been estimated to be 22% and as high as 36% in selected studies that met more rigorous scientific criteria

The open human defecation is risky for the transmission of diarrhoeal diseases. Improvements in sanitation will diminish the opportunity that flies have for contact with human excreta….



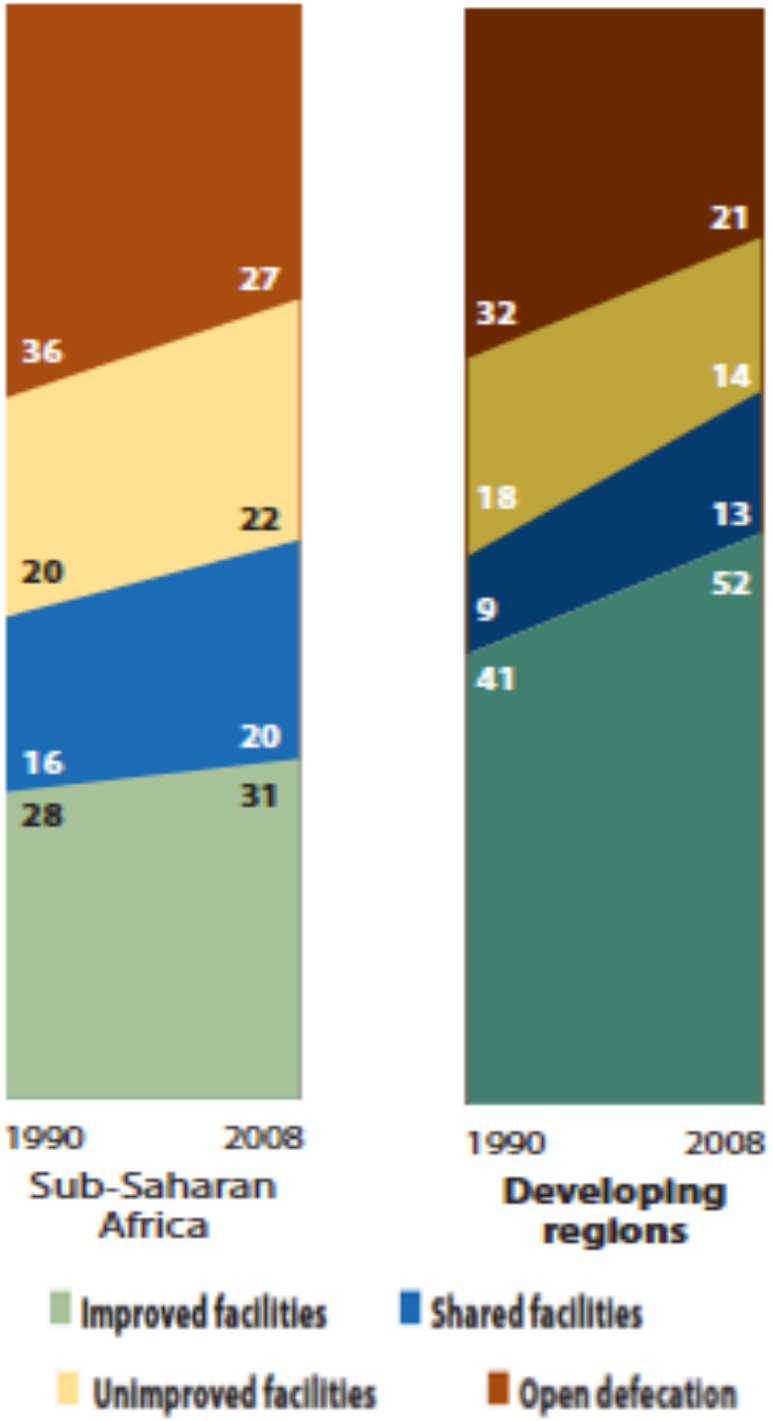
In 2008, 48% of the population in developing countries don't have access to improved sanitation (59% in 1990)

% of the population without access to improved sanitation

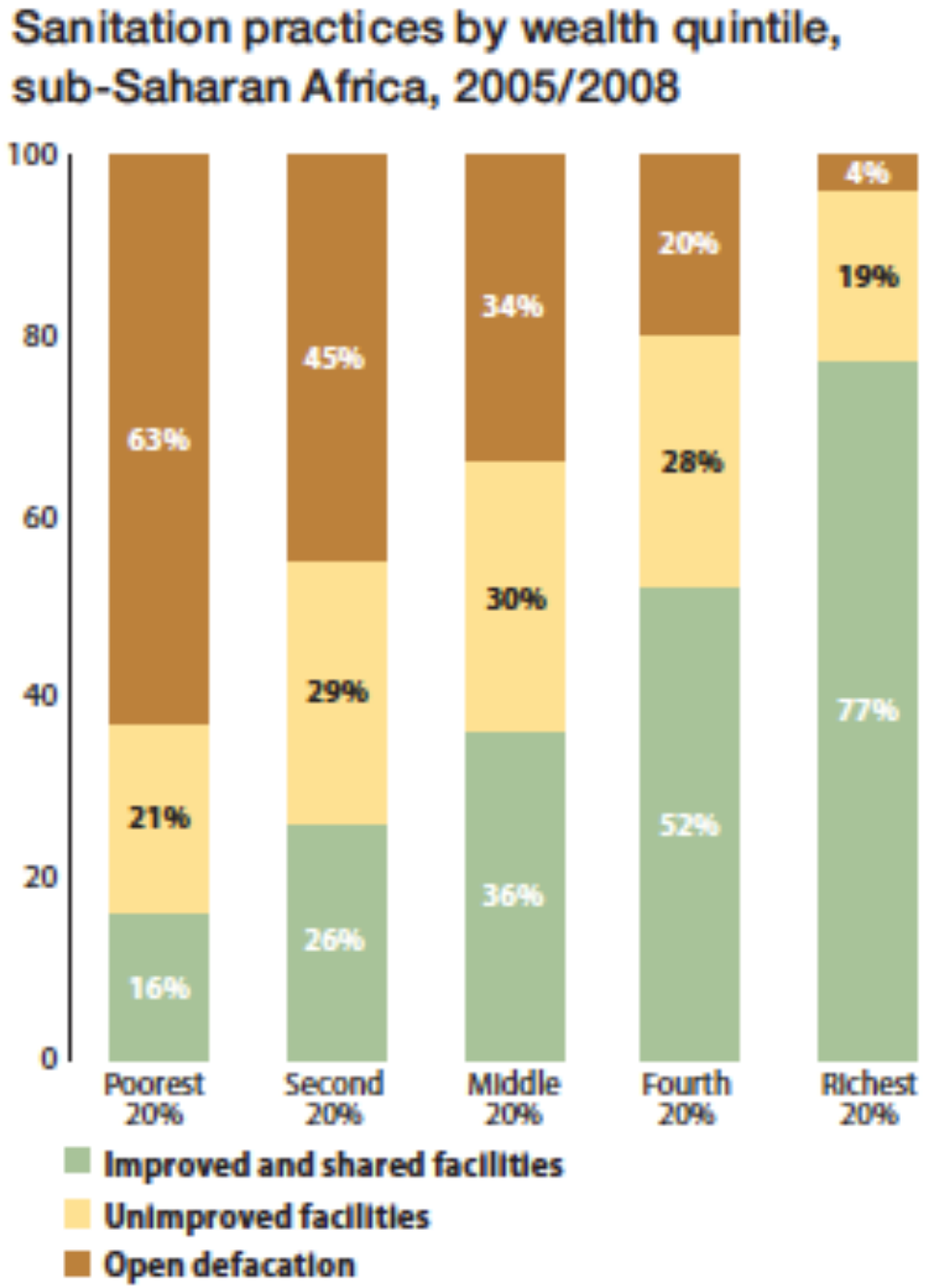
- sub-Saharan Africa
  - -1990: 72%
  - - 2008: 69%

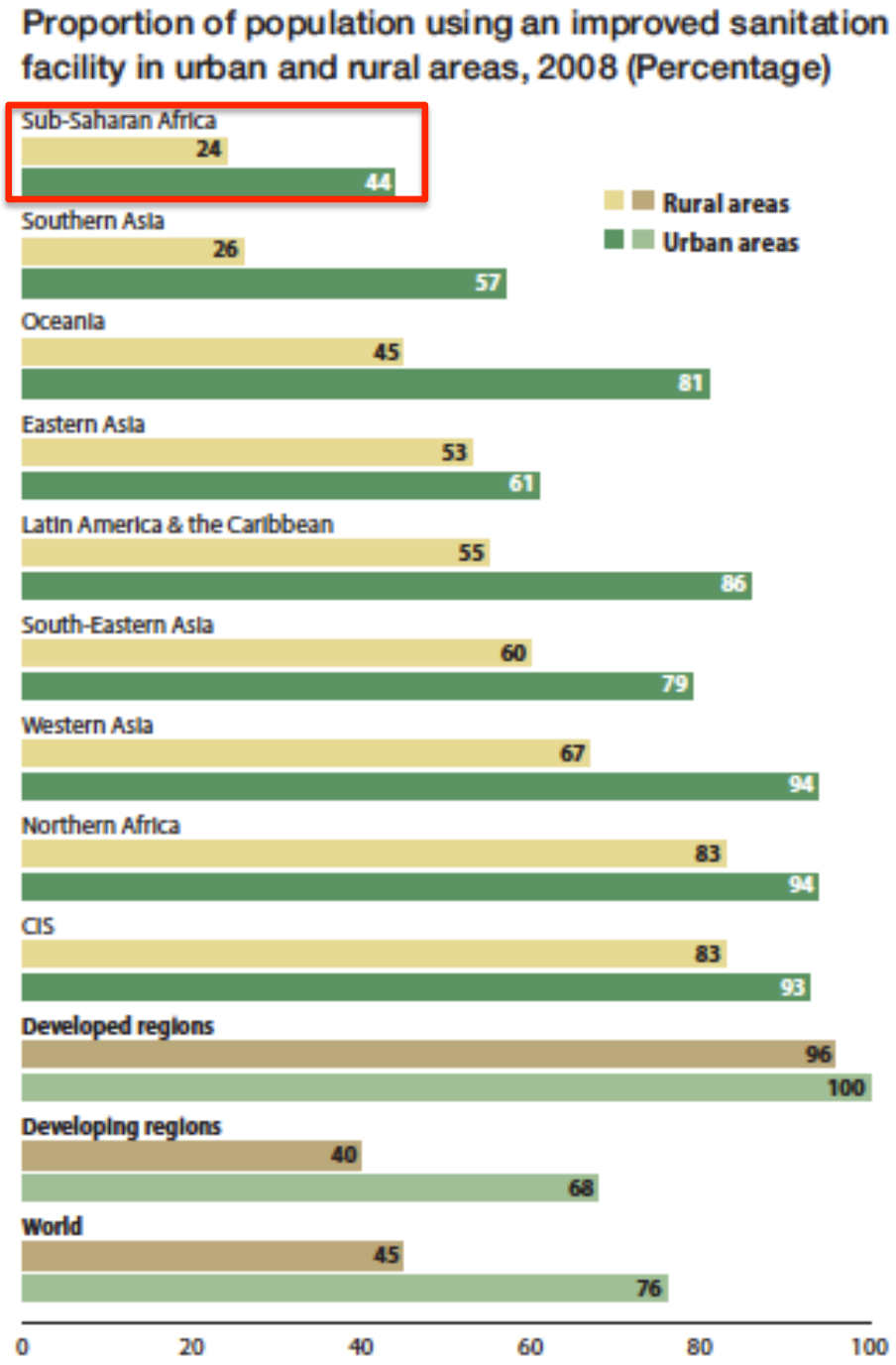
  - developing countries
  - - 1990: 59%
  - - 2008: 48%

In 2008, 21% of the total population of developing countries (27% in sub-Saharan Africa) was obliged to open defecation because of complete lack of sanitation



Improvements in sanitation are bypassing the poor





Most progress in sanitation has occurred in rural areas.

Over the period 1990-2008, sanitation coverage for the whole of the developing regions increased by only 5% in urban areas and by 43% in rural areas.

Hand washing

Where sanitation is poor, the potential for proper hygiene to prevent the transmission of diarrheal disease is high because of abundant environmental contamination with human and animal wastes.

A recent meta-analysis of 17 studies concluded that promotion of **hand washing interventions reduced the risk of diarrhoea by 47% and of severe intestinal infections by 59%.**

Washing with soap enhances the removal of pathogens from hands

Waterless hand sanitizing gels, such as the alcohol-based hand sanitizers now widely used in hospitals, eventually may be useful in developing countries where water is scarce, if they can be made available at very low cost.

Hand washing at critical times—**after defecating, after cleaning an infant or young child who defecated, before preparing food, before eating, and before feeding infants**—is important for maximal reductions in diarrheal disease transmission risk. Hand washing by key persons, including those who care for and prepare or serve foods to infants, and those who prepare and serve food as their vocation (eg, street vendors) should be targeted in promotional campaigns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