Incubation period: Average 60-90 days
Range 45-180 days

Clinical illness (jaundice):
<5 yrs, <10%
5 yrs, 30%-50%

Acute case-fatality rate: 0.5%-1%

Chronic infection:
<5 yrs, 30%-90%
5 yrs, 2%-10%

Premature mortality from chronic liver disease: 15%-25%
http://www.who.int/emc-documents/hepatitis/docs/who01shy0220022/virus/life_cycle.html

Spectrum of Chronic Hepatitis B Diseases

1. Chronic Persistent Hepatitis - asymptomatic
2. Chronic Active Hepatitis - symptomatic exacerbations of hepatitis
3. Cirrhosis of Liver
4. Hepatocellular Carcinoma
Structure and genomic organization of hepatitis B virus
Hepatitis Antigens-- HBsAg

- Hepatitis B surface antigen is the earliest indicator of acute infection and is also indicative of chronic infection if its presence persists for more than 6 months.
- It is useful for the diagnosis of HBV infection and for screening of blood.

Hepatitis Antigens-- HBcAg

Hepatitis B core antigen is derived from the protein envelope that encloses the viral DNA, and it is not detectable in the bloodstream. When HBcAg peptides are expressed on the surface of hepatocytes, they induce an immune response that is crucial for killing infected cells. The HBcAg is a marker of the infectious viral material and it is the most accurate index of viral replication.
Hepatatis Antigens-- HBeAg

Hepatitis Be antigen appearing during weeks 3 to 6 indicates an acute active infection at its most infectious period, and means that the patient is infectious. Persistence of this virological marker beyond 10 weeks shows progression to chronic infection and infectiousness. Continuous presence of anti-HBe indicates chronic or chronic active liver disease. HBeAg is not incorporated into virions, but is instead secreted into the serum.

Diagnosis

- HBsAg - used as a general marker of infection.
- HBsAb - used to document recovery and/or immunity to HBV infection.
- anti-HBe IgM - marker of acute infection.
- anti-HBeG - past or chronic infection.
- HBeAg - indicates active replication of virus and therefore infectiveness.
- Anti-Hbe - virus no longer replicating. However, the patient can still be positive for HBsAg which is made by integrated HBV.
- HBV-DNA - indicates active replication of virus, more accurate than HBeAg especially in cases of escape mutants. Used mainly for monitoring response to therapy.
Acute Hepatitis B Virus Infection with Recovery

Typical Serologic Course

Progression to Chronic Hepatitis B Virus Infection

Typical Serologic Course
Global Patterns of Chronic HBV Infection

- High (>8%): 45% of global population
  - lifetime risk of infection >60%
  - early childhood infections common
- Intermediate (2%-7%): 43% of global population
  - lifetime risk of infection 20%-60%
  - infections occur in all age groups
- Low (<2%): 12% of global population
  - lifetime risk of infection <20%
  - most infections occur in adult risk groups
Concentration of Hepatitis B Virus in Various Body Fluids

<table>
<thead>
<tr>
<th>High</th>
<th>Moderate</th>
<th>Low/Not Detectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>blood</td>
<td>semen</td>
<td>urine</td>
</tr>
<tr>
<td>serum</td>
<td>vaginal fluid</td>
<td>feces</td>
</tr>
<tr>
<td>wound exudates</td>
<td>saliva</td>
<td>sweat</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tears</td>
</tr>
<tr>
<td></td>
<td></td>
<td>breastmilk</td>
</tr>
</tbody>
</table>
Hepatitis B Virus
Modes of Transmission

- Sexual - sex workers and homosexuals are particular at risk.
- Parenteral - IVDA, Health Workers are at increased risk.
- Perinatal - Mothers who are HBeAg positive are much more likely to transmit to their offspring than those who are not. Perinatal transmission is the main means of transmission in high prevalence populations.
Primary Hepatocellular Carcinoma (PHC)

A rare tumour in the US and Europe (<2% fatal cancers) and most cases are alcohol-related.

In Southeast Asia, Asia and China, PHC is the most common fatal cancer—~5x10^5 deaths per year.
Cancer Screening

- Individuals with chronic hepatitis B are at increased risk for the development of hepatocellular carcinoma. Although precise recommendations do not exist, it is reasonable for such individuals to undergo periodic screening for cancer.
- Screening procedures include measurement of serum alpha-fetoprotein (a tumor marker that is elevated in about 85% of individuals with hepatocellular carcinoma) and ultrasound examination. The optimal frequency of such screening examinations has not been determined.

http://cpmcnet.columbia.edu/dept/gi/hepB.html

Viral Gastroenteritis

- It is thought that viruses are responsible for up to 3/4 of all infective diarrheas.
- Viral gastroenteritis is the second most common viral illness after upper respiratory tract infection.
- In developing countries, viral gastroenteritis is a major killer of infants who are undernourished. Rotaviruses are responsible for half a million deaths a year.
- Many different types of viruses are found in the gut but only some are associated with gastroenteritis.
Rotaviruses

- Naked double stranded RNA viruses, 80 nm in diameter.
- Also found in other mammals and birds, causing diarrhea.
- Causes disease in all age groups but most severe symptoms in neonates and young children.
- Asymptomatic infections common in adults and older children. Symptomatic infections again common in people over 60.
Rotaviruses

- Accounts for 50-80% of all cases of viral gastroenteritis.
- Usually endemic, but responsible for occasional outbreaks.
- 80% of the US population have antibody against rotavirus by age of 3.
- 2.5 million cases in children under 5 per year in US; 70,000 hospitalizations and 20-70 deaths per year in US
- Up to 30% mortality rate in malnourished children
- Responsible for up to half a million deaths per year, worldwide

Rotaviruses

- More frequent during the winter.
- Fecal-oral spread.
- 24-48 hr incubation period followed by an abrupt onset of vomiting and diarrhea, a low grade fever may be present.
- Diagnosed by electron microscopy or by the detection of rotavirus antigens in feces by ELISA or other assays.
Rotaviruses

- 1998--RotaShield vaccine introduced
- Increase in frequency of intussusception, a blockage or twisting of the intestine
- 20 deaths attributed to vaccine in first 1,000,000 children vaccinated
- Rotashield withdrawn
- 2006-RotaTeq vaccine approved by FDA for US use after large scale testing--no increase in intussusception reported

Adenovirus Particle

(Courtesy of Linda Stannard, University of Cape Town, S.A.)
Enteric Adenoviruses

- Naked DNA viruses, 75 nm in diameter.
- Fastidious enteric adenovirus types 40 and 41 are associated with gastroenteritis.
- Associated with cases of endemic gastroenteritis, usually in young children and neonates. Can cause occasional outbreaks.
- Possibly the second most common viral cause of gastroenteritis (7-15% of all endemic cases).
- Similar disease to rotaviruses
- Most people have antibodies against enteric adenoviruses by the age of three.
- Diagnosed by electron microscopy or by the detection of adenovirus antigens in faeces by ELISA or other assays.

Astrovirus Particles

(Source: ICTV database)
Astroviruses

- Small RNA viruses, named because of star-shaped surface morphology, 28 nm in diameter.
- Associated with cases of endemic gastroenteritis, usually in young children and neonates. Can cause occasional outbreaks.
- Responsible for up to 10% of cases of gastroenteritis.
- Similar disease to rota and adenoviruses.
- Most people have antibodies by the age of three.
- Diagnosed by electron microscopy only, often very difficult because of small size.

Calicivirus Particles

(Source: ICTV database)
Caliciviruses

- Small RNA viruses, characteristic surface morphology consisting of hollows. particles 35 nm in diameter.
- Associated mainly with epidemic outbreaks of gastroenteritis, although occasionally responsible for endemic cases.
- Like Norwalk type viruses, vomiting is the prominent feature of disease.
- Majority of children have antibodies against caliciviruses by the age of three.
- Diagnosed by electron microscopy only, often difficult to diagnose because of small size.

Norwalk-like Virus Particles

(Source: ICTV database)
Norwalk-like Viruses

- Small RNA viruses, with ragged surface, 35 nm in diameter, now classified as caliciviruses.
- Always associated with epidemic outbreaks of gastroenteritis, adults more commonly affected than children.
- Associated with consumption of shellfish and other contaminated foods. Aerosol spread possible as well as faecal-oral spread.
- Also named "winter vomiting disease", with vomiting being the prominent symptom, diarrhea usually mild.
- Antibodies acquired later in life, in the US, only 50% of adults are seropositive by the age of 50.
- Diagnosis is made by electron microscopy and by PCR.

The Immune System is Active in the Intestine

- M cells and dendritic cells are specialized cells which collect antigen
- Immune response to antigens is carried out by T and B cells which collect in follicular regions
SUPERANTIGENS PRODUCED BY A BACTERIUM OR A VIRUS PRODUCE TOXIC SHOCK

SUPERANTIGEN INTERACTION WITH HOST T CELLS
**DIFFERENCES BETWEEN ANTIGEN AND SUPERANTIGEN**

<table>
<thead>
<tr>
<th>Typical antigen–MHC Class II interaction</th>
<th>Superantigen–MHC class II interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Diagram of typical antigen-MHC interaction" /></td>
<td><img src="image2" alt="Diagram of superantigen-MHC interaction" /></td>
</tr>
</tbody>
</table>

- Antigen processing and presentation
- Conventional antigen
- TCR
- MHC class II
- APC

- Superantigen
- Superantigenic exotoxin
- Bacteria
- TCR
- MHC class II

**ANTIVIRAL COMPOUNDS**

- MUST ATTACK A BIOCHEMICAL VULNERABILITY OF THE VIRUS DISTINCTIVE FROM THE BIOCHEMISTRY OF THE HOST
- EXAMPLE: ACYCLOVIR AND HERPES VIRUS
ACYCLOVIR IS PREFERENTIALLY CONVERTED TO ACY-MP BY HERPES VIRUS ENCODED THYMIDINE KINASE

A Broad Spectrum Antiviral?

- Each virus class has very different molecular biology—a drug which attacks a specific point of vulnerability for one type of virus is unlikely to target other types
Some Major Food Borne Bacterial Pathogens of Humans

• Shigella dysenteriae,
• Salmonella enteritidis and typhi
• Campylobacter jejuni
• Listeria monocytogenes
• Bacillus cereus

PATHOGENIC E. COLI

• ENTEROTOXIGENIC (ETEC) (secretory diarrhea)
• ENTEROPATHOGENIC (Malabsorptive diarrhea) (EPEC)
• ENTEROHEMORAGGHIC (Malabsorptive diarrhea and dysentery) (EHEC) (E. coli 0157)

All three types are major causes of infant deaths worldwide
Bacterial Toxins

- Endotoxins - bacterial lipopolysaccharides
- Exotoxins - specific polypeptides produced by bacteria which cause toxic effects

**BACTERIAL EXOTOXIN GENES ARE OFTEN ACQUIRED BY GENE TRANSFER**

*Figure 9-1*  Lysogenic bacteriophages carry toxin genes that integrate into the bacterial chromosome, thus making the bacterium capable of producing the toxin.
MECHANISM OF ACTION ST AND LT TOXINS IN ETEC

INTERFERENCE WITH cAMP or cGMP METABOLISM LEADS TO LOSS OF CONTROL OVER WATER FLOW AND INTESTINAL WATER LOSS
Cholera

- The profuse diarrhea and subsequent fluid and electrolyte loss associated with infection with enterotoxigenic Escherichia coli and Vibrio cholerae arise following binding of the terminal epithelium of the intestine by the toxins Etx andCtx, respectively.
- (a) Binding to the cell is mediated by the ability of the B subunit of the toxin to interact and crosslink with ganglioside GM1 receptors.
- (b) Cytoskeletal rearrangement and vesicular uptake and
- (c) Trafficking, a process that is also influenced by the presence of an RDEL (or KDEL in the case ofCtx) sequence on the A2 fragment.
- (d) Enzymatic cleavage allows the A1 fragment to enter the cytosol, where
- (e) It catalyses adenosine diphosphate (ADP) ribosylation of Gs, a soluble guanylyl cyclase-activating protein that regulates the activation of adenylate cyclase.
- (f) Once activated, adenylate cyclase accelerates the conversion of adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP), which subsequently induces phosphorylation of protein kinase A (PKA) and leads to the opening of the cystic fibrosis transmembrane regulator (CFTR) chloride ion (Cl−) channel.
- (g) Efflux of Cl− from the cell results in a simultaneous osmotic shift of water from the cell into the intestinal lumen, accompanied by cell death. This results in the watery diarrhea characteristic of infection by V. cholerae and E. coli.
DELIVERY OF EPEC TOXIC PROTEIN TO HUMAN INTESTINAL CELLS BY A TYPE III SECRETION SYSTEM

EPEC PILI BIND TO INTESTINAL EPITHELIAL CELLS; CHANNEL IS FORMED MAKING DIRECT CONNECTION BETWEEN EPEC CYTOPLASM AND INTESTINAL CELL CYTOPLASM TOXIC PROTEIN INJECTED WITHOUT EXPOSURE TO HUMAN IMMUNE SYSTEM

Effects of EPEC infection on host intestinal epithelial cells

- EPEC initially adheres to the host cell by its bundle-forming pili, which also mediate bacterial aggregation.
- Following initial attachment, EPEC secretes several virulence factors by a type III secretion system.
- Signal transduction events occur within the host, including activation of phospholipase C (PLC) and protein kinase C (PKC), intracellular triphosphate (IP3) fluxes, and Ca2+ release from internal stores.
- The bacterium intimately adheres to the cell by secreting its own receptor, Tir, into the host and binding to it with its outer membrane ligand, intimin.
- Intimin can also bind beta-integrins.
- Several cytoskeletal proteins are recruited to the site of EPEC attachment, including actin, alpha-actinin, talin, and ezrin.
- Cytoskeletal rearrangements occur following Tir-intimin binding, resulting in the formation of a pedestal-like structure upon which the pathogen resides.
EHEC

- Shiga like toxin circulates through bloodstream, enters kidney and causes kidney damage

Pedestal Formation by EPEC and EHEC occurs by different mechanisms

- EPEC Tir becomes tyrosine-phosphorylated in the host-cell plasma membrane and binds the adaptor protein Nck.
- Nck recruits N-WASP or a WIPIN-WASP complex to trigger activation of the Arp2/3 complex, which leads to actin assembly.
- EHEC Tir localizes to the plasma membrane, but is not tyrosine phosphorylated.
- Other EHEC proteins (X) in addition to Tir are translocated into host cells.
- This combination of Tir and other factors promotes recruitment and activation of N-WASP by an unidentified mechanism (designated with a question mark).
- N-WASP then stimulates Arp2/3-based actin nucleation.
The Immune System is Active in the Intestine

- M cells and dendritic cells are specialized cells which collect antigen
- Some pathogens have systems which allow them to invade M cells and pass through into the body

PATHOGENICITY OF SALMONELLA

Mucin

- nucleus
- Salmonella spp.

Macrophages

Inflammation

Systemic infection (uncommon)
Salmonella invasion into host epithelial cells

- Salmonella secrete virulence proteins, including SopE and SptP, into host cells by the type III-secretion system.
- SopE functions as a guanine exchange factor for small GTP-binding proteins, probably mediating the exchange of GDP for GTP on a Rho subfamily member, CDC42.
- SptP is a tyrosine phosphatase required for invasion, probably by disrupting the cytoskeleton.
- Invasion also stimulates phospholipase C (PLC) activity, leading to inositol triphosphate (IP3) and Ca2+ fluxes, which in turn may be involved in cytoskeletal rearrangements leading to membrane ruffling and Salmonella internalization.

Shigella-mediated cytoskeletal rearrangements

- The outer membrane protein, LsaK, is sufficient to drive actin-based motility of Shigella.
- Vinculin undergoes proteolysis within the host cell upon Shigella infection, producing a 90-kDa fragment that can bind to LsaK and to the Wiskott-Aldrich-stimulated phosphoprotein (VASP).
- VASP in turn can recruit profilin to the bacterial surface, which can provide actin for tail construction.
- N-WASP binding of LsaK can also recruit profilin to the bacterial surface and may be another means of obtaining monomeric actin for tail formation and subsequent bacterial motility.
Figure 16-39. The actin-based movement of a bacterium within and between mammalian cells. (A) The bacterium Listeria monocytogenes spreads from cell to cell by inducing the assembly of actin filaments in the host cell cytoplasm. (B) Fluorescence micrograph of the bacterium moving in a cell that has been stained to reveal both bacteria and actin filaments. Note the comet-like tail of actin filaments (green) behind each moving bacterium (red). Regions of overlap of red and green fluorescence appear yellow. (B, courtesy of Tim Mitchison and Julie Theriot.)
HELICOBACTER PYLORI INFECTION: PRODUCTION OF AMMONIA PROTECTS AGAINST DESTRUCTION BY STOMACH ACIDS

H. Pylori Pathogenicity is Dependent on vacA Genotype

- *H. pylori* strains that contain vacA alleles of the s1 type are associated with an increased risk for development of peptic ulcer disease and gastric cancer compared with strains containing vacA alleles of the s2 type.
a Addition of VacA to many different cell types in the presence of weak bases results in the formation of large intracellular vacuoles. The image shows HeLa cells incubated with VacA and stained with neutral red dye.

b Schematic illustration of a model for the mechanism of VacA-induced vacuole formation. After binding of VacA to the cell surface, VacA is internalized and forms anion-selective VacA channels in the membranes of late endocytic compartments. Conductance of chloride through these channels results in an increased intraluminal chloride concentration. To compensate for this increased anion concentration, vacuolar ATPase activity increases, resulting in increased proton pumping and a reduction in intraluminal pH. Membrane-permeant weak bases such as ammonia diffuse into late endocytic compartments and become protonated and trapped in these compartments. Osmotic swelling of these compartments ultimately results in cell vacuolation.

Some Major Bacterial Pathogens of Humans

- Staphylococcus aureus and epidermis
- Streptococcus pyogenes and pneumonia
- Neisseria gonorrhoeae and meningitidis
- Pseudomonas aeruginosa
- Vibrio cholerae
- Haemophilus influenzae
- Bordetella pertussis
- Clostridium tetani, botulinum and perfringens
- Mycobacterium tuberculosis
- Yersinia pestis
Pathogens can be normal flora of the human body

- Example: staphylococcus aureus normally found on nasal passages, skin and mucous membranes
- Staphylococcus aureus can cause pneumonia, mastitis, phlebitis, meningitis, urinary tract infections and deep-seated infections, such as osteomyelitis and endocarditis. It can also cause superficial skin lesions such as boils, styes and furuncles
THE GRAM STAIN DISTINGUISHES TWO FUNDAMENTALLY
DIFFERENT BIOCHEMISTRIES OF BACTERIAL CELL WALLS
GRAM STAIN OF SPUTUM SAMPLE INFECTED WITH STREPTOCOCCUS PNEUMONIAE

Gram negative Pseudomonas
STRUCTURE OF MUREIN OR PEPTIDOGLYCAN: A HIGHLY CROSS-LINKED POLYSACCHARIDE PEPTIDE MATRIX WHICH MAKES UP THE CELL WALL OF BACTERIA
DIFFERENCE IN MUREIN STRUCTURE BETWEEN GRAM POSITIVE AND GRAM NEGATIVE BACTERIA

TEICHOIC ACID IS AN IMPORTANT COMPONENT OF GRAM POSITIVE CELL WALLS

GLYCEROL TEICHOIC ACID

RIBITOL TEICHOIC ACID
LIPID A ANCHORS LPS IN THE OUTER LEAFLET OF THE MEMBRANE

LIPID A is composed of disaccharides attached to short chain fatty acids and phosphate groups.

CORE CONSISTS OF A SHORT SERIES OF SUGARS INCLUDING KETO-DEOXYOCTONOOIC ACID AND A HEPTOSE

O antigen is a long carbohydrate chain up to 40 sugars in length. Hydrophilic sugars cover the bacterial surface and exclude hydrophobic compounds protecting bacteria from bile salts.

GRAM NEGATIVE CELL WALL

Major Targets of Antibacterial Antibiotics.

DNA

Transcription

mRNA

Translation

Protein

Inhibition of cell wall synthesis
Penicillins, cephalosporins, bacitracin, vancomycin

Inhibition of protein synthesis
Chloramphenicol, erythromycin, tetracyclines, streptomycin

Inhibition of nucleic acid replication and transcription
Quinolones, rifampin

Injury to plasma membrane
Polylysine B

Inhibition of synthesis of essential metabolites
Subtilisins, interpeptids

Enzymatic activity

Copyright © 2001 Benjamin Cummings, an imprint of Addison Wesley Longman, Inc.
Inhibition of bacterial protein synthesis by antibiotics

Aminoglycosides

Streptomycin
Changes shape of 30S portion, causes code on mRNA to be read incorrectly

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FIGURE 13-7 Inhibition of nucleic acid synthesis. 1. Rifampin (R) binds to DNA-dependent RNA polymerase and inhibits RNA synthesis. 2. Quinolones (Q) inhibit DNA gyrase and prevent supercoiling of DNA.
Rifampicin binds to a pocket in the channel that is normally occupied by the newly formed RNA-DNA hybrid. Thus the antibiotic blocks elongation after only two or three nucleotides have been added.

Mechanism of inhibitors of folic acid (metabolic) pathway
Sites of action of some antibiotics which inhibit cell wall synthesis

STRUCTURE OF MUREIN

N-Acetyl muramic acid
N-acetylmuramic acid
N-acetylglucosamine
N-acetylglicosamine

Cross-linked peptide
Penicillin acts by irreversibly inactivating the enzyme glycopeptide transpeptidase which cross links the bacterial cell wall through addition to the enzyme active site via the beta lactam ring.
(a) Natural (antibiotic) penicillins

(b) Semi-synthetic penicillins
ANTIBIOTIC RESISTANCE IN BACTERIA

• ALTERATION OF STRUCTURE OF TARGET ENZYME SO THAT DRUG NO LONGER BINDS, BUT ENZYME STILL FUNCTIONS
• ENZYME PRODUCED WHICH DESTROYS DRUG
• EFFLUX SYSTEM REMOVES DRUG FROM CELL
• ALTERNATIVE BIOCHEMICAL PATHWAY DEVELOPED TO EVADE ACTION OF DRUG

Resistance to Penicillin and Structurally Related Drugs

Hydrolysis of the β-lactam ring by β-lactamase inactivates penicillin since the hydrolysed β-lactam ring no longer binds to glycopeptide transpeptidase
Inactivation of Chloramphenicol by Acetylation of the Drug

Chloramphenicol resistance mediated by chloramphenicol acetyltransferases (CATs)

Acetylation prevents chloramphenicol from binding to the ribosome and inhibiting protein synthesis.

Vancomycin is currently a drug of last resort in bacterial infection
BUT
Vancomycin resistance has become a serious clinical problem
Emerging Vancomycin-resistant Enterococcal Infections*

* in U.S. NNIS Hospitals

CDC

VANCOMYCIN RESISTANCE: A NEW BIOCHEMICAL SYSTEM FOR CELL WALL SYNTHESIS

Figure 71-3 Mechanism of vancomycin resistance. (A) Action of vancomycin in susceptible bacteria: three enzymes are involved, one (VanD) that catalyzes conversion of pyruvate to lactate; a second one (VanA or VanD) that catalyzes the synthesis of d-Ala-d-Ala instead of d-Ala-d-Ala, and a third one (Van X) that cleaves the terminal d-Ala from the d-Ala-d-Ala that is synthesized by the normal pathway.
Multidrug Resistance

Membrane proteins which can pump molecules out of cells are termed multidrug resistance proteins (mdr or mrp).

These proteins are normal constituents of the cell membranes of all cells—bacterial and eukaryotic; they use ATP to provide the energy for pumping molecules out of the cell.

Increased expression levels of mdr and/or mrp proteins can lead to drug resistance for one or more classes of drugs.

Multidrug resistance is a problem in chemotherapy for treatment of bacterial infections, parasitic infections (such as malaria) and cancer.

Antibiotic Resistance in Bacteria

- Genes for resistance to multiple antibiotics are carried on a single plasmid which can be transferred from one bacterial species to another.
- Use of antibiotics in agriculture as a significant contributor to development of antibiotic resistant bacterial pathogens for humans.
Spread of antibiotic resistance genes

- Movement of antibiotic resistance genes between bacteria can lead to the accumulation of multidrug-resistant bacteria.

Spread of antibiotic-resistant bacteria from animals to humans

- Food of animal origin is the source of a majority of food borne bacterial infections caused by non-typhoid *Salmonella, Campylobacter, Yersinia, E. coli 0157* and other pathogens
- Spread of resistance genes from bacteria in farm environment to farm workers documented in a number of instances
Potential Environmental Sources of Drug Resistance Gene

- Therapeutic, prophylactic, and growth promotion in animal feeds –, streptogramins, everinomycins, quinolones, aminoglycosides, and cephalosporins
- Salmon farming uses large quantities of tetracyclines and quinolones
- Fruit-growers spray their crops with tetracycline or streptomycin to prevent fireblight
- Industrial uses of antibiotics--cleaning of oil pipes.

Staphylococcus aureus can cause many types of pathological infection
S. aureus expresses many potential virulence factors:

- (1) surface proteins that promote colonization of host tissues
- (2) invasins that promote bacterial spread in tissues (leukocidin, kinases, hyaluronidase)
- (3) surface factors that inhibit phagocytic engulfment (capsule, Protein A)
- (4) biochemical properties that enhance their survival in phagocytes (carotenoids, catalase production)
- (5) immunological disguises (Protein A, coagulase)
- (6) membrane-damaging toxins that lyse eukaryotic cell membranes (hemolysins, leukotoxin, leukocidin)
- (7) exotoxins that damage host tissues or otherwise provoke symptoms of disease (SEA-G, TSST, ET)
- (8) inherent and acquired resistance to antimicrobial agents