INFECTIOUS COMPLICATIONS IN PATIENTS WITH CIRRHOSIS: WHAT SHALL WE DO?

Jenny Lim Limquiaco, MD
Epidemiology

- present in about 30% of patients with cirrhosis at admission or during hospitalization
- 60% are community-acquired
- 30% exhibit acute on chronic liver failure
- Mortality reaches 38%

Clin Gastroenterol Hepatol 2010;8:979–985
Gastroenterology 2013;144:1426-37
PATHOGENESIS OF SEPSIS IN CIRRHOSIS
Pathophysiological Mechanisms of Increased Susceptibility to Infections

- Immune Dysfunction
- Kupffer Cells
- Neutrophils
- Monocyte
  - Cytokine STORM
- Genetic predisposition
  - NOD2 (nucleotide-binding oligomerization domain containing 2)
  - Mannose-binding lectin deficiency
- Intrinsic cellular defect
- GUT permeability
- Endotoxin
- Lipoprotein
- Albumin dysfunction
- Toll Like receptors
  - Toll-like receptor (TLR)2 polymorphisms
OTHERS:

- Impairment of macrophage Fcg-receptor-mediated clearance of Ab-coated bacteria
- Deficiencies in the complement system
- Down-regulation of monocyte HLA-DR expression
TLR mediated Induction of Proinflammatory Genes in Immune Cell
Mechanisms involved in the pathogenesis of infections in cirrhosis

Portal Hypertension

- Altered intestinal motility
- Decreased Intestinal IgA or bile acids

Intestinal Bacterial overgrowth

- Submucosal edema, inflammation
- Altered permeability

Bacterial translocation

- RES dysfunction
- Impaired cellular and non specific humoral immunity

Regional mesenteric lymph nodes

Bacteremia

- Transient
- Prolonged

- Depends on bacterial activity (good, moderate, poor)

SBP | CNNA | MNB

SBEM

<table>
<thead>
<tr>
<th>Type of infection in CLD</th>
<th>Common Causes</th>
</tr>
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<tbody>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>Escherichia coli, Klebsiella species, Streptococcus species Enterococcus species. Infrequently anaerobic organisms</td>
</tr>
<tr>
<td>Spontaneous bacterial empyema</td>
<td>E. coli</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>Gram-negatives</td>
</tr>
<tr>
<td>Community acquired pneumonia</td>
<td>Streptococcus pneumonia, Hemophilus influenzae, Klebsiella, Mycoplasma pneumoniae, Legionella species, Peptostreptococcus, Bacteroides melaninogenicus, Fusobacterium nucleatum</td>
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<tr>
<td>Hospital acquired pneumonia</td>
<td>Gram negatives and staphylococci</td>
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<tr>
<td>Bacteremia</td>
<td>Escherichia coli, Klebsiella pneumoniae, Aeromonas hydrophila, Staphylococcus aureus, Streptococcus group</td>
</tr>
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<td>Pulmonary or peritoneal tuberculosis</td>
<td>Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>Lymphangitis of lower extremities or cellulites</td>
<td>Gram-positives and Gram-negatives</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>Streptococcus pneumonia, Escherichia coli, Staphylococcus aureus</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Streptococcus pneumonia, Escherichia coli, Listeria monocytogenes</td>
</tr>
</tbody>
</table>
Limitations of common clinical and analytical markers of infection

GENERAL POPULATION: SIRS Diagnosis

- 2 or more of the ff:
  1) a core T ≥38 °C or ≤36 °C
  2) a HR≥90 beats/min
  3) tachypnea ≥20 breaths/min or partial carbon monoxide pressure (PaCO2) ≤32mmHg or the need of mechanical ventilation
  4) WBC ≥12 × 10^9/L or ≤4 × 10^9/L or >10% of immature neutrophils
Limitations of common CLINICAL and analytical markers in cirrhosis

- SIRS diagnostic criteria
  - more difficult to use; less diagnostic accuracy in cirrhosis

HEART RATE:
- hyperdynamic circulation leads to tachycardia in the absence of infection
- beta-blockers: reduces heart rate
- hepatic encephalopathy: presents w tachypnea

WHITE BLOOD COUNT
- hypersplenism decreases white blood cell count

Management of bacterial infections in cirrhosis Javier Fernandez and Thierry Gustot
Journal of Hepatology 2012
Limitations of common clinical and analytical markers of infection

- C-reactive protein (CRP) and procalcitonin (PCT)
  - Conflicting results exist regarding threshold values and diagnostic accuracy in cirrhosis
  - CRP: produced predominantly by hepatocytes
  - PCT: produced ubiquitously by thyroidal and extra-thyroidal tissues including the liver in septic patients

J Clin Endocrinol Metab 2001;86:396–404
Limitations of common clinical and analytical markers of infection

Patients with liver failure – attenuated response

- CRP (AUC: 0.64 to 0.91)
  - LOW CRP:
    - interpret with caution in Child–Pugh C patients
- PCT (AUC: 0.68–0.89)
- Cut off: 0.5ng/ml

- some studies showing a superiority of PCT over CRP and others showing similar results

Factors predisposing to infection in cirrhosis

- Severity of the underlying liver disease (Childs Pugh C)
- Ascitic fluid total protein concentration <1gr/dl
- Ascitic fluid C3 level <13mg/dl
- Total bilirubin level of >3.2 mg/dl
- Gastrointestinal bleeding
- Previous spontaneous bacterial peritonitis episodes
- Urinary, respiratory tract or other source of infection
- Iatrogenic factors (e.g. urinary bladder, intravascular catheters)
- Low platelet count (<98,000/mm3)

Annals of Gastroenterology 2003
SPONTANEOUS BACTERIAL PERITONITIS
Spontaneous Bacterial Peritonitis

ETIOLOGY:

- 60 to 72% - aerobic Grm (-) enteric bacteria
  - *Escherichia coli*: majority
  - Grm (+) *Cocci* - 29%
  - *Streptococcus* species - 19%
  - *Klebsiella* species - 13%
  - *Enterococcus* species - 5% Isolation of an
  - anaerobic organism – 5%

- *ascites has too high an oxygen tension to permit anaerobic growth*
Spontaneous Bacterial Peritonitis

- 87% - asymptomatic at the time of diagnosis
  - Fever (62-69%)
  - Abdominal pain (59-64%) - diffuse
    - Rigid abdomen - infrequent even if bowel perforation occurs
  - Other clinical features:
    - hepatic encephalopathy (44- 54%)
    - abdominal tenderness (49%)
    - diarrhea (7-32%)
    - ileus (5-30%)
    - shock (8-21%)
    - hypothermia (17%)
Spontaneous Bacterial Peritonitis

- Mortality rates at 1 and 2 yrs: 50-70% and 70-75%
- Predictors:
  - Higher MELD score (25+//-8 vs 19+//-7)
  - Hepatic encephalopathy
  - Hepatorenal syndrome
  - Mechanical ventilation
  - ICU stay during hospitalization

Bajaj GUT 2012 August; 61(8): 1219-1225
<table>
<thead>
<tr>
<th>Types</th>
<th>PMN ascitic fluid</th>
<th>Culture</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture negative neutrocytic ascites (CNNA)</td>
<td>≥250 cells /mm³</td>
<td>(-)</td>
<td>Should exclude: &gt; Previous antibiotic treatment &gt; hemorrhage &gt; HCC &gt; peritoneal carcinomatosis &gt; TB &amp; pancreatitis</td>
</tr>
<tr>
<td>Monomicrobial nonneutrocytic bacterascites (MNB)</td>
<td>&lt;250 cells/mm³</td>
<td>single</td>
<td>underling liver disease is usually less</td>
</tr>
<tr>
<td>Polymicrobial bacterascites</td>
<td>&lt;250 cells/mm³</td>
<td>multiple</td>
<td>Consequence of needle perforation of the gut during a diagnostic or therapeutic paracentesis</td>
</tr>
</tbody>
</table>

Other diagnostics:
Ascitic lactoferrin concentration: >242ng/ml Sensi: 96%/speci:97%
Spontaneous Bacterial Peritonitis

- Secondary bacterial peritonitis SHOULD be differentiated!
  - represents less than 10% of ascitic fluid infections in cirrhotic patients
  - usually polymicrobial and PMN≥250mm3 due to surgically treatable intraabdominal source of infection (e.g. perforated gut, perinephric abscess)
  - ascitic fluid analysis shows two or more of the following criteria:
    - total protein >1gr/dL and glucose <50mg/dL
    - LDH >225 U/mL (or higher than ULN of serum)
Integrated treatment of bacterial infections in cirrhotic patients
Diagnostic paracentesis

- NO: Ascites PMN >250
- YES: Start IV antibiotics

Repeat diagnostic paracentesis after 48 hours

- NO: Ascites PMN reduced by at least 50%
- YES: Broad spectrum antibiotic
  Investigate secondary peritonitis

Creatinine >1.0

- YES: Bilirubin >4.0
- NO: IV albumin

Switch to oral antibiotics for 3-5 days

Norfloxacin prophylaxis

No treatment unless clinical suspicion is high

SEMINARS IN LIVER DISEASE 2008
Treatment of infection
Early empirical IV antibiotics considering:
  * Type and severity of infection
  * Origin of infection (nosocomial vs. healthcare-associated vs acquired)
  * History of recent colonization or infection by multiresistant bacteria
Surgical or radiological interventions if needed

Prevention of renal failure in SBP
* IV administration of 20% albumin:
  - In patients at risk for renal failure (serum creatinine >1 mg/dl and/or bilirubin >4 mg/dl)
  - Dose: 1.5g/k at diagnosis and 1g/kg on Day3
* Diuretic withdrawal
* Avoidance of large volume Paracentesis

Prevention of renal failure in non-SBP infections
a. Diuretic withdrawal
b. Adequate IV and oral hydration
c. IV albumin?

Treatment or prevention of other complications
* Nonabsorbable disaccharides (lactulose or lactitol) to prevent or treat encephalopathy
* Maintenance of B blockers for EV bleeding prophylaxis
* Coagulation factors if bleeding?

Journal of Hepatology 2012
Treatment of SBP

- CEFOTAXIME
  - a 3rd generation cephalosporin
  - can achieve resolution of infection in 85% of patients with SBP

- **Dose**: 2.0 gr cefotaxime IV q8 or 12 hours

- **Duration**: 5 days of therapy has been shown to be as effective as a long course (10 days)

Annals of Gastroenterology 2003
Spontaneous Bacterial Peritonitis

- Risk factors for Recurrent episode of SBP
  - low (<1 g/dl) ascitic fluid protein levels
  - survived from a previous episode of SBP
  - gastrointestinal bleeding are at high risk to develop

- Prophylaxis
  - reduce the risk of recurrence
  - Improve the survival of this group of patients
  - mean % of patients free of infection is increased
## Current indications of antibiotic prophylaxis in cirrhosis

<table>
<thead>
<tr>
<th>Indication</th>
<th>Antibiotic and dose</th>
<th>Duration</th>
</tr>
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<tbody>
<tr>
<td>GI bleeding</td>
<td>Norfloxacin 400 mg/12 h PO&lt;br&gt;IV ceftriaxone 1 g/d in patients with advanced cirrhosis&lt;br&gt;(at least 2 of the following: ascites, jaundice, hepatic encephalopathy, and malnutrition)</td>
<td>7 days</td>
</tr>
<tr>
<td>Primary prophylaxis in patients with low protein ascites (&lt;15g/L)</td>
<td>Norfloxacin 400 mg/d PO in patients with advanced cirrhosis:&lt;br&gt;CPT&gt;9 points with Bili&gt;3mg/dl and/or impaired renal function (Crea&gt;1.2mg/dl; BUN&gt;25mg/dl or Na&lt;130meq/L)</td>
<td>Until OLT or death</td>
</tr>
<tr>
<td>Secondary prophylaxis</td>
<td>Norfloxacin 400 mg/d PO</td>
<td>Until OLT or death</td>
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Emergence of MDR

- Prevalence rate: 23%
  - higher incidence of treatment failure, septic shock and hospital mortality.
  - lack of efficacy of the currently recommended empirical antibiotic therapy
  - clearly ineffective in nosocomial infections (60% of treatment failure)

- CULPRIT:
  - ESBL producing Enterobacteriaceae – 14%
  - Enterococcus faecium – 12%
  - P. aeruginosa – 6%
  - MRSA – 6%
<table>
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<tr>
<th>Risk Factor</th>
<th>HR</th>
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<tbody>
<tr>
<td>Nosocomial infection</td>
<td>4.43</td>
</tr>
<tr>
<td>Long term Norfloxacin prophylaxis</td>
<td>2.69</td>
</tr>
<tr>
<td>Infection by MDR bacteria (last 6 months)</td>
<td>2.45</td>
</tr>
<tr>
<td>Use of B lactam (past 3 months)</td>
<td>2.39</td>
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Proposed Empiric Treatment Strategy for Nosocomial Infection

- **Nosocomial SBP and SB:**
  - carbapenems or with tigecycline to cover ESBL-E

- **Uncomplicated UTI:**
  - oral nitrofurantoin or fosfomycin

- **UTI associated with SIRS:**
  - carbapenem plus a glycopeptide (to cover ESBL-E and E. faecium)

- **Cellulitis:**
  - ceftazidime plus a glycopeptide (to cover MRSA and P. aeruginosa)

- **HCA and nosocomial pneumonia:**
  - carbapenems or ceftazidime plus levofloxacin plus a glycopeptide

HEPATOLOGY 2012;55:1551-1561
Antibiotic prophylaxis is not recommended in patients with ascites who are not hospitalized with an episode of GI hemorrhage and who do not have a history of SBP.
Initial resuscitation, early diagnosis, and antibiotic treatment

GOLDEN PERIOD: first 6 hours

- Treat sepsis-induced tissue hypoperfusion
  - mean arterial pressure ≥65 mmHg
  - CVP between 8 and 12 mmHg
  - central venous oxygen saturation ≥70%
  - urine output ≥0.5 ml/k/h

Crit Care Med 2008;36:296–327
Initial resuscitation, early diagnosis, and antibiotic treatment

- Broad-spectrum antibiotics within the FIRST hour of recognizing severe sepsis or septic shock

- De-escalation
  - should be done once the susceptibility profile of the responsible bacteria is known

- Prompt admission of the patient to the ICU
Fluid and Vasoactive Agents

- **FLUIDS**
  - *Crystalloids*
    - Requires > fluid to achieve the same goals
    - > edema
  - *Albumin*
    - associated with a decrease in mortality compared to other solutions in non-cirrhotic patients with sepsis

*norepinephrine and dopamine*
  - FIRST LINE

*Vasopressin*: second-line therapy

Intravenous Albumin

- reduces the incidence of renal impairment (from 33% to 10%)
- improves hospital survival (from 71% to 90%) in patients with SBP

**Mechanism of Action:**

- plasma expander increasing cardiac preload
- attenuates endothelial dysfunction increasing peripheral vascular resistance.

- Dose: 1.5 g/kBW D1 → 1g/kBW on day 3

- High risk patients that will benefit with IV albumin:
  - bilirubin >4mg/dl
  - creatinine >1.0mg/dl
  - high risk for the development of HRS (incidence between 33% and 57%)
STRESS Dose Steroids

- improves shock reversal
  - Relative adrenal insufficiency (RAI) - an inappropriate adrenal response to stress
  - frequent in non-cirrhotic patients with septic shock and is associated with refractory shock and mortality

- Current guidelines only recommend stress dose steroids in patients with vasopressor-unresponsive septic shock
- The clinical impact of stress dose steroids on the outcome of cirrhotic patients with septic shock is unclear

Hepatology 2006;44:1288–1295
Glucose Control

- Tight blood glucose control (80-110 mg/dL) with insulin therapy did not reduce mortality rates, but induced more hypoglycemic events compared to conventional strategy (180-200 mg/dL).

- Intensive insulin therapy increased the 90-day mortality rate compared to targeting 144-180 mg/dL.
Vaccination

- Pneumococal Vaccination
  - influenza virus
    - the risk of direct damage or allograft reinfection is substantial
  - Adequate protection: 92% to 95% of liver transplant recipients

- Vaccination in Chronic Liver Disease
  - Hepatitis A and B superinfection
    - higher morbidity and fatality rates than in healthy persons
  - advocated in patients with chronic liver disease, including those waiting for transplantation

*Semin Crit Care Med 2012;33:80–95*
Nutrition

- branched-chain amino acids
  - effective in restoring neutrophil phagocytosis

- mixture of arginine, omega-3 fatty acids, and nucleic acids
  - hepatic encephalopathy

Parenter Enteral Nutr 2006;30(2):91–96
Measures to decrease bacterial translocation

**ANTIBIOTIC**

(1) “selective intestinal decontamination” (SID)

**NON ANTIBIOTIC approach**

(1) changing the composition of gut bacterial flora through the administration of pre/probiotics or bile acids

(2) by accelerating intestinal transit (thereby decreasing IBO) through the use of prokinetics or b-blockers
NON ANTIBIOTIC PROPHYLAXIS
Probiotics

- Mechanism is largely speculative
- promotes the integrity of the gut barrier by normalizing intestinal permeability
- controls intestinal inflammatory responses by modulating the release of cytokines
- **Lactobacillus casei**
  - improves neutrophil phagocytic capacity and modulates cytokine production and TLR expression
B blocker

- slows intestinal motility in cirrhosis

- pharmacologically induced reductions in portal pressure have been associated with reductions in the development of SBP

Bile acids

- affect the microflora and integrity of the SI
- oral administration of conjugated bile acids, such as cholylsarcosine and cholylglycine in ascitic cirrhotic rats, results in a reduction in bacterial overgrowth, BT, and endotoxemia and an increase in survival
- RCTs needed

CIRRHOSIS

Sources other than gut

Systemic antibiotics

Bacterial infections

SIRS / Sepsis

Relative adrenal insufficiency

Norfloxacain
Probiotics
Prokinetics
Bile Acids

↑ Vasodilatation

↑ Hyperdynamic circulation

Hydrocortisone

Further vasodilatation

- Hypotension
- Renal dysfunction
- Encephalopathy
- Coagulopathy

- Variceal growth and hemorrhage
- Ascites

Albumin
VCs
ECAD?

Septic shock

Death

Seemars in Liver Disease/Volume 28, Number 1 - 2008
Spontaneous Bacterial Empyema
Cirrhotic hydrothorax
- large pleural effusion (>500ml) in cirrhotic patients, +/- ascites, in the absence of primary pulmonary or cardiac disease
- 4% to 6% and up to 10% in advanced liver disease
- almost half also have spontaneous bacterial peritonitis.

Annals of Gastroenterology 2003
Spontaneous Bacterial empyema

- **MECHANISM:**
  - transfer of peritoneal fluid directly via defects in the tedious portion of diaphragm from the abdominal cavity to the pleural space.
  - The unidirectional flow of fluid from the abdomen to the chest and the evidence of pressure gradient between the two cavities

Annals of Gastroenterology 2003
Spontaneous Bacterial empyema

- most frequent causative organisms:
  - Gram (-) bacilli particularly E. coli.
  - same pathogenesis as that of SBP
  - infection of the fluid in the thoracic cavity as an effect of spontaneous bacteremia or the passage of infected ascites from the abdomen through the diaphragm
- should be suspected when fever and dyspnea
Spontaneous Bacterial empyema

Diagnosis:
- (+) pleural fluid culture and PMN >250 cells /mm3
- (-) culture with PMN > 500 cells/mm3

EXCLUDE:
- HIV infection
- parapneumonic infections with CXR and CT
- Patients who underwent variceal sclerotherapy during the previous week
Spontaneous bacterial empyema

- **Treatment:**
  - cefotaxime 2 g/12 h IV or ceftriaxone 1 g/12-24 h IV or amoxicillin-clavulanic acid 1-0.2 g/6-8 h IV

- Intestinal decontamination with norfloxacin appears to be effective in preventing the recurrence of infection
  - may decrease with time because of emergence of MDR
Spontaneous bacterial empyema

Criteria for chest tube insertion:
- frank pus
- pH < 7.1
- glucose levels < 40 mg/dl
Pneumonia

7% to 23% - aspiration of oropharyngeal contents
Organisms:
- Streptococcus pneumonia
- Hemophilus influenzae
- Klebsiella
- Mycoplasma and Legionella species
- Anaerobes (mostly Peptostreptococcus, Bacteroides melaninogenicus and Fusobacterium nucleatum)

TREATMENT:
Macrolide or a quinolone (levofloxacin), along with cephalosporin
- HAP: gram negative organisms and staphylococci
Pneumonia

- Other risk factors:
  - Gastrointestinal bleeding
  - upper GI endoscopy
  - ascites

- Empiric treatment with cefipime is a reasonable first choice with the addition of clindamycin if aspiration pneumonia is possible

Soft Tissue Infection

- Lymphangitis of lower extremities
- Cellulitis of lower extremities or abdominal wall
- Organisms:
  - Gram (+) cocci; Gram (-) bacilli
    - frequent in cirrhotic patients with ascites and generalized edema
- DOC: amoxicillin-clavulanic acid 1-0.2 g/6-8 h IV or ceftriaxone 1 g/12-24 h IV + cloxacillin (2 g/6 h IV)

Annals of Gastroenterology 2003
Endocarditis

- prior invasive procedures that increase the risk of bacteriemia
- Incidence: 0.34% cirrhosis vs 0.1% without cirrhosis
- ? aortic or mitral valve (unclear)
- Pathogens: S. pneumonia, E. coli and S. aureus

Potential sources:
- upper gastrointestinal bleeding
- pneumonia
- SBP
- heart catheterization
- abdominal abscess
- TIPS placement and hip replacement
### Other infections in patients With Cirrhosis

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<thead>
<tr>
<th>Infectious Complication</th>
<th>Incidence, Characteristics, and Risk Factors in Cirrhosis</th>
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</table>
| RTI                     | - Bacterial decontamination may significantly influence incidence, but not mortality, of septicaemia  
* Incidence ranging from 13.6% to 48.1% of all infections |
| UTI                     | - Incidence: 7% to 74.1% of all infections  
* *Enterococcus faecalis* - 20% of cases  
* Possible relationship with hepatic encephalopathy  
* Recurrent UTIs implicated in PBC as AMA inducers  
Tx: cefotaxime 2 g/12 h IV or ceftriaxone 1 g/12-24 h IV  
or amoxicillin-clavulanic acid 1-0.2 g/6-8 h IV in patients with sepsis.  
Ciprofloxacin 500 mg/12 h PO or cotrimoxazole (160-800 mg/12 h PO) in uncomplicated infections* |
### Other infections in Patients With Cirrhosis

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<thead>
<tr>
<th>Specific Infectious Complication</th>
<th>Incidence, Characteristics, and Risk Factors in Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Meningitis</strong></td>
<td>More commonly reported in alcoholic cirrhosis; overall one month case fatality rate may exceed 50%; <em>Streptococcus pneumoniae</em>, <em>Escherichia coli</em>, and <em>Listeria</em> the commonest pathogens implicated; nuchal rigidity may be a delayed or even absent clinical sign; mortality may reach 80% in Child-Pugh stage C</td>
</tr>
<tr>
<td><strong>Hepatic abscess</strong></td>
<td>• Mortality exceeding 60% for nonalcoholic cirrhotic patients</td>
</tr>
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American Journal of Gastroenterology  2005
Special Population
Alcoholism

- most important predisposing factor for the development of pneumonia
- S. pneumonia
- anaerobic bacteria
- H. influenzae
- G(-)bacilli, particularly K. pneumoniasiae

- prone to develop pulmonary or peritoneal TB
- Dx: Laparoscopic investigation
- Symptoms:
  - low grade fever
  - high protein ascitic fluid
  - lymphocyte elevation
Esophageal Variceal Ligation

Infectious complications:

- Bacteremia
  - introduction of microorganisms via the sclerotherapy needle or contaminated water solution
- meningitis
- subdural empyema
- Perinephric abscess
- cerebral abscess
- Endocarditis
- bacterial peritonitis
Esophageal Scleotherapy

- bacteria translocate through intestinal walls
- calculated risk of developing peritonitis:
  - Elective EVS: 0.5%
  - Emergency EVS: 3%

Isolates:
- Klebsiella pneumoniae
- streptococcus sanguis
- Enterococcus, Streptococcus group B, Staphylococcus aureus, Escherichia coli, Citrobacter freundii.
EVL vs EVS

- 10x LOWER after EVL than after EVS

- Mechanical strangulation of varices by EVL using small elastic rings, may obliterate the submucosal venous channels and thereby diminish the entrance of bacteria to the blood stream

- Gram positive skin and oropharyngeal microorganisms (EVL):
  - Streptococcus pyogenes
  - Staphylococcus epidermidis
  - Staphylococcus aureus and Dipheroid species
Prophylaxis prior to EVL/EVS

- valvular heart disease
- prosthetic valves
- previous endocarditis
- previously undergone splenectomy
- patients with Childs C class cirrhosis
- recent history of variceal bleeding
- past history of bacterial peritonitis
- co morbid immunosuppressive condition
Key Points

- Bacterial infection is one of the most frequent complications and the first cause of death in cirrhosis.

- Immune defects, mainly acquired but also genetic, and bacterial translocation are the main mechanisms involved in its pathogenesis.
Key Points

- Early diagnosis of infection is pivotal. CRP, prolactin and SIRS criteria have less diagnostic accuracy in cirrhosis. New diagnostic tools are clearly needed.

- Whole third generation cephalosporins continue to be the gold standard antibiotic treatment of many of the infections acquired in the community.
Key points

- IV albumin reduces the incidence of renal impairment and improves hospital survival in patients with SBP and poor liver or renal functions.

- Restriction of prophylactic antibiotics to the high risk populations will reduce the spread of multidrug resistant bacteria in cirrhosis.