INFEZIONI DELLE BASSE VIE RESPIRATORIE (LRTI): ASPETTI CLINICI E DIAGNOSI MICROBIOLOGICA

I percorsi diagnostici microbiologici nel paziente immunocompromesso

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The term “immunocompromised host” describes a patient who is at increased risk for life-threatening infection as a consequence of a congenital or acquired abnormality of the immune system.

During the past few decades, the population of immunocompromised hosts has expanded enormously, reflecting the increased use of immunosuppressive therapies used in solid-organ and haematopoietic transplantations, cancer and systemic illnesses. In addition, acquired immunodeficiency syndrome (AIDS) has resulted in the existence of many immunocompromised patients.

The respiratory system, which is extensively connected with the environment, is a favourite target for microorganisms, usually pathogenic, or otherwise with scarce pathogenic activity (opportunistic), both exacerbating their virulence in immunocompromised patients.
In the immunocompromised hosts, enhanced susceptibility to a subset of pathogens depending upon the nature of the underlying immune defects:

- abnormalities in neutrophils
- T lymphocytes
- B lymphocytes

In clinical practice, mixed patterns of immunodeficiency are frequently present.

The etiologic agents of pneumonia in the immunocompromised host consist not only of the same agents that cause pneumonia in the immunocompetent host but also of a large number of opportunistic agents:

- bacterial infections
- viral infections
- fungal infections
- parasitic infections
Timeline of infectious complications (pulmonary and nonpulmonary) after solid organ transplantation.

Fishman and Rubin  (NEJM;338:1741-1751)
Pneumonia is defined as the presence of clinical signs and symptoms of LRTI, along with radiological changes that are consistent with pneumonia. An assessment of illness severity should be made clinically.

On this basis, this algorithm deals with the investigation of patients presenting with pneumonia that is judged to be either clinically mild or severe. Pneumonia that may be judged to be moderate can still reflect a significant risk of mortality and therefore, should be investigated as for severe pneumonia.

The collection of diagnostic samples (respiratory, urine and blood) should be carried out before the administration of antimicrobials in order to increase the likelihood of a microbiological diagnosis but initiation of treatment should not be delayed in severe cases.

If this is not possible, then samples taken for bacterial diagnosis should be collected at a maximum of 24 hours from the start of antimicrobial therapy whenever possible.

In patients who are immunocompromised, microbiological investigation should be carried out to the same extent if they are judged to have mild or severe pneumonia. This is due to the fact that the presentation of pneumonia in this patient group can be atypical and the CURB-65a scoring system has not been validated for them. In addition, progression from mild to severe illness can be rapid.
LRTI nel paziente immunocompromesso

Le differenze fondamentali rispetto all’approccio nel paziente immunocompetente consistono nella ricerca maggiormente orientata all’individuazione di virus, batteri, funghi e parassiti che caratterizzano il diverso inquadramento etiologico delle LRTI che insorgono nel paziente immunocompromesso.
Pneumonia in immunocompromised adults

Clinical History / Patient group

Mild / Moderate / Severe pneumonia

Sample type

Blood

Respiratory sample for virus and atypical bacteria detection

Urine

Sputum or induced sputum

BAL

Primary testing

Blood culture

Respiratory virus PCR screen

Mycoplasma pneumoniae

Chlamydia sp.

Secondary testing

CMV

Specific Aspergillus / Cryptococcus investigation

Mycoplasma pneumoniae

Chlamydia sp.

CMV

Mycoplasma pneumoniae

Chlamydia sp.

CMV

Legionella

Mycobacterium sp.

Legionella

Nocardia Investigation

NTM

Blood → Blood culture → MALDI-TOF-MS / PCR-ESI-MS

Multiplex PCR (bacterial, fungal infections) / MALDI-TOFMS / PCR-ESI-MS
### Fungal infections in immunocompromised hosts

| **Aspergillus spp.** | Invasive pulmonary aspergillosis: increasingly common problem in hospitalised patients, especially in patients immunocompromised, those receiving systemic corticosteroids and those with prior pulmonary disease. The majority of cases occurred within the first 90 days. **Diagnosis of invasive aspergillosis can be problematic**

- *Aspergillus* is cultured from sputum in only 8-34%, from BAL in 45-62% in patients with invasive disease, from respiratory tract cultures 28-55% in organ transplant recipients, with the highest rates of airway colonization after lung transplantation. **Serological** studies have historically been unhelpful.

- Detection of *serum galactomannan antigen* (a polysaccharide cell wall component of aspergillus) EIA has a sensitivity of 80-96% (HSCT, neutropenia, hematologic disease), 30% in lung transplant for the diagnosis of invasive aspergillosis.

- Detection of *galactomannan antigen in BAL*: greater sensitivity and specificity (67-100% and 91-98%)

- **PCR Aspergillus DNA in BAL**: sensitivities similar to galactomannan detection. Use of both has been recommended to improve sensitivity.

| **Candida spp.** | *Candida sp.* are the most frequent cause of nosocomial fungal colonization/infection in solid organ transplant patients causing 98% of fungal infections in a series of patients in a transplant ICU (*C. albicans*, *C. tropicalis*, *C. krusei*). In lung transplant recipients < 10% of patients colonized with *candida* species develop invasive disease. Pulmonary candidiasis is quite rare, more often in conjunction with disseminated candidiasis. Proving a «true» *Candida* pulmonary infection can be difficult. Therefore, the diagnosis often requires lung biopsy.

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Wheat LJ Transpl Infect Dis 2006;8 :128-139
**Fungal infections in immunocompromised hosts**

**Pneumocystis jiroveci**

P. *jiroveci* is the **commonest cause of severe pneumonia** in patients with advanced HIV infection, and defines AIDS. It also occurs in numerous other immunocompromised adults and children, although co-trimoxazole prophylaxis is effective in the majority of cases.

The greatest risk of *Pneumocystis jiroveci* pneumonia falls between 2 - 6 post-transplantation months. The risk declines significantly beyond the first year for all groups except lung transplant recipients.

**Pneumocystis pneumonia** before chemoprophylaxis organ-specific prevalence rates:

- kidney and heart transplant recipient  4%
- liver transplant patients  11%
- allogenic HSC transplant recipient  16%
- heart-lung recipients up to  33%
- HIV infected person (before 1995 from 4,9 cases/100 person-years to 0,3 cases/100 person-years after 1998

**Laboratory diagnosis**

- Lack of a reliable culture system
- Microscopy: cytological stain or immunofluorescence assay (cysts and/or trophic forms)
- **Molecular methods**: several PCR/ Realtime PCR ⇒ BAL and sputum most useful clinical samples

**Pneumocystis colonization**

Healthy children ⇒ 10,5%; infant with respiratory symptoms and/or bronchiolitis ⇒ 15%
Adults most healthy people are not colonized; patient with respiratory disorder ⇒ 7%-19%;
pregnant women ⇒ 16%; HIV-infected ⇒ 10-69%

⇒ ⇒ ⇒ Quantitative molecular methods

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Cryptococcus Neoformans

*Cryptococcus neoformans* causes the **vast majority of cryptococcal infections** in immunosuppressed hosts, including patients with AIDS: it is the most common fungal pulmonary infection in AIDS patients who have CD4 < 100 cell/mmc (usually coexists with cryptococcal meningitis).

**Cryptococcosis prevalence rate**
- 19 patients/31 patients with cancer- pulmonary involvement (61%).
- SOT 2.8%, the CNS was the most commonly affected site: 55% of patients had CNS infection alone, 6% of patients had pulmonary infection only, and 24% had infection at more than 1 site.

**Laboratory diagnosis**

*C. neoformans* can be isolated on most **routine media**: detected from **3 to 7 days** after

- Standard **blood culture** methods routinely identify *C. neoformans* and confirm a diagnosis of cryptococcemia (up to 75% of patients with HIV-1–associated cryptococcal meningitis will have positive blood cultures).

**Clinical specimens staining** India ink staining (encapsulated yeast cells): yeasts are easily highlighted on routine Gram stains.

**Antigen detection (capsular polysaccharide)**
- **Serum**: especially in patients with AIDS
  - In cryptococcal lung disease test highly effective at identifying active disease, it does not discriminate the site of infection. Often require a second diagnostic procedure: biopsy or sputum examination
- **Cerebrospinal fluid** (CSF) in patients who have meningitis or meningoencephalitis detection of is both sensitive and specific (90%, 95%)
- **BAL** in patients with pneumonia (BAL 100%, serum 2/3 of patients, fungal stain only 1/3)

**Serology**: antibody response no role in diagnosis of cryptococcosis
Bacterial infections in immunocompromised hosts

*Nocardia spp.*

Infections caused by *Nocardia* are **infrequent but challenging** to clinicians: the incidence of *Nocardia* pneumonia has declined substantially with the use of trimethoprim-sulfamethoxazole **prophylaxis**, however, it continues to be reported

- **In the early era** of organ transplantation, *Nocardia* infections were relatively common, with a prevalence of 2–13% documented in several large series
- **More recent case series** have suggested a lower frequency of infection, on the order of 0.2–2.1%, mainly lung transplant and heart transplant recipients

**Mortality** directly attributable to *Nocardia* infection ranges from 0 to 30% among the various SOT populations

Infection due to this aerobic, gram-positive filamentous rod is **most common beyond the first month after transplantation**

**Laboratory diagnosis is difficult and requires a high index of suspicion**

- **Diagnostic specimens**: BAL, lung biopsy, pleural fluid and sputum culture
- **Microscopy**: initial visualization is often not possible with routine stains
- **Standard culture methods**: growth slowly on the standard medium for bacterial cultures; identification (routine phenotypic testing; a real-time PCR assay (of 16S rDNA) ⇒ melting-curve analysis to identify *Nocardia* spp.)
- **Serological methods**: usefulness limited by the variety of species, potential lack of sensitivity in immunocompromised patients

If *Nocardia* is suspected, cultures should be held longer to ensure that this diagnosis is not missed

# Viral infections in immunocompromised hosts

<table>
<thead>
<tr>
<th>CMV</th>
<th>CMV is still the most important virus affecting immunocompromised patients (in the absence of antiviral prophylaxis 20-35%)</th>
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<tbody>
<tr>
<td></td>
<td><strong>CMV pneumonia incidence</strong></td>
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<tr>
<td></td>
<td>– HSCT 10-30% in allogenic recipients (mortality rate 4 ⇒ 0,8%)</td>
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<tr>
<td></td>
<td>– SOT recipients: lung 10-55%; liver 9,2%; heart 0,8-8% , renal &lt;1%</td>
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<td><strong>Lungs are a major organ site of CMV latency and recurrence</strong></td>
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<td>higher burden of latent viral CMV genome than other organs</td>
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<td></td>
<td>– Lymphoma 82% (mortality rate 30%); non-Hodgkin lymphoma (89%)</td>
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<tr>
<td></td>
<td>– HIV patients connotation of CMV pneumonia is not clear, often not the only pathogen</td>
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## Diagnosis

**EDTA - blood samples ⇒ QNAT (QPCR) CMV DNA**

Dynamic determination of CMV-DNA may predict the occurrence of CMV-IP (Interstitial Pneumonia).

**Viral loads > 10^4 copies/mL plasma** continuing for 3 weeks may serve as a cutoff to predict CMV-IP (Renal transplant recipients)


**Monitoring CMV infection in both blood samples and lungs (BAL) may improve preemptive therapy efficacy** (Lung transplant Recipients)

Appears highly advisable to monitor HCMV infection in lungs of LTR for the following reasons:

(i) a high HCMV load in BAL (> $5 \times 10^5$ copies/mL) was clearly associated with HCMV pneumonia

(ii) early HCMV infection in blood has been associated with a greater risk of developing BOS (bronchiolitis obliterans syndrome) ($3.0 \times 10^5$ DNA copies/mL whole blood= cutoff for systemic infection)

(iii) lung infection may occur in the absence of systemic infection, as reported in other studies and as shown in this study, where two patients with histologically proven HCMV pneumonia had viral load in blood< cutoff for initiating pre-emptive therapy

In this report, for preemptive therapy we selected a cutoff of $1.0 \times 10^5$ DNA copies/mL BAL
## Viral infections in immunocompromised hosts-2

### HSV

<table>
<thead>
<tr>
<th>HSV1 and HSV2 have been reported to cause pneumonia in HSCT recipient, liver transplant, patients with solid tumors.</th>
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<tbody>
<tr>
<td>However, it is difficult to distinguish between asymptomatic shedding of the virus and disease.</td>
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</table>

**Quantitative detection of HSV DNA in BAL** is a potential diagnostic tool for detection of relevant viral infection of the lower respiratory tract.

- Patients with HSV DNA levels \( \geq 7.5 \) log had severe respiratory failure

### VZV

<table>
<thead>
<tr>
<th>Pneumonia HSCT or SOT recipients (lung transplant): evidence for the diagnosis of varicella pneumonia viral inclusion bodies on histology</th>
</tr>
</thead>
</table>

- Pneumonia HSCT recipients: visceral VZV disease \( \approx 6 \) months after transplantation
  - **PCR in whole blood** \( \Rightarrow \) VZV DNA detection
  - **PCR quantification** VZV DNA \( \Rightarrow \) possible usefulness for assessing the effectiveness of treatment
  - **Ishizawa J et al.** Int. J.Hemat. 2006: 242-245

### HSV1, HSV2 and VZV: rare causes of LRTI

- Pneumonia is typically due to reactivation of a latent infection and is now infrequent \( \leftrightarrow \) prophylaxis
### Viral infections in immunocompromised hosts-3

<table>
<thead>
<tr>
<th>ADENOVIRUS</th>
<th>Important causa of morbility and mortality in patients immunocompromised, particularly children, neonates and HSCT</th>
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<tbody>
<tr>
<td></td>
<td>Immunocompromised hosts may experience reactivation of latent infections</td>
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<tr>
<td></td>
<td>Infection usually occurs in the first 3 months post-transplant and may be organ specific (e.g., pneumonia) or infection disseminated</td>
</tr>
<tr>
<td>HSCT</td>
<td>Adenoviruses 2,5 (species C, often showing a more severe course of illness), 34,35 (sub-species B2), and 31 (species A) have been isolated from HSCT recipients with respiratory diseases (children incidence up to 31%)</td>
</tr>
<tr>
<td>SOT</td>
<td>Serotypes 1 and 2 (subgroup C) are more commonly associated with pneumonia</td>
</tr>
<tr>
<td>HIV</td>
<td>Adenovirus in 7.4% of patients with CAP, but is almost always associated with multiple other pathogens</td>
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#### Diagnosis

**Respiratory viruses screening**

- **Adenovirus DNA:** viral load quantification (qRT-PCR), in serum or plasma marker ⇒ detecting ⇒ monitoring disease progression ⇒ treatment response in patients immunocompromised, particularly in HSCT

- **PCR whole blood** ⇒ significant screening method in pediatric HSCT (asymptomatic patients who are at risk for progressive adenoviral disease)

- **No specific threshold** although **viral loads >1 x 10^6 copie/mL** ⇒ increased likelihood of death in HSCT recipients

- **Statistically significant differences between viral loads of different AV types**

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<table>
<thead>
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<th>EBV</th>
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| There is a **high prevalence** of EBV infection in immunocompromised patients, transplant receivers, acquired human immunodeficiency virus and non-Hodgkin lymphoma.

EBV has a **central role in the pathogenesis** of Post Transplantation Lymphoproliferative disorder (PTLD) although not all PTLD is EBV-related.

Rermitting-relapsing EBV infection is common in transplant recipients and may reflect relatively excessive immune suppression

Primary EBV infection presenting as pneumonia in recent HSCT recipient (donor seropositive ⇒ EBV-seronegative transplant recipient)

**Quantitative PCR** for EBV DNA → samples of blood and nasopharyngeal secretions, were highly positive: 123000 copies/mL and 1344 copies/mL, respectively


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**Diagnosis acute EBV infection or PTLD**

- **Seroologic testing** is not useful
- **Quantitative EBV viral load** testing helpful for the diagnosis and management PTLD
  - serial assays of whole blood may be useful in individual patients
  - specific diagnostic levels of viral loads are not available

**EBV assays are not standardized and cannot be easily compared between centers**

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<thead>
<tr>
<th><strong>Serology</strong></th>
<th>In general is not useful for initial diagnosis and has reduced sensitivity among transplant recipients</th>
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</thead>
</table>
| **Virus culture** | • For most of the common DNA /RNA virus except Rhinovirus, Coronavirus....  
• Special cell lines and condition are need to grow these viruses and culture tend to be inefficient:  
  several cell lines (3-21 days) >> shell vial assay/ fixed mixture of cells  
  + monoclonal/polyclonal antibodies-FITC (24-48 h) |
| **Direct fluorescent assay (DFA)** | Direct antigen detection in a specimen (IFA, enzyme-linked immunoassay, immune chromatography)  
  - Can detect several viruses from a single specimen  
  - Good clinical specificity and short turn-around time < 2 h  
  - Sensitivity can be lower than reported in licensing studies  
Lack of reagents for some the viruses (eg. rhinovirus,coronavirus) , Less sensitivity in detecting dual infections, sensitivity can be substantially Lower among immunocompromised patient |
| **Nucleic acid testing** | Nucleic acid amplification assays  
  **Most sensitive diagnostic tool** available to screen for a wide range of pathogen in tandem  
  ⇒ multiplex testing platform  
  ⇒ microbead-based assay ⇒ microarray and nanotechnologies  
Many have been tested in transplant population  
PCR is the preferred testing method for immunocompromised patients |
### Respiratory virus screening

**Viral PCR screen** is the same for patients who are immunocompetent and immunocompromised.

Respiratory samples for viral PCR screening are ideally **lower respiratory tract samples** such as an induced sputum, BAL or endo-tracheal aspirate. Where this is not possible, a nose/throat swab is acceptable.

<table>
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<th>Types of samples</th>
<th><strong>Upper Respiratory Tract</strong></th>
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<tr>
<td></td>
<td>• nasopharyngeal aspirate</td>
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<tr>
<td></td>
<td>• nasopharyngeal swab, nose /throat swabs (combined) preferably flocked for nasal sampling</td>
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<tr>
<th><strong>Lower Respiratory Tract infections</strong></th>
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<tr>
<td>Bronchoalveolar lavage (BAL) is the preferred sample, but is not commonly available</td>
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**Sputum** is an acceptable sample although this may present problems in processing due to the nature of the specimen which is frequently mucoid.

If a cough is non-productive and not severe enough to warrant taking a BAL sample then a sample from the upper respiratory tract may be the only sample available.

The quality of the sample is paramount in diagnosing respiratory virus infection.
### Respiratory viruses - old viruses: Influenza, parainfluenza, RSV, HMPV, Adenovirus

<table>
<thead>
<tr>
<th>SOT</th>
<th>Greater propensity for these pathogens to involve the lower respiratory tract ⇒ severe illness</th>
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<tr>
<td></td>
<td>SOT populations: the highest rates of infection in lung transplant recipients, up to 21% of whom develop respiratory viral infections</td>
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<td></td>
<td>Mortality rates in the range of 0–20% have been reported in association with respiratory viral infections in the various solid organ transplant populations</td>
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<tr>
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<td>Seasonality</td>
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<td><strong>RSV</strong> and <strong>Influenza virus</strong> infections ⇒ epidemics in the winter and spring months</td>
</tr>
<tr>
<td></td>
<td><strong>Adenovirus</strong> and <strong>Parainfluenza</strong> ⇒ infections throughout the year</td>
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<table>
<thead>
<tr>
<th>HSCT</th>
<th>These pathogens are recovered from up to 1/3 of HSC transplant recipients hospitalized with acute respiratory illnesses: <strong>RSV is most commonly isolated</strong></th>
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<tr>
<td></td>
<td>Outbreaks among the HSCT population tend to coincide with community outbreaks</td>
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<td></td>
<td>Most patients present initially with <strong>URI ⇒ pneumonia</strong> occurs frequently in association with <strong>RSV</strong> and <strong>parainfluenza</strong> infection but considerably less so with <strong>influenza</strong>, although postinfluenza bacterial pneumonias are a concern</td>
</tr>
<tr>
<td></td>
<td>Among patients with <strong>RSV</strong> infection, the <strong>risk of pneumonia ≈ 80%</strong> for those who are &lt; 1 month posttransplantation or still in the preengraftment stage, but falls to less than 40% for those beyond this critical period</td>
</tr>
<tr>
<td></td>
<td>Once pneumonia develops, <strong>mortality from untreated RSV infection approximates 80%</strong></td>
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<tr>
<td></td>
<td>Mortality associated with parainfluenza and influenza pneumonia is considerably lower</td>
</tr>
<tr>
<td></td>
<td><strong>hMPV (2001)</strong>: similar epidemiology and clinical course to RSV. Presence of copathogens, particularly RSV ⇒ more severe disease</td>
</tr>
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### Viral infections of LRT: new viruses and the role of diagnosis

**Rhinovirus**
- **Rhinoviruses** are the most common cause of URI, detection in asymptomatic persons is relatively common. Recent studies: rhinovirus can replicate at higher temperatures and infect the lower respiratory tract
  - ⇒ **genotypes** with **greater capacity** for LRT disease and severe disease
- Viral quantification may prove **helpful** to determine when an **isolate is associated** with severe disease
  - At high viral loads (> $10^6$ RNA copies/ml): HRVs may cause severe LRTI
  - At medium-low viral loads (<$10^5$ RNA copies/ml): may represent only bystander
- **Coinfections** with other pathogens ⇒ high morbidity and mortality of this infection

**Coronaviruses**
- **Human coronavirus NL63** (HCoV-NL63, Netherlands 2004) clearly been associated with croup and bronchiolitis and occasionally with pneumonia
- HKU1, NL63, OC43, and 229E were **isolated** from 2.2% of children hospitalized with respiratory disease
- Coronaviruses are being increasingly found in immunocompromised patients and those with underlying pulmonary disorders, but there is little information on risk of progression to pneumonia

**HBoV**
- **Bocavirus** **isolated** in 2005 (DNAss, family *Parvoviridae*) in NPA specimens (also in stool and in serum) from children with respiratory tract infection
- Bocavirus frequently in conjunction with other pathogens and detected for prolonged periods ⇒, viral load were significantly higher in patients with only bocavirus than in those with coinfection
  - ⇒ accumulating data support the **role of bocavirus as a true pathogen** ⇒ clinical profile and role as a causative agent of respiratory disease **is still not clear**
The challenge of respiratory virus infections in hematopoietic cell transplant recipients

Improved molecular detection

- RSV, hMPV, PIV and Influenza virus are well known for their potential ⇒ fatal pneumonia
- New viruses hMPV, coronavirus, bocavirus, and rhinovirus

Early identification allow effective cohorting and isolation

For transplant recipients with respiratory infection, the ability to detect the full range of viral pathogens is critical

Largest potential societal benefit may come from reduction unnecessary use of antibiotics for LRTI in children: respiratory tract infections remain the most common reason for prescribing antibiotics, and each course of antibiotics adds selective pressure
Multiplex PCR: 490 specimens tested, 336 (68.6%) were positive for at least one respiratory virus

RSV A/ B (30%) > RHINO (16%) > AD (7%) > MPV (6%) > PIV (6%) > BOCA (5%) > COR (4%) > IA (3%) > IB (1%) ; Enterovirus (1%). Dual respiratory virus infections (8%), and only 4 triple virus infections

RV12 and RV15 increased our understanding of the epidemiology of respiratory viral infections and assist us in the diagnosing the etiology of respiratory tract infections in individual and in outbreak situation

Epidemiology of respiratory virus infections in children, the virus-specific positivity rates, and seasonality for respiratory virus infections, over a 24 months period (February 2010-2012)
Amplified PCR products using Seeplex® RV15 ACE Detection and result analysis.

B | B set
1. PIV2, PIV1
2. 229E/NL63, PIV3
3. AdV
4. AdV
5. 229E/NL63

A | A set
1. PIV2, PIV1
2. 229E/NL63, PIV3
3. AdV
4. AdV
5. 229E/NL63

C | C set
1. PIV4
2. MPV
3. HBoV, Flu B
4. HEV
5. HBoV

1~5: Clinical samples, N: Negative Control

Seeplex® RV15 OneStep ACE Detection is designed to test most currently known respiratory viruses by one-step multiplex RT-PCR:

- Flu A virus; Flu B virus; RSV A, B; MPV; PIV 1-4, Adenovirus A/B/C/D/E; Enterovirus; Bocavirus 1/2/3/4; Coronavirus 229E/NL63-OC43, Rhinovirus A/B/C
Multiplex Real-time PCR
Simultaneous detection of 16 respiratory viruses

Panel A
- Adenovirus (AdV)
- Influenza A virus (FluA)
- Influenza B virus (FluB)
- Parainfluenza virus1 (PIV1)
- Parainfluenza virus2 (PIV2)
- Parainfluenza virus3 (PIV3)
- Parainfluenza virus4 (PIV4)
- Rhinovirus A/B/C (HRV)
- Internal control (IC)

Panel B
- Respiratory syncytial virus A (RSV A)
- Respiratory syncytial virus B (RSV B)
  - Bocavirus 1/2/3/4 (HBoV)
- Coronavirus 229E (CoV 229E)
- Coronavirus NL63 (CoV NL63)
- Coronavirus OC43 (CoV OC43)
  - Metapneumovirus (MPV)
  - Enterovirus (HEV)
  - Internal control (IC)
LRTI nel paziente immunocompromesso

Le differenze fondamentali rispetto all’approccio nel paziente immunocompetente consistono nella ricerca maggiormente orientata all’individuazione di virus, batteri, funghi e parassiti che caratterizzano il diverso inquadramento etiologico delle LRTI che insorgono nel paziente immunocompromesso.

In questo contesto clinico e immunologico, se si intende garantire una diagnostica davvero efficiente ed efficace, non si può prescindere dai metodi molecolari, che permettono di rilevare anche microrganismi altrimenti non diagnosticabili con la medesima efficacia e sensibilità.

A. Camporese
Le Infezioni in Medicina, n. 4, 237-244, 2012