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Polmoniti non batteriche

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Le più comuni forme di polmoniti non batteriche: micotiche

Eziologia	Immunocompetente	Immunodepresso
Muffe angioinvasive Aspergillus, Mucomircosi		
Lieviti invasivi Criptococco, Candida		
Pneumocystis		
Funghi endemici Istoplasmosi, Blastomicosi, Coccidiomicosi		
Funghi emergenti Rasamsonia Argillacea, Emergomyces species		

Diagnostic Tests for Angioinvasive Molds

Organism	Clinical Manifestations	Gold Standard	Culture	Antigen Testing	PCR	Comments
Aspergillus spp. [1]	Respiratory colonization ABPA Aspergilloma IPA	Angioinvasion by acute angle, branching septate hyphae on histopathology with positive culture [6]	Sputum BAL	BAL GM Serum GM Serum BDG	Serum PCR BAL PCR	GM is commonly used to aid in diagnosis. Positive serum result should be repeated to confirm. PCR is not widely used in US.
		Limitations *Requires invasive biopsies*	*Limitations* *May represent infection or colonization; sensitivity is low [9]*	*Limitations* *GM low sensitivity, some false positive [13]* *BDG non-specific* *Effect of AF unknown*	*Limitations* *Single serum test with high sensitivity, repeated serum with high specificity [6]* *Effect of AF unknown*	
Mucor	Rhino-orbital-cerebral infection Cutaneous Pulmonary	Tissue invasion of wide-branching hyphae without septation [23]	Tissue Sputum BAL	BAL GM Serum GM	Currently unavailable for clinical use	GM is not used to diagnose Mucor and is classically negative. Positive GM may help identify co-infection or aide in AF selection.
		Limitations *Requires invasive biopsies*	*Limitations* *Low sensitivity; takes up to 7 days [25]*	Characteristically negative, but may be positive in some sub-species		

Abbreviations: ABPA- Allergic Bronchopulmonary Aspergillosis, AF- Antifungal, BAL- Bronchoalveolar Lavage, BDG- β-1,3-D glucan, GM- Galactomannan, IPA- Invasive Pulmonary Aspergillosis, PCR- Polymerase Chain Reaction, US- United States

[1] Tests are referring to the diagnostic tests used for IPA.

Diagnostic Tests for Invasive Yeast

Organism	Clinical Manifestations	Gold Standard	Culture	Antigen Testing	Molecular Testing	Comments
Candida spp.[1]	Blood stream infection Deep tissue infection	Blood or deep tissue culture [6]	Blood Urine Tissue	Serum BDG Mannan/ antimannan IgG	T2Candida panel	BDG may help rule out IC but lacks the specificity to be used as a stand-alone diagnostic test. Mannan/ anti-mannan IgG is not widely used in the US. T2Candida panel is not widely available.
		Limitations *Blood cultures only positive during candidemia; May require invasive biopsy*	*Limitations* *Prolonged time to positivity [31]*	*Limitations* *BDG is non-specific, should not be used in isolation to make diagnosis [6]* *Mannan/ anti-mannan have low sensitivity, but specific [32]*	*Limitations* *Only for Candidemia; may remain positive for several days after Candidemia has cleared [31]*	
Cryptococcus spp.	Pneumonia Meningoencephalitis	Culture Direct visualization of narrow budding, encapsulated yeast	Sputum BAL CSF Tissue	Latex agglutination EIA Lateral flow immunoassay *Can be tested on sputum, BAL, serum, CSF, urine, pleural fluid	Currently unavailable for clinical use	Antigen testing on serum or CSF is used most to make the diagnosis. Evaluate for CNS disease in immunocompetent patients with neurologic findings and high serum titer Evaluate for CNS disease in all immunocompromised patients
		Limitations *Delayed time to positivity [36]*	*Limitations* *Sensitivity dependent upon culture specimen [40]*	*Limitations* *False positive RF or other infections [35]*		

Abbreviations: BDG- β-1,3-D glucan, CSF- Cerebrospinal Fluid, EIA- Enzyme Immunoassay, IC- Invasive Candidiasis, RF- Rheumatoid factor, US- United States, CNS- Central Nervous System

[1] Tests are referring to the diagnostic tests used for IC, which includes candidemia and deep-seated tissue infections

Aspetti clinici

Fungo	Clinica	Note
Aspergillosi *	Dolore pleuritico, emottisi	Pazienti neutropenici e trapiantati
Mucomircosi	Versamento pleurico, >10 noduli, «alone inverso» Più comune: infezione dell'orbita.	Neutropenici, immunodepressi, diabetici, terapia steroidea
Candidosi	Forme sistemiche	Neutropenia, terapia antibiotica, device.
Cryptococcosi	Da asintomatico a ARDS. N.B. Meningoencefalite	Cryptococcus gattii nell'immunocompetente
Pneumocystis	Variabile	Comune in HIV con CD4<200/mm3

* Respiratory colonization, Aspergilloma, Allergic Bronchopulmonary Aspergillosis, and Invasive Pulmonary Aspergillosis (IPA)

Perché neutropenia è importante fattore di rischio?

- Perché i neutrofili, interagendo con funghi non fagocitabili, estrudono la cromatina (suicidio finalizzato), inglobando il fungo nella rete (NETOSI dove NET: neutrophil extracellular trap).
- Resta fermo che la linfocitopenia predispone a infezioni da Pneumocystis, Criptococcus, Blastomyces, Coccidioides.
- Invece, il difetto funzionale dei MN espone a infezioni da Aspergillus, Blastomyces, Cryptococcus neoformans, Coccidioides e Histoplasma.

Fungo	Visualizzazione	Antigeni	PCR	Altro
Aspergillo	Ife ramificate ad angolo acuto. Coltura nel BAL: specificità 90%, ma sensibilità 50%	Galattomannano: alta sensibilità in neutropenici, immunodepressi e su BAL. Beta glucano meno utile	Sensibilità e specificità>90% su **BAL**	Colture+ nell'immunocompetente: in genere colonizzazione
Mucorales	Grandi ife ad angolo aperto. Coltura difficile		In sviluppo	
Candida	Emocoltura negativa in forme localizzate, time to positivity lungo	Mannano e AB antimannano: spec 90%, sens 60%. Glucano: spec 60% e sens 80%, ma solo per forme invasive	+ per giorni dopo risoluzione della candidemia	Screening rapido: ricerca ife fungine nelle urine
Cryptococco	In coltura, non su striscio. Bene su BAL e biopsia transbronchiale	Ottimo su BAL		
Pneumocystis	Non si coltiva. Visualizzazione, anche di forme cistiche, con Ab	Beta glucano: in HIV sensibilità 90% e specificità 75% se vi sono sintomi	+Anche nei colonizzati Quantitativa: soglia per polmonite?	

Limiti di alcuni antigeni

- Galattomannano
- Contenuto in yogurt, formaggi e gelati e può essere assorbito (mucosite). Può essere prodotto da altri funghi (Penicillus, Fusarium, Zygomicetes)
- >> effettuare due dosaggi

- Beta Glucano
- Possibile falso + in rapporto a trasfusioni, emodialisi, altre micosi (ma non Cryptococcus e Mucorales), Ig endovena, by pass cardiopolmonare

Aspergillosis: an important complication of Covid19 presenting with nodules, cavitary nodules, airway thickening and bronchiectasis (Marr KA et al. Emerging Infect Dis 2021)

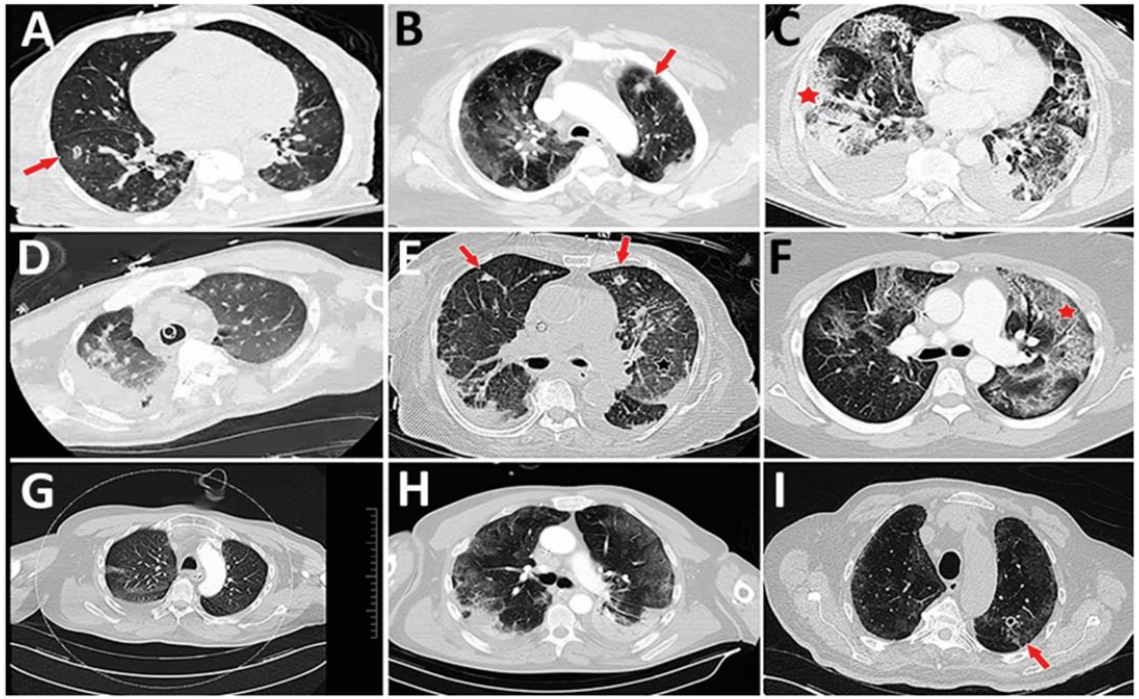
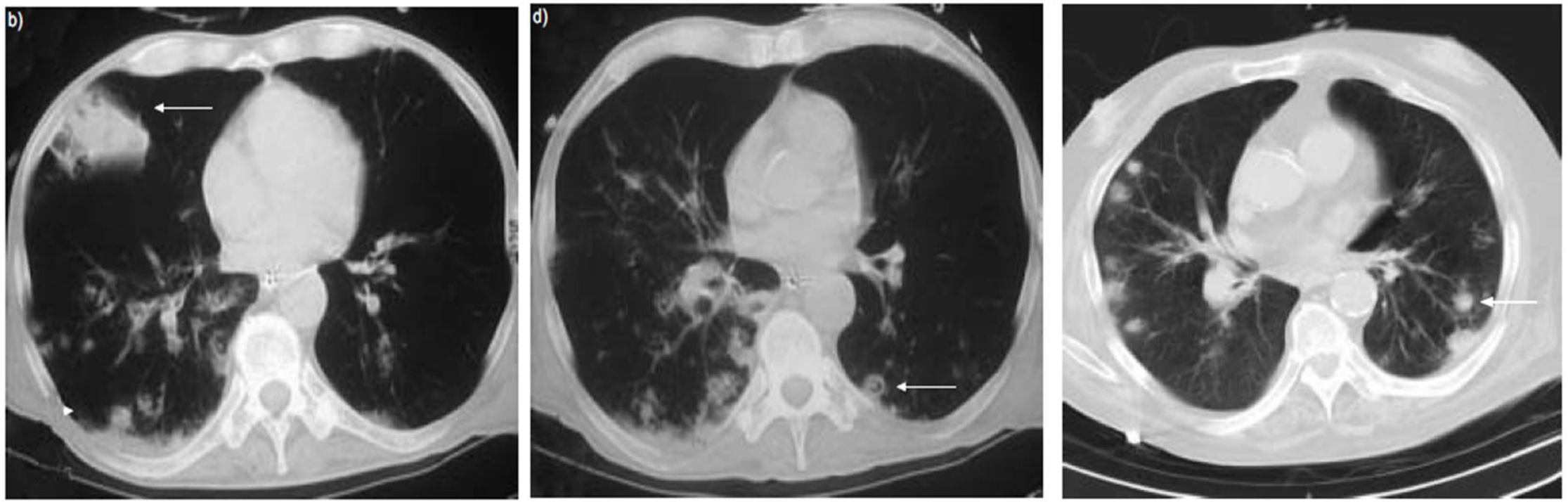


Figure 1. Representative computed tomography (CT) scans for 9 patients with aspergillosis complicating severe viral pneumonia in patients with coronavirus disease. Scans were obtained at or around diagnosis of coronavirus disease–associated pulmonary aspergillosis in this series of patients, described in the Table (https://wwwnc.cdc.gov/EID/article/27/1/20-2896-T1.htm). Corresponding case-patients are indicated with lettered superscripts in the radiology column of Table 1. Examples of nodules and cavitating nodules are indicated by red arrows, and prominent airway thickening and bronchiectasis in ground glass opacities are indicated by red stars.

Alcuni esempi di lesione da Aspergillo



Aspergillosi, la più comune forma di VAP

- Sempre più comune in malati critici, TBC, BPCO e sarcoidosi.

- Perché speso resiste agli azolici in difetto di esposizione?
- - Tratto genetico
- - Azolici usati in agricoltura e in altri setting
- - Resistenza CYP51A mediata o no, panazolica o selettiva (voriconazolo) o basata su pompa di efflusso o altre mutazioni
- (Livelli di voriconazolo inefficaci)

Profilo di rischio comune nell'anziano

(Fortùn J. Rev Esp Quimioter 2022; 35 (Suppl. 1): 97-103)

Table 1 Risk Factors for IPA in ICU Patients

1. High risk
Neutropenia (500/mm³)
Hematological malignancy
Allogeneic HSCT
2. Intermediate risk
Prolonged treatment with corticosteroids before admission to the ICU
Autologous HSCT
COPD
Liver cirrhosis
Solid organ cancer
HIV infection
Lung transplantation
Systemic immunosuppressive therapy
3. Low risk
Severe burns
Solid organ transplant
Steroid treatment for > 7 days
Prolonged stay in the ICU (> 21 days)
Malnutrition
Post cardiac surgery
Near drowning

COPD chronic obstructive pulmonary disease, HIV human immunodeficiency virus, HSCT hematopoietic stem cell transplantation, ICU intensive care unit, and IPA invasive pulmonary aspergillosis. Modified from reference [6].

Aspergillo: nella BPCO associazione tra contaminazione ambientale e tasso anticorpale (Fréalle E et al *** 2021)

	Total counts		
	≤30 CFUs/cm^2	>30 CFUs/cm^2	P-values
Aspergillus section *Fumigati* detection in sputum			
Inclusion (n=48)	7/41 (17%)	2/7 (29%)	0.39
Final visit (n=25)	0/20 (0%)	1/5 (20%)	0.20
Detection of anti-*Aspergillus* antibodies			
Inclusion (n=51)	13/43 (30%)	5/8 (63%)	0.09
Final visit (n=32)	6/25 (24%)	5/7 (71%)	**0.03**

Bold type represents statistical significance at p<0.05.

"Beyond the significant association between anti-Aspergillus 313 antibodies and total fungal counts in EDCs, the higher frequency of patients with anti Aspergillus antibodies in dwellings with total mould contamination levels of >30 CFUs/cm2 314 315 suggests that this threshold could be used to define abnormal indoor mould exposure, as well 316 as the need for patient's home assessment by a professional (such as a medical indoor317 environment counsellor) and remediation measures. "

Aspergillo: nella BPCO una disagevole diagnosi (Bulba P et al. Eur Respir J 2007; 30: 782–800)

TABLE 1 Definitions of invasive pulmonary aspergillosis (IPA) in chronic obstructive pulmonary disease (COPD) patients

Proven IPA	Histopathological or cytopathological examination, from needle aspiration or biopsy specimen obtained from any pulmonary lesion present for <3 months, showing hyphae consistent with Aspergillus and evidence of associated tissue damage, if accompanied by any one of the following: 1) Positive culture of Aspergillus spp. from any LRT sample. 2) Positive serum antibody/antigen test for *A. fumigatus* (including precipitins). 3) Confirmation that the hyphae observed are those of Aspergillus by a direct molecular, immunological method and/or culture.
Probable IPA	As for proven IPA but without confirmation that Aspergillus is responsible (points 1, 2 and 3 are not present or tested). OR COPD patient, usually treated with steroids and severe according to GOLD (stage III or IV), with recent exacerbation of dyspnoea#, suggestive chest imaging¶ (radiograph or CT scan; <3 months+) and one of the following: 1) Positive culture§ and/or microscopy for Aspergillus from LRT. 2) Positive serum antibody test for *A. fumigatus* (including precipitins). 3) Two consecutive positive serum galactomannan tests.
Possible IPA	COPD patient, usually treated by steroids and severe according to GOLD (stage III or IV), with recent exacerbation of dyspnoea#, suggestive chest imaging¶ (radiograph or CT scan; <3 months+), but without positive Aspergillus culture or microscopy from LRT or serology.
Colonisation	COPD patient with positive Aspergillus culture from LRT *without* exacerbation of dyspnoea, bronchospasm or new pulmonary infiltrate.

Data from references [23] and [38]. LRT: lower respiratory tract; *A. fumigatus*: *Aspergillus fumigatus*; GOLD: Global Initiative for Chronic Obstructive Lung Disease; CT: computed tomography. #: Exacerbation of dyspnoea and/or bronchospasm resistant to appropriate treatment including antibiotics; ¶: pulmonary lesion(s) unresponsive to appropriate antibiotics (refers to dose, route, spectrum and activity against cultured bacteria); +: pulmonary lesions, especially cavitary, present for >3 months are better classified as chronic pulmonary aspergillosis (see text), unless direct tissue invasion is demonstrated; §: standard or sabouraud culture, or molecular detection test when licensed.

…anche perchè la malattia è proteiforme (Bulba P et al. Eur Respir J 2007; 30: 782–800)

TABLE 2 Characteristics of the patient population

Total number of patients	56
Sex	
Male	42 (75)
Female	14 (25)
Age yrs	
Mean±SD	65.5±9.3
Median (IQR)	66 (57–73)
Steroid treatment	
At admission	43
Systemic use	40
Inhaled only	3
In hospital (systemic use)	49
None	2
NA	5
Clinical signs (total patients available)	
Antibiotic resistant pneumonia	53 (56)
Dyspnoea exacerbation	48 (48)
Wheezing increase	22 (28)
Fever >38°C	15 (39)
Haemoptysis	5 (12)
Parietal pain	4
Tracheobronchitis during bronchoscopy	6 (33)
Duration between symptoms and diagnosis days	
Mean±SD	12.5±11.3
Median (IQR)	8.5 (6–16.5)
Ventilation	
Invasive	43
Noninvasive ventilation	1
None	10
NA	2
Total leukocytes	
<12000	10
>12000	30
NA	16
Outcome[¶]	
Death	53 (95)
Survival	3 (5)

TABLE 3 Number of patients[#] with radiological signs

Chest radiographs	
Nonspecific consolidation	36
Specific images	10
Nodules	3
Cavitation	3
Wedge consolidation	3
Round consolidation	1
No infiltrate	2
NA	8
Chest CT scan	
Contributive	11
Halo sign	1
Nodule + cavitation	2
No description	8
Noncontributive	5
Not done	40

Data from [12, 13, 34, 36, 37, 39–54]. NA: not available; CT: computed tomography. [#]: total n=56.

Terapia dell'Aspergillo: voriconazolo problematico nell'anziano, spesso inefficace <1 mg/l, tossico>5 mg/l (Fortùn J. Rev Esp Quimioter 2022; 35 (Suppl. 1): 97-103)

Table 4 Comparative inhibition of selected CYP450 isoenzymes by triazoles

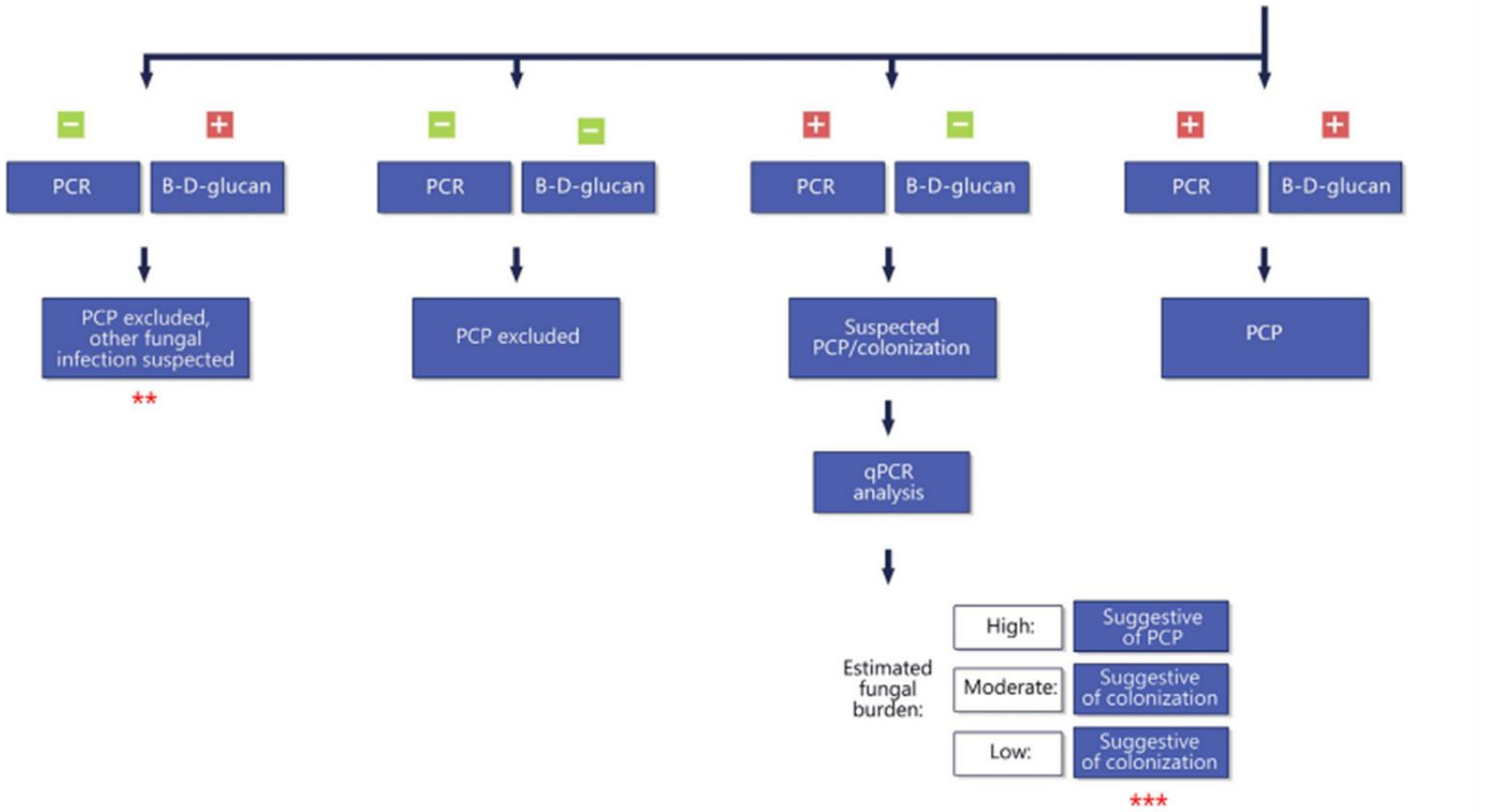
Azole	CYP2C8	CYP2C9	CYP2C19	CYP3A4
Fluconazole	++	++	+	++
Itraconazole	+	+	-	+++
Voriconazole	++	++	+++	++
Posaconazole	-	-	-	+++
Isavuconazole	-	-	-	+/++

Notes: -, no inhibition; +, mild inhibition; ++, moderate inhibition; +++, strong inhibition.
Modified from reference [30].

Candida non-albicans species: C. glabrata, C. krusei, C. parapsilosis, C. tropicalis…

- C Auris: origine ignota, colonizza anche cute e narici, il suo biofilm resiste ai comuni disinfettanti, inclusi quelli a base di Ammonio quaternario
- Aggressiva, spesso resistente, può coinfettare con Covid-19.
- Negli USA 90% resiste agli azolici, 30% all'anfotericina B, 5% alle echinocandine, ma % in aumento rapido da esposizione.
- Comune in nursing home che assistono pazienti ventilati.

Uno schema binario plus per la diagnosi di polmonite da Pneumocystis (PCP) (Szydłowicz M et al. Trends in Parasitology, 2021; 37: 859-862)



Funghi emergenti e relativi correlati

(Wiederhold NP. Clinical Chemistry 2022; 68: 83-90)

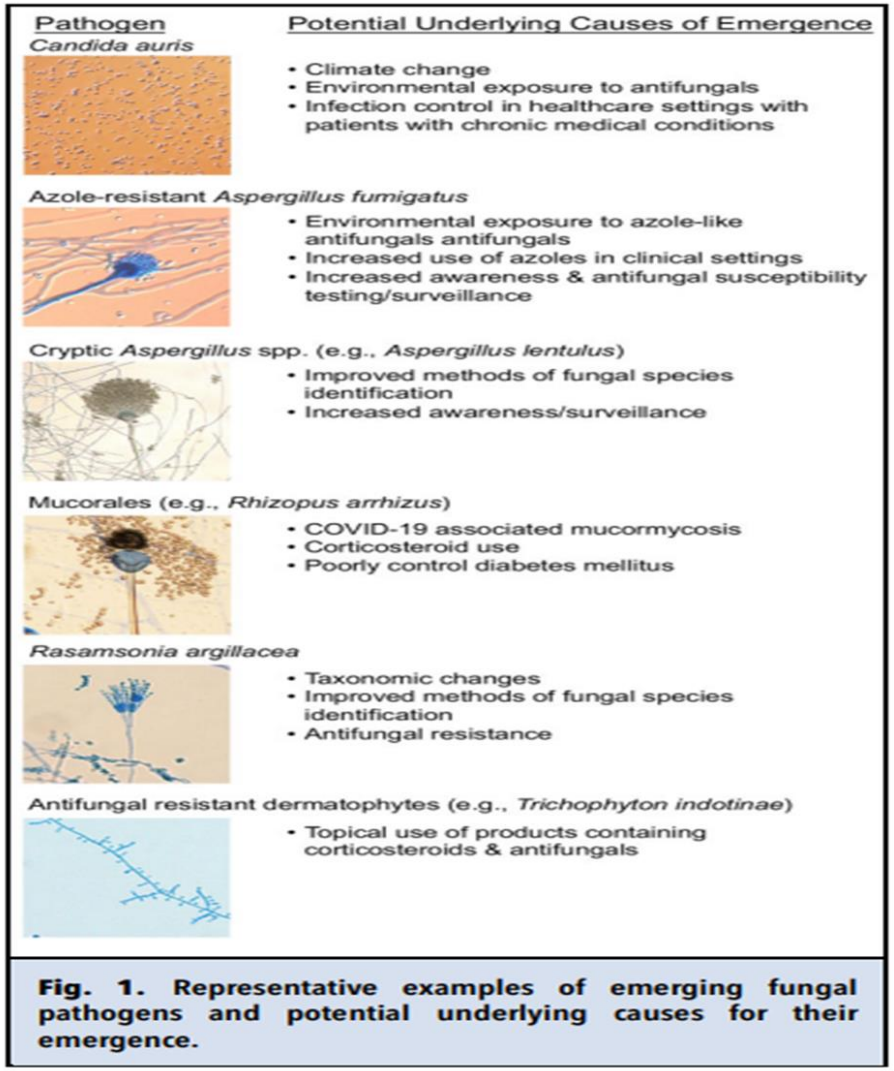


Fig. 1. Representative examples of emerging fungal pathogens and potential underlying causes for their emergence.

E i funghi non finiscono qui…

(Wiederhold NP. Clinical Chemistry 2022; 68: 83-90)

Table 1. Examples of other newly recognized or reclassified fungal species of clinical significance, including some with resistance to antifungals.

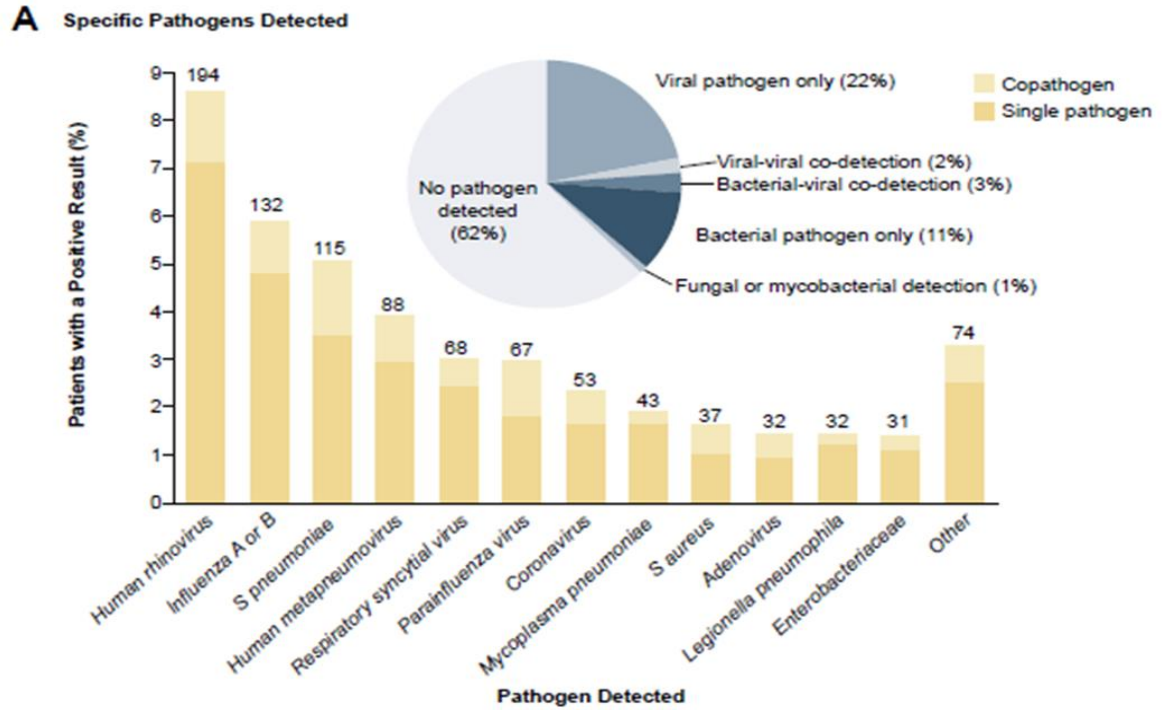
Current name/classification	Previous name/classification	Clinical relevance
Blastomyces helicus	*Emmonsia helica*	• Atypical and disseminated blastomycosis in immunocompromised humans and companion animals [Schwartz et al. (57)]. • Cases reported in western states and provinces of US and Canada.
• *Emergomyces* species • *Emergomyces africanus* • *E. canadensis* • *E. europaeus* • *E. orientalis* • *E. pasteurianus*	*Emmonsia*-like species	• Disseminated infections in patients with advanced-HIV/AIDS [Kenyon et al. (58)]. • Systemic infections in other immunocompromised patients [Schwartz et al. (59) and Spallone et al. (60)].
Rasamsonia argillacea species complex	*Geosmithia* species	• Invasive disease in those with chronic granulomatous disease and hematologic malignancies, and colonization in cystic fibrosis patients [Houbraken et al. (61)]. • Intrinsic resistance to voriconazole and isavuconazole [Houbraken et al. (61) and Steinmann et al. (62)]. • Often misidentified as *Penicillium* or *Paecilomyces*.
Sporothrix brasiliensis	*Sporothrix schenckii*	Zoonotic transmission can occur with outbreaks in humans reported due to infected cats [Barros et al. (63) and Brandolt et al. (64)].
Trichophyton indotineae	*Trichophyton mentagrophytes* species complex (*T. interdigitale*)	Outbreaks of dermatophytosis with emerging resistance to terbinafine, fluconazole, and griseofulvin in patients in Northern India, leading to clinical failures in the treatment of tinea corporis/cruris infections [Singh et al., Tang et al., and Kano et al. (65–67)].

Principali polmoniti non batteriche: virali (incidenza circa doppia rispetto alla forma batterica)

- <u>Nell'immunocompetente</u>
- Adenovirus
- Meta-pneumovirus
- Para-influenza virus *
- Respiratory syncytial virus (RSV)
- Infuenza A and B viruses
- Covid-19
- Rhinovirus *
- Others (Echo, Coxachie, Hantav, Mimiv…)

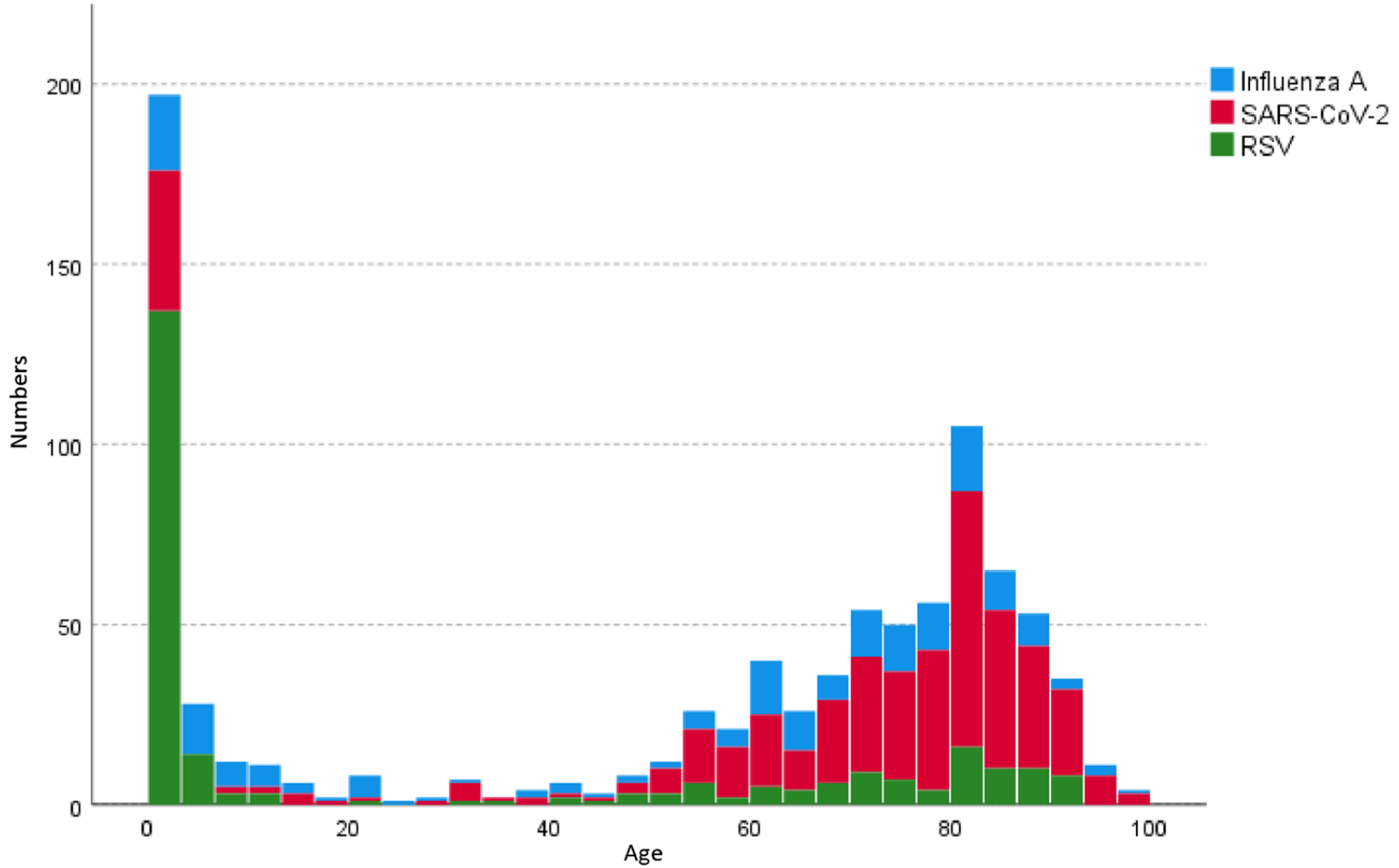
- <u>Nell'immunodepresso</u>
- Adenovirus
- Herpes Virus (HSV)
- Cytomegalovirus (CMV)
- Epstein-Barr Virus (EBV)
- Varicella Zoster (VZV)
- * Maggiore gravità, non prevalenza.

Dallo studio EPIC i dati di prevalenza nell'adulto (Jain S. Clin Chest Med 38 (2017) 1–9)



Among the 2259 adults enrolled in the EPIC study with clinical and radiographic pneumonia who had specimens available for bacterial and viral diagnostic testing, a pathogen was detected in 853 (38%) with one or more viruses in 530 (23%), bacteria in 247 (11%), bacteria and viruses in 59 (3%), and a fungal or mycobacterial pathogen in 17 (1%). Among the 2259 adults, the most commonly detected viruses were HRV (9%), influenza A and B viruses (6%), HMPV (4%), RSV (3%), PIV (2%), CoV (2%), and AdV (1%) (Fig. 1A).3 Importantly, the incidence of pneumonia hospitalization with influenza was almost 5 times higher among adults 65 years and older than among younger adults, and the incidence of HRV was almost 10 times as high.

Nei ricoverati, prevalenza di tre eziologie in rapporto all'età in un ospedale tedesco… (Quarg C et al. Eur J Med Res (2023) 28:568)



...e relativi outcome (Quarg C et al. Eur J Med Res (2023) 28:568)

Table 3 Outcome data of the three major infection groups stratified according to age

Age group	< 18 years			≥ 18 years		
Infection	n	ICU admission	Mortality	n	ICU admission	Mortality
Sample size	254	17 (6.7%)	0 (0%)	637	103 (16.2%)	56 (8.8%)
Influenza A	51	2 (3.9%)	0 (0%)	147	24 (16.3%)	10 (6.8%)
SARS-CoV-2	46	0 (0%)	0 (0%)	391	60 (15.3%)	35 (9.0%)
RSV	157	15 (9.6%)	0 (0%)	99	19 (19.2%)	11 (11.1%)

Numbers (percentages) are given. For the results of statistical comparisons, see text. Mortality refers to in-hospital mortality. ICU = intensive care unit

Ogni virus ha la sua stagione (Falsey R et al. Clinical Infectious Diseases 2006; 42:518–24)

Table 2. Characteristics of common respiratory viruses.

Virus	Season	Periodicity	Duration of incubation period	Primary means of transmission
Influenza	Winter	Yearly	1–2 days	Small particle aerosols
RSV	Late fall to early spring	Yearly	2 –8 days	Large droplets and fomites
hMPV	Late winter	Every other year	5–6 days	Large droplets and fomites[a]
PIV	Fall through spring	Every 2–3 years	2 –8 days	Large droplets and fomites
Coronavirus	Winter	Every 2–3 years	1–3 days	Large droplets and fomites[a]
Rhinovirus	All year; fall	Yearly	8 h to 2 days	Fomites

NOTE. hMPV, human metapneumovirus; PIV, parainfluenza virus; RSV, respiratory syncytial virus.

[a] Presumptive mode of transmission.

Ma quasi nessuno ha un preciso biglietto da visita (Falsey AR. Clin Geriatr Med 23 (2007) 535–552)

Table 2
Common respiratory viruses

Virus	Season	Clinical clues	Incubation	Treatment
Influenza	Winter	Abrupt onset, fever, myalgias	1–2 days	Oseltamivir, aanamivir
RSV	Late fall to late winter	Rhinorrhea, wheezing	2–8 days	Aerosolized ribavirin[a]
hMPV	Late winter	Nonspecific	5–6 days	None available
PIV	Fall to spring	Hoarseness	2–8 days	None available
Coronaviruses	Winter	Nonspecific	1–3 days	None available
Rhinoviruses	All year, fall	Rhinorrhea	8 hours to 2 days	None available

[a] Not approved for use in adults.

Le forme virali più spesso identificate in corso di CAP (Cavallazzi R et al. Clin Chest Med 39 (2018) 703–721)

Table 1
Characteristics and taxonomy of commonly identified respiratory viruses in patients with community-acquired pneumonia

Virus	Genome	Family	Important Antigenic Structures
Influenza	RNA	Orthomyxoviridae	Surface glycoproteins hemagglutinin (HA) and the neuraminidase (NA).[8]
Respiratory syncytial virus	RNA	Paramyxoviridae	Attachment glycoprotein (G) and fusion (F) glycoprotein.[9]
Human rhinovirus	RNA	Picornaviridae	Viral capsid proteins VP1, VP2, VP3, and VP4.[10]
Adenovirus	DNA	Adenoviridae	Capsid major structures: hexon (the building block of the capsid), penton base, and polypetides.[11]
Parainfluenza	RNA	Paramyxoviridae	Surface glycoproteins hemagglutinin-neuraminidase and fusion protein. Membrane protein.[12]
Coronavirus	RNA	Coronaviridae	Membrane glycoprotein and spike protein.[13]
Human metapneumovirus	RNA	Paramyxoviridae	Virus fusion (F) glycoprotein.[14]
Human bocavirus	DNA	Parvoviridae	Capsid viral proteins (VPs), VP1, and VP2.[15]

Polmoniti virali nell'anziano

- A Swiss study enrolling patients ageing>65 years with suspected CAP screened for viral pathogens by PCR analysis of nasopharyngeal swabs demonstrated the presence of a viral genome in 31% of the cases. Rhinovirus and Infuenza A/B viruses were those most identified and evidence of both bacterial and viral infection was detected in about 10% of the cases [14]

Le polmoniti virali: diagnostica differenziale (Galvàn GM et al. Arch Bronconeumol. 2015; 51(11): 590–597)

Table 1
Differential Factors Between Viral Pneumonia and Bacterial Pneumonia.

	Suggestive of viral origin	Suggestive of bacterial origin
Age	Younger than 5 and older than 65 years	Adults
Epidemic status	Seasonal or epidemic outbreaks	Throughout the year
Disease course	Slow onset	Rapid onset
Clinical profile	Most frequently rhinitis and wheezing	Most frequently high fever and tachypnea
Total leukocyte count on admission	$<10\times10^6$ c/L	$>15\times10^6$ c/L and $<4\times10^6$ c/L
C-reactive protein on admission	<20 mg/L	>60 mg/L
Serum procalcitonin on admission	<0.1 μg/L	>0.5 μg/L (>1 μg/L with greater specificity)
Chest X-ray	Bilateral, interstitial infiltrates	Lobar alveolar infiltrates
Response to antibiotic treatment	Slow response or no response	Rapid

Adapted from Ruuskanen et al.[3]

NIV	Molto efficace nell'anziano
PCR	Permane + per diverso tempo dopo risoluzione: limiti diagnostici della positività Utilissima nell'anziano, data la minore carica virale nasofaringea rispetto al giovane
RSV	Notevole latenza tra esordio dei sintomi e accesso in PS. Ribavirina rivelatasi efficace in immunodepressi.
Procalcitonina elevata esclude polmonite virale, salvo co-infezione	La sintesi di interferon gamma stimolata dai virus riduce quella di procalcitonina in adipociti e cellule neuroendocrine
Rhinovirus	Forme gravi, rare in assoluto, ci concentrano in tarda età e negli immunocompromessi
Inibitori neuraminidasi	Uso precoce, pre conferma immunologica, privilegiando Zanamivir: il virus A spesso resiste a oseltamivir. Laninamivir pare efficace per inalazione.
Valanciglovir, Ganciglovir	Efficaci anche in polmoniti gravi da CMV
Amantadina	Efficace solo contro il virus A, induce spesso resistenza, ha importanti effetti avversi
Steroidi a piccole dosi	Mediamente efficaci

Principi di terapia antivirale (Pagliano P et al. Infection (2021) 49:607–616)

Table 1 Main antiviral treatments active in patients with viral pneumonia

Main indication for the treatment	Medication	Dosage	Notes
Uncomplicated Influenza Influenza pneumonia	Oseltamivir	Oral 75 mg twice daily for 5 days	Dose adjustment for CrCl < 50 ml/'
	Peramivir	Intravenous 600 mg single dose (5 days for complicated Influenza)	Efficacy is not established for severe Influenza A and for Influenza B
	Zanamivir	Intravenous 300 mg daily for 5–10 days 10 mg inhaled q12hr for 5–10 days	Bronchospasm can occur in patients with asthma
RSV infection in immunocompromised	Ribavirin	Aerosolized 2 g over 2 h every 8 h Systemic oral or intravenous (dosage variable)	Inhalatory formulation can deposit in the delivery system if ventilated Hemolytic anemia Teratogenic
Severe adenovirus infection	Cidofovir	Intravenous 5 mg/kg/weekly, until symptoms resolve	Very limited data Nephrotoxicity
Varicella pneumonitis	Acyclovir	Intravenous 10 mg/kg/dose every 8 h for at least 7 days	Nephrotoxicity
CMV pneumonia	Ganciclovir	Intravenous 5 mg/kg/dose every 12 h for at least 2 weeks	Hematologic toxicity Nephrotoxicity (dose adjustment for CrCl < 70)
COVID-19	Remdesivir	Day 1 loading dose: 200 mg IV over 30–120 min Day 2—6: 100 mg IV q Day	Hepatotoxicity

CMV cytomegalovirus, *CrCl* creatinine clearance, *HCW* healthcare workers, *HMPV* human metapneumovirus, *PIV* parainfluenza viruses, *RSV* respiratory syncytial virus

Terapia in funzione dello stato immunitario? (Cavallazzi R et al. Clin Chest Med 39 (2018) 703–721)

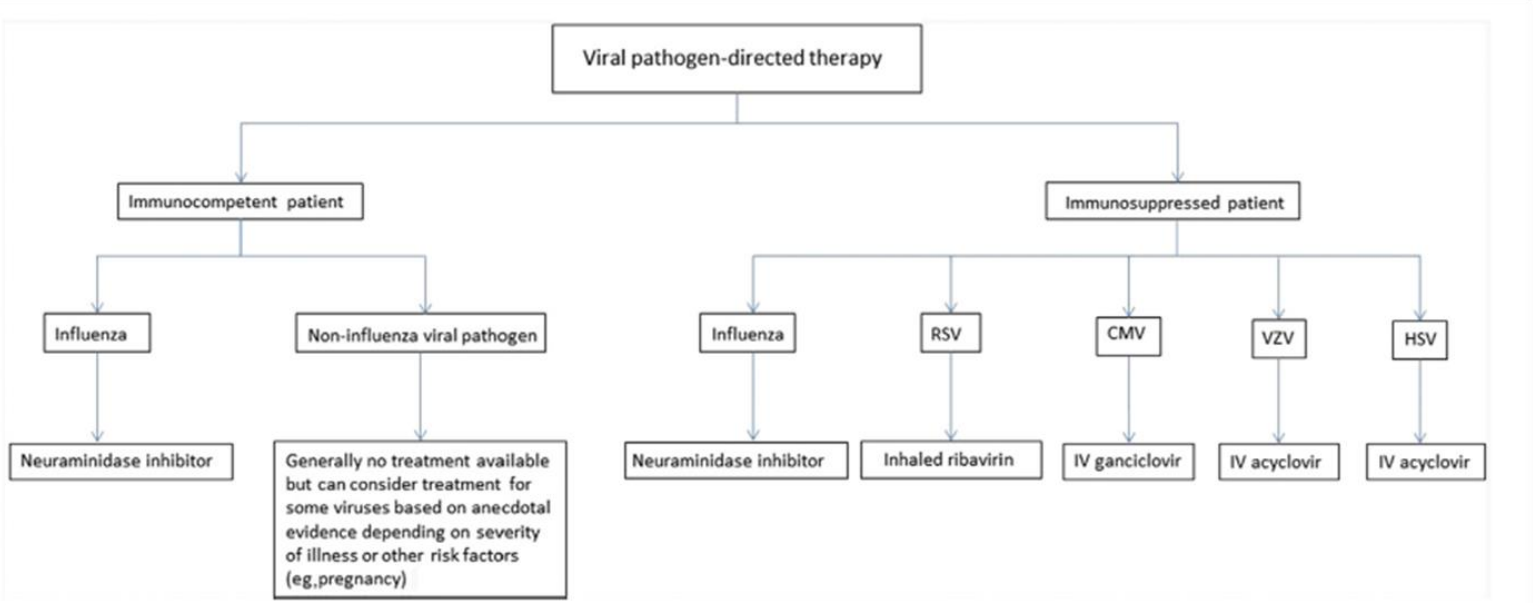


Fig. 7. Viral pathogen-directed therapy. CMV, cytomegalovirus; HSV, herpes simplex virus; IV, intravenous; RSV, respiratory syncytial virus; VZV, varicella zoster virus.

L'eterogena letteratura sugli steroidi nelle polmoniti virali (Pagliano P et al. Infection (2021) 49:607–616)

Table 2 Studies assessing the effectiveness of steroids in patients with viral pneumonia

Article	Study type	Therapy	Etiology	Patients (n)	Effects
63	Meta-analysis	CS vs No CS treatment	Influenza virus	4916	Higher mortality (OR 1.98, 95% CI 1.62–2.43, $p < 0.00001$) in CS group
64	Retrospective cohort study	Early CS treatment vs Non early CS treatment	Influenza virus	241	Higher hospital mortality rate in CS group
65	Case control study	Low-to-moderate dose vs High-dose CS	Influenza A (H1N1)	2141	Reduced 30-day and 60-day mortality in patients receiving low-to-moderate-CS dose with $PaO_2/FiO_2 < 300$ mm Hg
66	Randomized controlled trial	Dexamethasone vs Standard of care	COVID-19	6425	Reduced 28-day mortality rate in the dexamethasone group receiving ventilatory support
67	Meta-analysis	CS vs Standard of care	COVID-19	1703	Advantage after treatment with dexamethasone (6 mg daily)

CS: corticosteroid, ARDS: Acute Respiratory Distress Syndrome, aHR: adjusted Hazard Ratio, IMV: invasive mechanical ventilation

Viral coinfections of Covid-19: RSV

(Kim D et al. JAMA 2020 Apr 15;323(20):2085-2086. doi: 10.1001/jama.2020.6266)

Table 2. Proportions of Specimens Positive for Non–SARS-CoV-2 Respiratory Pathogens and Mean Patient Ages for Each Subgroup, by SARS-CoV-2 Result[a,b]

	SARS-CoV-2 status			
	Negative (n = 1101)		Positive (n = 116)	
Pathogen	Proportion positive for other respiratory pathogen, No. (%)[b]	Mean age of positive patients, y	Proportion positive for other respiratory pathogen, No. (%)[b]	Mean age of positive patients, y
Influenza				
A	29/1101 (2.6)	45.9	1/116 (0.9)	74.0
B	8/1101 (0.7)	21.6	0/116 (0)	
RSV	32/1101 (2.9)	26.0	6/116 (5.2)	52.3
Parainfluenza				
1	1/1101 (0.1)	71.0	1/116 (0.9)	43.0
2	0/1101 (0)		0/116 (0)	
3	2/1101 (0.2)	40.0	1/116 (0.9)	45.0
4	5/1101 (0.5)	26.6	1/116 (0.9)	36.0
Metapneumovirus	47/1101 (4.3)	41.1	2/116 (1.7)	67.0
Rhinovirus/enterovirus	133/1101 (12.1)	32.6	8/116 (6.9)	42.1
Adenovirus	10/1101 (0.9)	14.1	0/116 (0)	
Other Coronaviridae	39/1101 (3.5)	42.2	5/116 (4.3)	40.8
Chlamydia pneumoniae	0/1060 (0)		0/116 (0)	
Mycoplasma pneumoniae	6/1101 (0.5)	14.8	0/116 (0)	

Esistono anche polmoniti parassitarie!

(Cheepsattayakorn A et al. BioMed Research International Volume 2014, Article ID 874021)

Table 1: Parasitic diseases, chest roentgenographic features, and chemotherapeutic agents.

Disease	Chest roentgenographic features	Reference	Chemotherapeutic agents	Reference
Malaria	Diffuse interstitial pulmonary edema, pleural effusion, lobar consolidation, bilaterally pulmonary infiltrates, diffuse bilateral alveolar opacities, bilateral basal ground glass opacities	[12–15]	Chloroquine (all *Plasmodium* species), Artemisinin-based combination regimens (all *Plasmodium* species)	[1, 11, 20, 22–25]
Amoebiasis	Pleural effusion, basal pulmonary involvement, elevation of hemidiaphragm	[1]	Metronidazole, diloxanide, lactoferrin, lactoferricin	[34, 35]
Leishmaniasis	Pleural effusion, mediastinal lymphadenopathy, pneumonitis (immunocompromised status)	[39, 40]	Pentavalent antimonials, pentamidine, amphotericin B, miltefosine	[48]
Trypanosomiasis	Pulmonary alveolar hemorrhage, alveolitis, pneumonitis, pulmonary emphysema (*in vivo*)	[52, 54]	Eflornithine, melasoprol (*in vivo*)	[8, 56, 57]
Pulmonary larval migrans	Localized patchy infiltrates	[1]	Diethylcarbamazine, Mebendazole, Albendazole	[67–69]
Toxoplasmosis	Interstitial pneumonia, diffuse alveolar damage, necrotizing pneumonia, obstructive or lobar pneumonia	[71, 72]	Combination regimen of pyrimethamine and sulfadiazine	[1]
Babesiosis	Noncardiogenic diffuse-bilateral-interstitial pulmonary edema and adult respiratory distress syndrome (complicated case)	[78]	Combination of clindamycin and quinine, or atovaquone and Azithromycin	[79, 80]
Filariasis	Bilateral military infiltrates, prominent hila with increased lung markings, normal	[84–89]	Diethylcarbamazine	[101–106]
Dirofilariasis	A solitary-coin or multiple nodules (usually less than 3 cm. in size, usually in the periphery of the right lower lobe)	[1, 109, 113, 114, 117, 118]	No specific medical therapy, but ivermectin may be useful, usually curative by wedge resection of the pulmonary nodule	[126, 127]
Strongyloidiasis	Bronchopneumonia, alveolar hemorrhages	[1]	Thiabendazole	[135]
Ascariasis	Peripherally basal opacities, unilateral or bilateral transient-migratory-non-segmental opacities of various sizes	[142]	Mebendazole, albendazole, pyrantel pamoate, piperazine citrate, ivermectin	[1]
Ancylostomiasis	Bronchitis, bronchopneumonia, transient pulmonary infiltrates	[128, 143, 144]	Mebedazole, albendazole, pyrantel pamoate, ivermectin	[128]
Paragonimiasis	Patchy consolidation, pleural thickening, pleural effusion, nodular lesions, cystic lesions, cavities, normal	[150, 153, 155–158]	Praziquantel, triclabendazole, niclofolan, bithionol	[147, 150, 164, 165]
Schistosomiasis	Multiple ill-defined small nodular lesions with ground glass-opacity halo, prominent hila, increased lung markings, enlargement of the right ventricle, dilatation of the pulmonary arteries and trunk as well as their interlobar branches (pulmonary hypertension and cor pulmonale)	[166, 170–173, 176]	Praziquantel, artemisinin derivatives	[166]
Hydatidosis/echinococcosis	Solitary or multiple round opacities with air-fluid level, water-lily sign, onion-peel sign, crescent sign	[1, 184]	Praziquantel, mebendazole, albendazole,	[187]
Trichinellosis	Patchy infiltrates, exaggerated and fuzzy lung markings, hilar enlargement	[192, 194, 195]	Mebendazole, albendazole	[128, 192]

Polmoniti non batteriche nell'anziano: conclusioni

- Problematiche da diagnosticare e trattare
- E' fondamentale sospettarle
- Bisogna conoscere i pannelli diagnostici per singoli funghi
- Il supporto del laboratorio è vitale, ma va stimolato
- Dovremmo limitare i fattori di rischio
- Non v'è specificità clinica rispetto all'adulto, ma maggiore impatto sullo stato di salute
- Anche alcune forme virali si giovano di terapia medica mirata