Strumenti attuali per accelerare e facilitare una diagnosi differenziale

Valore dell'appropriatezza nei percorsi di diagnosi e cura del paziente fragile

Focus on

INFEZIONI RESPIRATORIE

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Infezioni respiratorie: patogeni

Figure 1. Classification of the URIs with the associated most relevant causative agents.

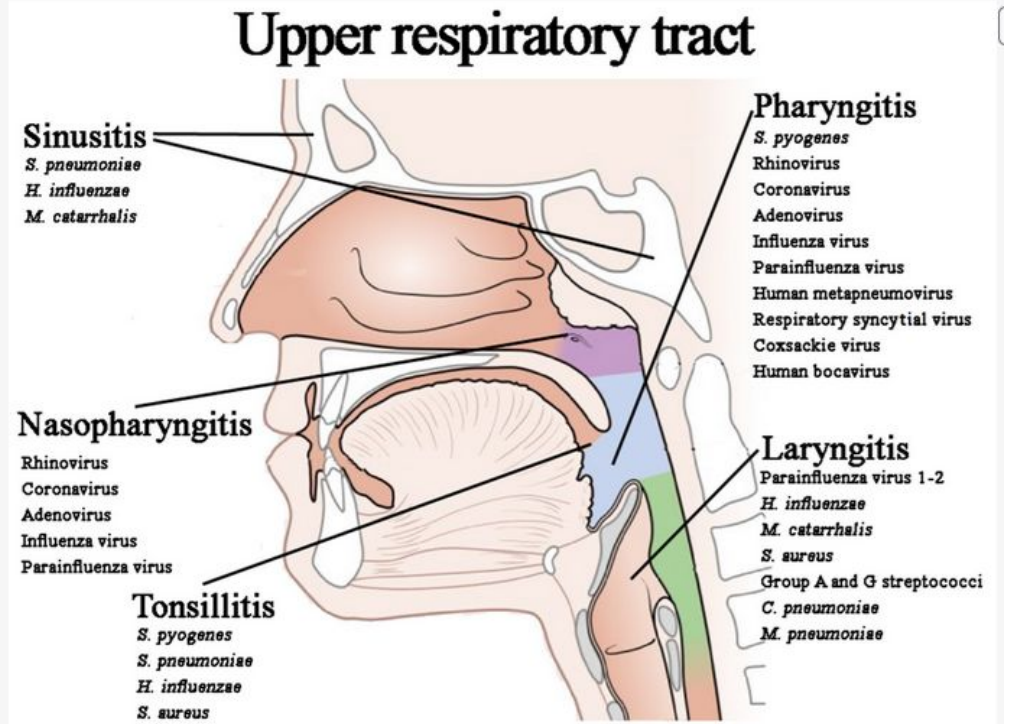
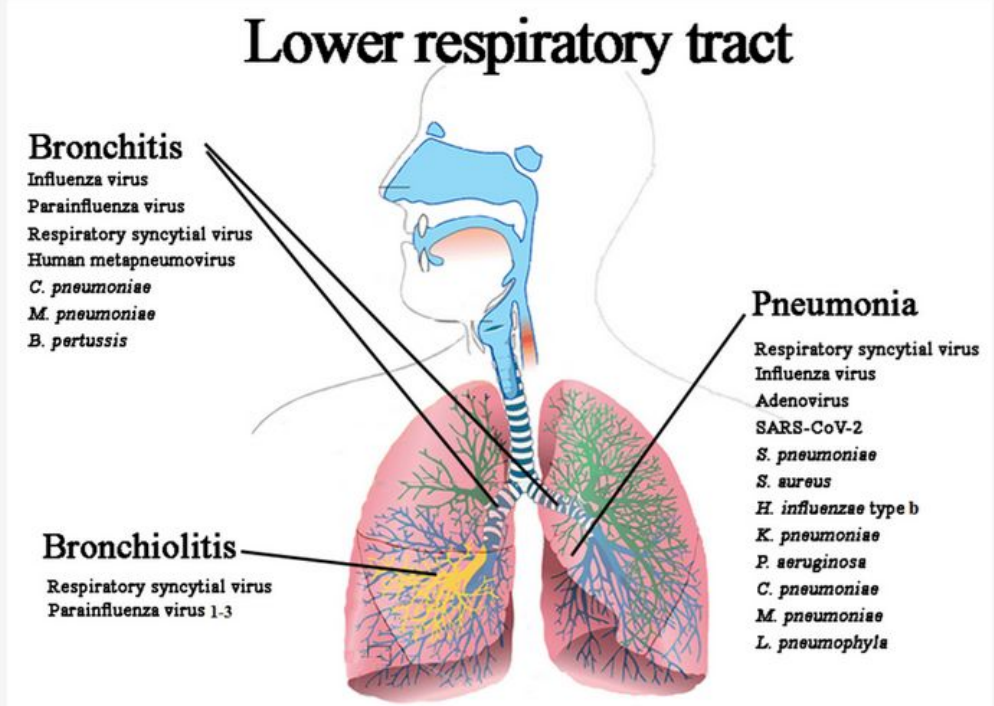


Figure 2. Classification of LRIs with the associated most relevant causative agents.



Microorganisms **2022**, *10*(9), 1856;
https://doi.org/10.3390/microorganisms10091856

Diagnostica rapida

Può fornire informazioni per le decisioni cliniche

15 min → 2h → 3-4 h

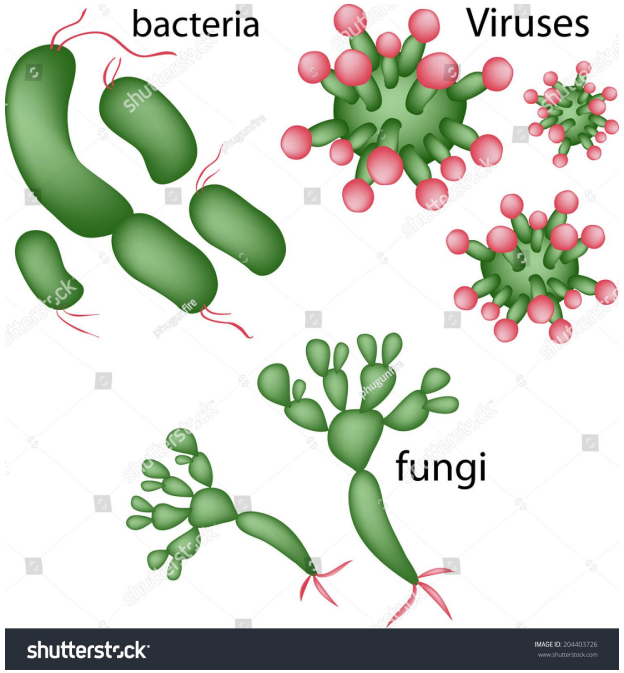
Tempo? → POCT?

≠test convenzionali di laboratorio

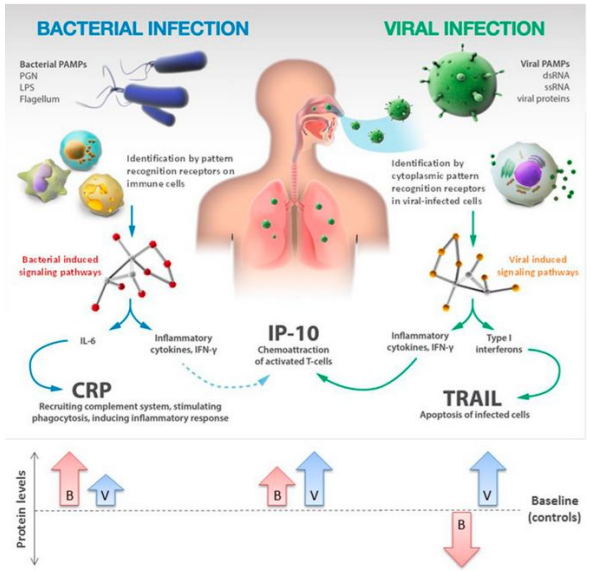
Training tecnico, dispositivi di sicurezza e expertise per interpretazione

Poco consenso sulle definizioni

Diagnostica rapida:



- Approcci
  - Patogeno
    - Antigene
    - Metodi molecolari
  - Biomarker



Biomolecules **2024**, *14*(1), 97;
https://doi.org/10.3390/biom14010097

Patogeno: eziologia dell’infezione

Antigenici

- Buona specificità
- Sensibilità variabile

Molecolare

- Alta sensibilità
- Alti costi
- Interpretazione più complessa

Rapid Antigenic Detection Test (RADT)

Rilevazione di antigeni specifici mediante anticorpi

PRO

- Relativamente economici
- Facile esecuzione
- Risultati rapidi (15 min)

cons

- Bassa sensibilità comparata PCR
- Possibili falsi negativi

Rilevano i principali virus respiratori:

RSV,
Influenza A e B
SARS-CoV2

World Health Organization (WHO) and European Centers for Disease Prevention and Control (ECDC) recommend to apply only RADTs of high diagnostic accuracy (≥80% sensitivity and ≥97% specificity

Urine Antigenic Test

Antigene urinario *Legionella*

Permanenza e rilevazione dell'antigene anche dopo la risoluzione del'infezione

Immunocompromessi può persistere per mesi

Risultati rapidi

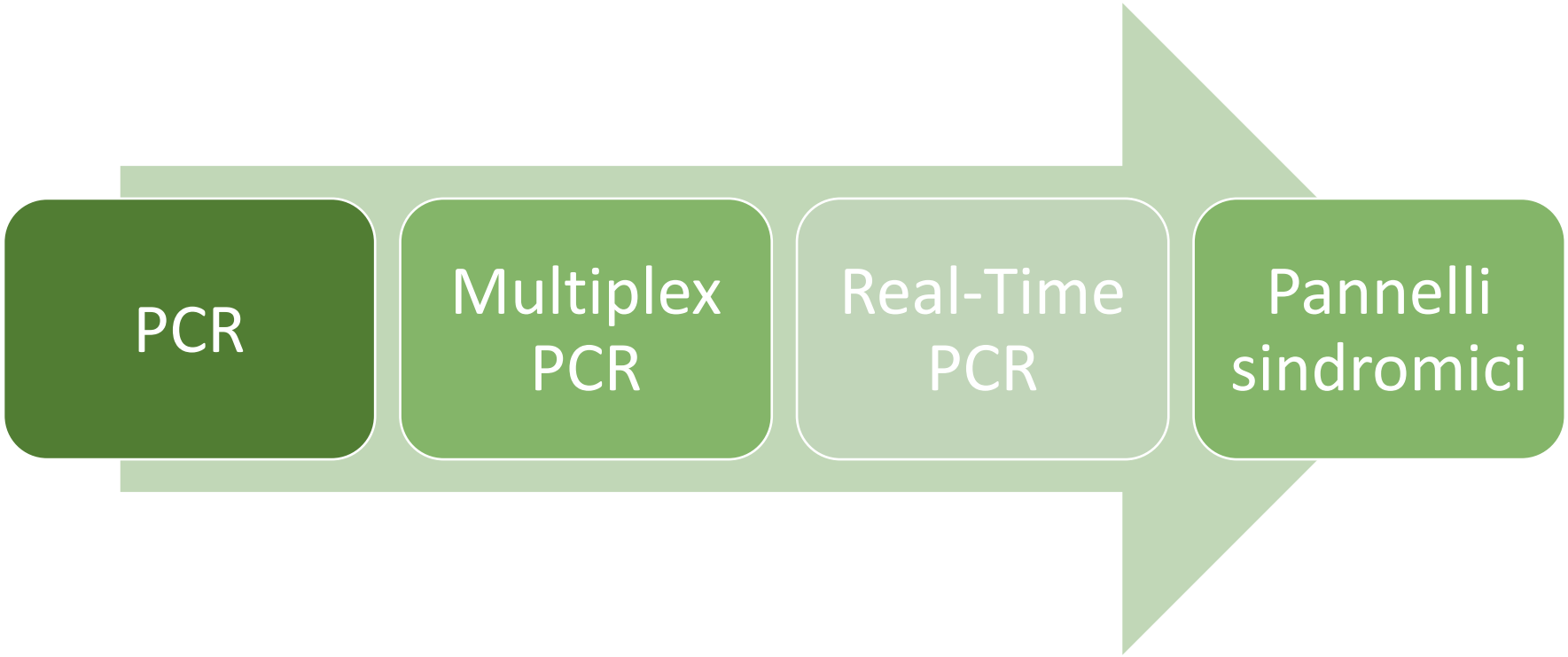
Antigene urinario Pneumocco

Specificità elevata ma non la sensibilità

In laboratorio sensibilità aumentata con lettura strumentale e pretrattamento del campione

Test rivelazione acidi nucleici

NAAT (nucleic acid amplification test)



Alta specificità
Alta sensibilità
Rapidi: 1h-3h

Neccessità di strumentazione
Richiesta di processazione in biosicurezza
Expertise per interpretazione e validazione

Pannelli sindromici

Cosa sono?

Test basati su metodiche di PCR che permettono l'identificazione di materiale genetico proveniente da più patogeni in modo contemporaneo

Risultati in tempi brevi dell'agente eziologico = trattamento tempestivo

L'uso di questi dovrebbe essere considerato solo per gruppi specifici di pazienti con forme respiratorie severe, come immunocompromessi e pediatrici

Non tutti ma i più frequenti

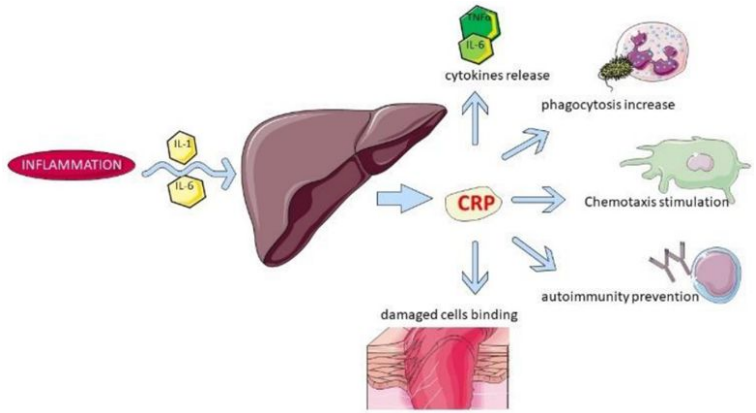
Ditte diverse hanno liste di patogeni che possono differerire

Negativo NON significa non infetto

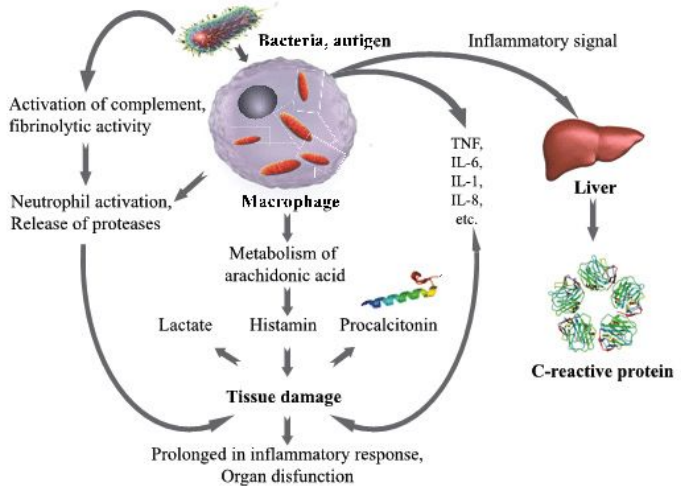
Biomarker

Rilevazione di molecole che misurano la risposta dell'ospite

Proteina C reattiva (PCR)

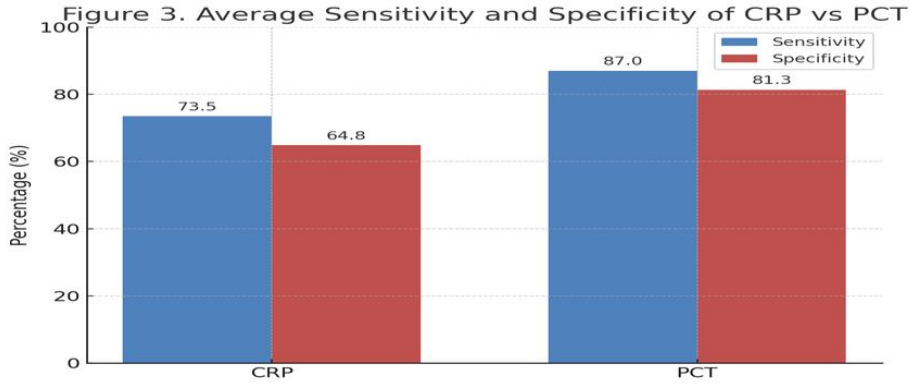


Procalcitonina



Biomarker

Non tutte le infezioni batteriche presentano un innalzamento di questi marker



I batteri aticipi: Legionella, Micoplasma, Clamidia sono intracellulari e non richiamano polimorfinucleati

DOI:10.63969/5axbjt60

The IDSA guidelines do not recommend routine CBC, CRP, ESR, and procalcitonin collection in the outpatient setting.[7] A systematic review demonstrated an elevated procalcitonin was not necessarily associated with increased odds of bacterial pneumonia.[36]

Biomarker nuove prospettive

3 marcatori

PCR
Proteina C reattiva

Infezioni batteriche

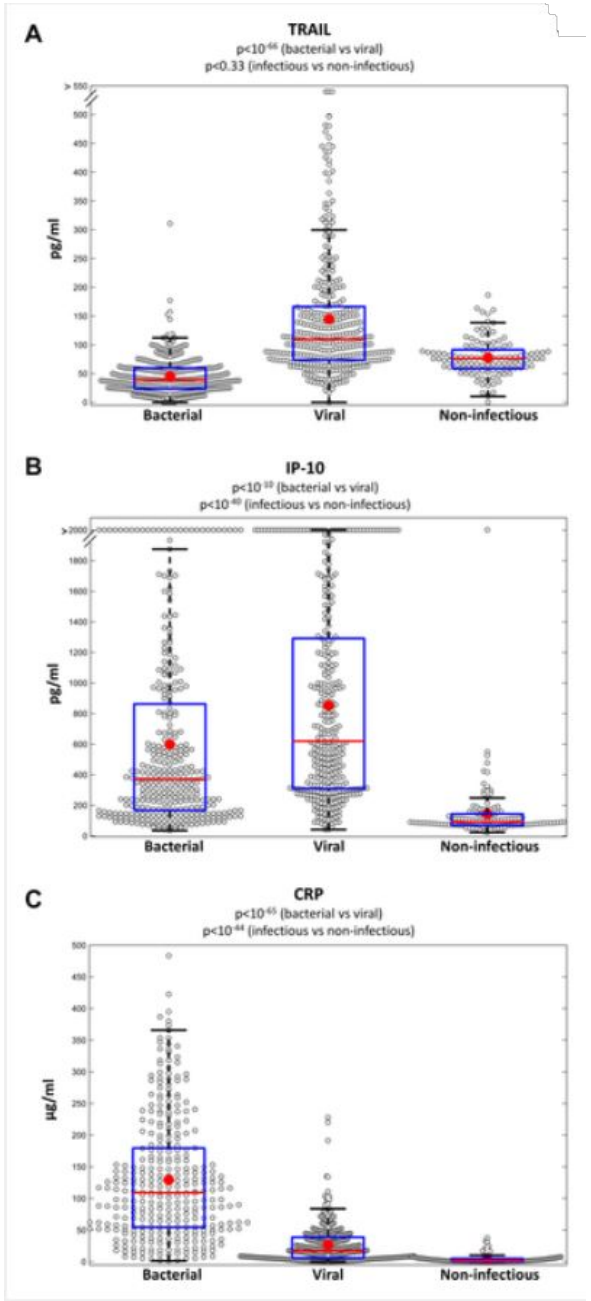
TRAIL
TNF-realted apoptosis inducing ligand

Infezioni virali

IP10
Interferon gamma induced protein-10

Aumenta maggiormente nelle infezioni virali

https://doi.org/10.1371/journal.pone.0120012



MeMed BV test

Index probabilistico

Triverity test missing some bacterial infections and MeMed BV misclassifying most viral infections as bacteria

•DOI: 10.1016/j.jinf.2024.106360

Table 2 Considerations for practical use of ID test systems in PHC

From: How to identify respiratory pathogens in primary health care – a review on the benefits, prospects and pitfalls in using point of care tests

Category	Topic	Practical recommendations
Pre-analytical	Indications for microbiologic testing	Microbiologic testing should be integrated into diagnostic algorithms and stewardship programs [37, 112].
	Clinical syndrome	Consider the reported symptoms and clinical signs to indicate appropriate microbiological sampling and diagnostic work-up [239].
	Epidemiologic situation	Consider the pathogen activity in the community and possible exposure to assess pre-test probability of a specific infection [240].
	Travel history	Consider the travel history and possible exposure to assess pre-test probability of a specific infection [241].
	Type of specimen collected	Approved clinical specimens vary by test system. Consult the manufacturer's instructions for use (IFU) for each test's approved specimens. Combining specimens, such as nasal and oropharyngeal swabs, may increase sensitivity for respiratory viruses– if approved. Note that nasopharyngeal swabs are ideal for the detection of *B. pertussis* by PCR and that sputum samples (not nasopharyngeal swabs) are required for the diagnosis of infections with *S. pneumoniae*, *L. pneumophila* and *M. pneumoniae* by PCR [242, 243]. Specimens initially taken for RADTs may not be suitable for RT-PCR, and samples for PCR may not be suitable for subsequent culture.
	Timing of specimen collection	Respiratory samples for RADTs, PCR and culture are best taken in the first 1 to 3 days after symptom onset [48]. Urinary samples for UATs are also best taken in the first days after symptom onset, yet may contain a pathogen's antigens for weeks [244, 245]. Expect serum samples for the diagnosis of *M. pneumoniae* or *B. pertussis* infections to be negative for pathogen-specific antibodies in previously unexposed/unvaccinated individuals in the first 7 to 10 days of the disease. Serial serum sampling may thus be required [39].

https://doi.org/10.1007/s15010-025-02600-1

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Analytical	In Vitro Diagnostic Regulations (IVDR)	Use IVDR-compliant or CLIA-waved tests.
	IFU	Follow the manufacturer's IFUs carefully and ensure that the personnel performing a diagnostic test is documented to be trained and competent for the procedure.
	Overall diagnostic accuracy	Healthcare providers ought to verify that their chosen test system meets the requirements of diagnostic accuracy e.g. by comparing it to the gold standard in collaboration with their ID laboratory or microbiologic/virologic institute [111, 246].
	Sensitivity	RADTs for clinical use should ideally have a sensitivity of at least 80% aligning with recommendations from the ECDC, FDA, and WHO [109, 110].
	Specificity	RADTs for clinical use should ideally have a specificity of at least 97%, aligning with recommendations from the ECDC, FDA and WHO [109, 110].
Post-analytical	Clinical information	The exchange of clinical information including the patient's history of contacts, travels and anti-infective therapy between physicians and the ID/microbiological laboratory is key for a correct interpretation of test results [112, 247].
	Other laboratory results	Consider other laboratory parameters such as CRP. A CRP threshold of > 5 mg/dL offers a sensitivity of 75% and a specificity of 75% for the classification of LRTIs as of bacterial etiology [105]. CRP is transcriptionally induced in the liver upon cytokine stimulation. CRP levels may thus be within the reference range (i.e. false negative for indication of a bacterial infection) at early stages of disease onset (< 24 h). However, in patients being symptomatic for > 24 h, normal CRP levels offer a good negative predictive value to rule out bacterial infection [107].
	Imaging studies	Consider the results imaging studies such as chest X-ray and lung ultrasound [104].
	Therapeutic consequences	Microbiologic testing should be integrated into therapeutic algorithms and stewardship programs ensuring that testing focuses on clinical cases in which test results are likely to have therapeutic consequences [37, 90, 164].

https://doi.org/10.1007/s15010-025-02600-1