CHIMICA ANALITICA CLINICA

Prof. Elisa Michelini- Dipartimento di Chimica "Giacomo Ciamician" (4 CFU, II Ciclo)

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Conoscenze e abilità da conseguire

Al termine del corso lo studente possiede

- le conoscenze di base relative ai più comuni metodi di analisi chimico-clinica
- ed è in grado di selezionare la metodica più adatta alla risoluzione di un dato problema clinico e
- è in grado di valutare in senso critico il dato analitico ottenuto.

Modalità di verifica dell'apprendimento

La verifica dell'apprendimento avviene attraverso l'esame finale, che accerta l'acquisizione delle conoscenze e delle abilità attese tramite una prova orale.

Foreword

Health care delivery and the practice of medicine and clinical laboratory science have undergone exponential change in the last decade. There have been, and continue to be, many factors contributing to that change. Rising costs and concern regarding unequal access to health care and the growing number of uninsured have made health care one of the top issues for this country. Politicians and regulators are faced with the need to provide accessible health care while trying to control costs. Policy makers and payers have increased influence over medical and diagnostic decisions through managed care. Consumers and payers alike expect easy access and the highest quality of care with the most economic prices. Reports on medical errors have raised the visibility for the need for enhanced patient safety and quality initiatives. Emphasis has shifted from simply diagnosing and treating disease to identifying and controlling disease risk factors and maintaining health. There is increased concern about public health issues and bioterrorism as well as environmental effects on health. As a result of these and other factors, laboratory testing is expanding and playing an increasingly valuable and prominent role in health care delivery.

Technological advances have dramatically changed the way we practice clinical laboratory science. Molecular diagnostic testing is allowing earlier detection of disease. Advances in biotechnology including the "omics"—genomics, proteomics, and pharmocogenomics—have given rise to the advent of personalized medicine. We can now determine inherited predisposition to disease, identify protein profiles associated with disease status, and tailor treatment options based on genetic make-up. Testing techniques have shifted from test tubes, beakers, and large, automated analyzers to microanalytic systems ("lab on a chip") that allow reduced sample size, fewer reagents, and smaller instruments. The walls of the laboratory are disappearing, with increasing numbers of tests that can be performed at the "point of care."

The demographics of health care are also changing. As a result of the aging population and longer life expectancy, we are seeing an increase in chronic disease, which is impacting the health care system. These demographics not only affect the number and types of individuals accessing the health care system, but also the workforce that is delivering the care. There is a growing shortage of educated and trained clinical laboratory professionals. This is a result of many factors, including the aging workforce, reduction in educational programs, and competing career opportunities.

As a result of all of these issues, the role of clinical laboratory practitioners is changing. We can no longer afford to be simply analysts that perform, report, and assure the quality of laboratory test results. Clinicians recognize and acknowledge the need for help in test selection and result interpretation. It is essential that laboratory professionals work with physicians in helping them understand testing options and optimize clinical outcomes. In order to do this, clinical laboratory practitioners must be educated and trained not only in test performance and utilization but also in pathophysiology, differential diagnosis, and how diagnostic information contributes to patient care and outcomes.

The sixth edition of *Clinical Chemistry: Techniques, Principles, Correlations* was written with these changing needs in mind. The text provides a comprehensive view of pathophysiology as it relates to clinical chemistry diagnostic testing. It emphasizes the preanalytical, analytical, and post-analytical aspects of diagnostic testing. This text not only provides comprehensive information but also includes case studies and other strategies that will enhance critical thinking and problem-solving skills. Furthermore, Web-based support is provided with the text. Utilization of the text and supportive materials will enhance theoretical, technical, and consultative skill development. This text is not only an excellent resource for clinical laboratory and medical students, but also for clinical laboratory practitioners, clinicians, and other health care providers.

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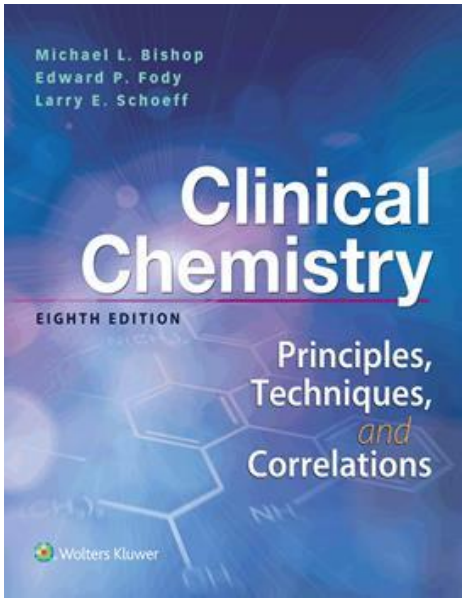
Some keywords

Public health issues
Environmental effects on health
Bioterrorism
Molecular diagnostics
Omics
Personalized medicine
Lab on a chip/point of care
Chronic disease management
Biomarker
Microbiota



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IL PROCESSO ANALITICO NEL LABORATORIO CHIMICO-CLINICO

Come per tutte le analisi, anche nelle analisi chimico-cliniche è possibile definire un ***processo analitico***, in cui ogni fase deve svolgersi correttamente per garantire l'attendibilità del risultato finale.

Prelievo del campione

Trasporto, accettazione e conservazione del campione

Fase preanalitica

Trattamento del campione

Fase analitica

Analisi

Refertazione

45% e il 70% degli errori in fase pre-analitica

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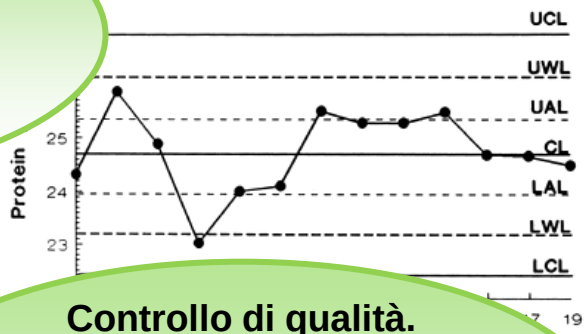
Matrice del campione
Principalmente fluidi biologici facilmente prelevabili → ***sangue, urina***, ma anche altri fluidi, feci, capelli, biopsie, ecc.

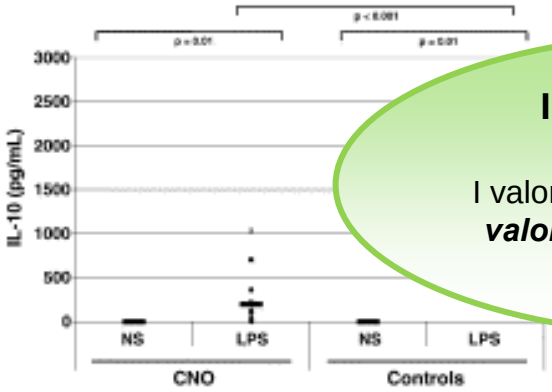
Natura degli analiti
Analiti presenti a basse concentrazioni e di varia natura → ***gas, ioni, piccole molecole organiche, zuccheri, lipidi, proteine, enzimi, DNA***



Problematiche nella chimica analitica clinica

Controllo di qualità.
Necessità di garantire la validità del risultato analitico → ***validazione*** delle procedure, ***controllo di qualità*** intra- ed interlaboratorio

Campionamento
Preparazione del paziente, modalità di prelievo dei campioni, trattamento e conservazione dei campioni



Interpretazione del risultato
I valori fisiologici sono variabili → ***valori "normali", sensibilità e specificità***

PRESTAZIONI DI UNA TECNICA ANALITICA

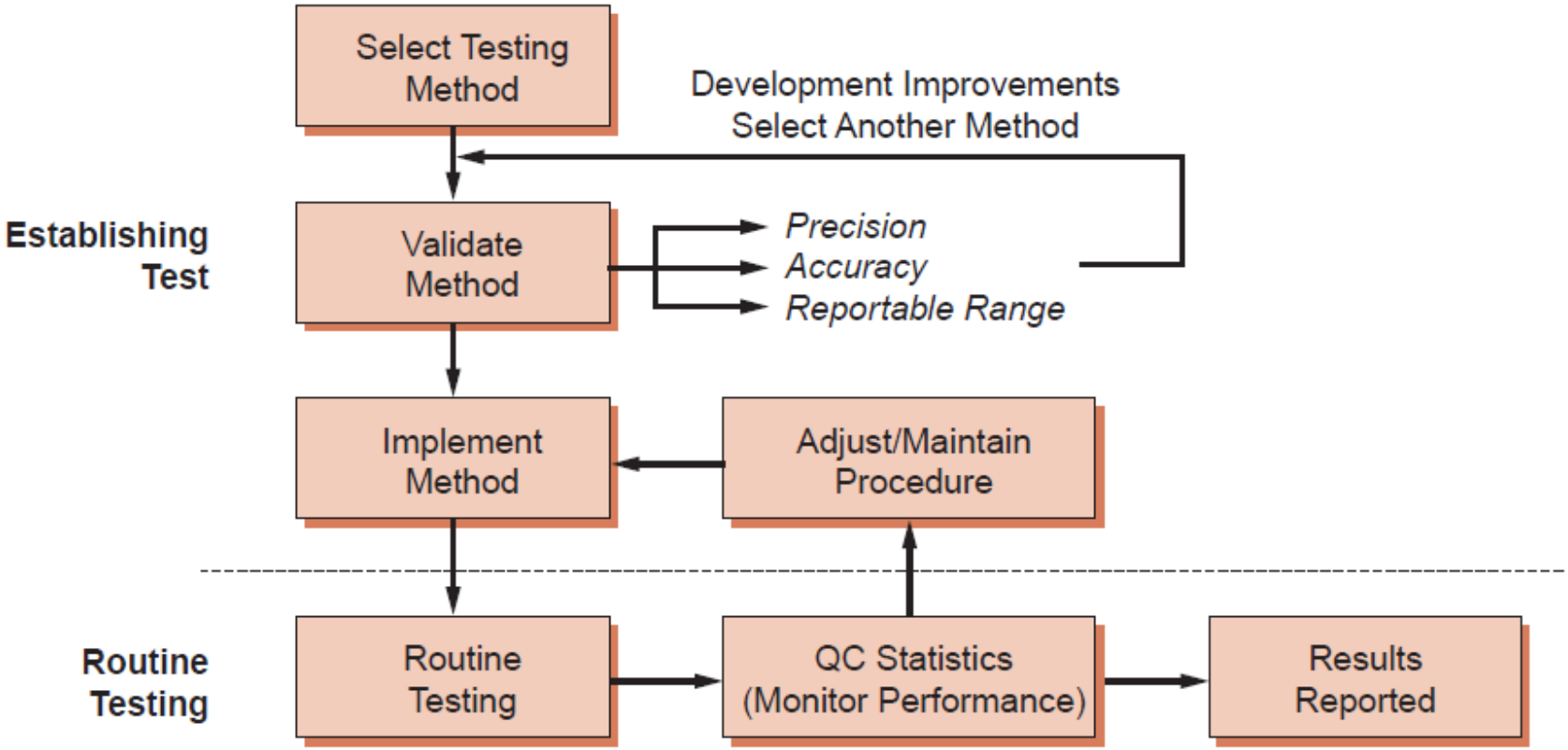
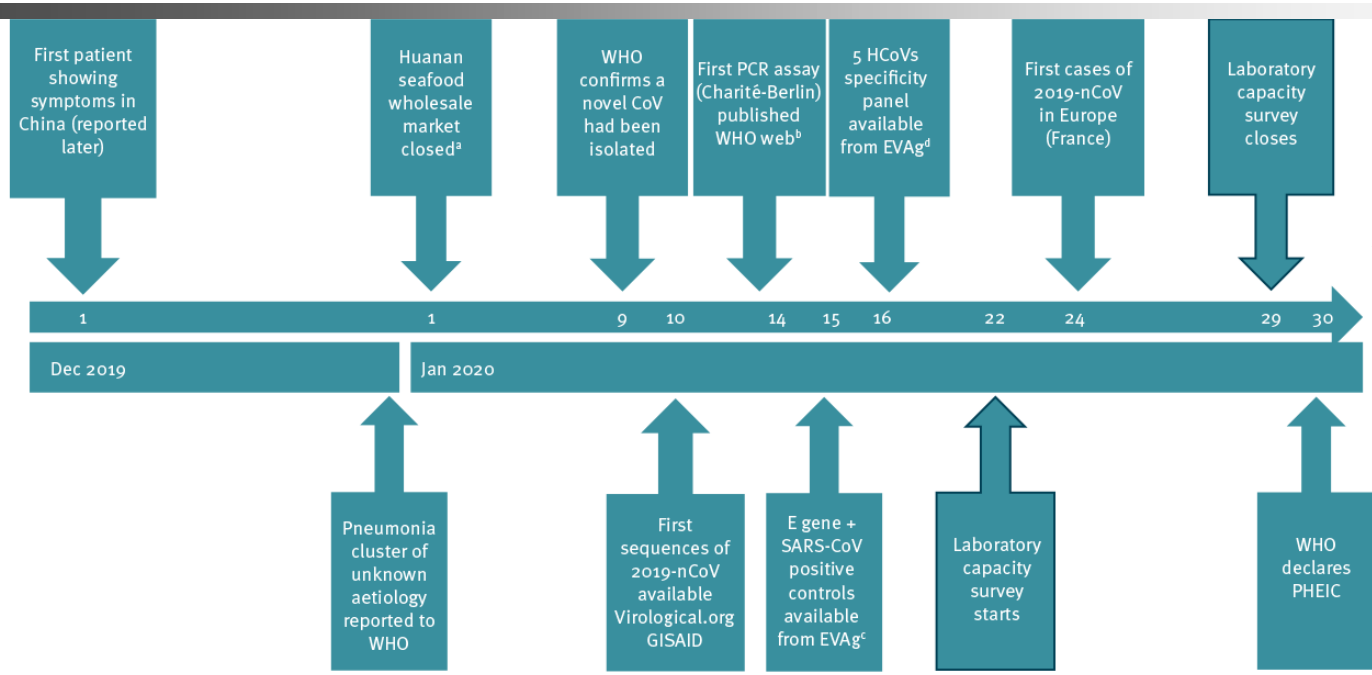


FIGURE 3-10 A flowchart on the process of method selection, evaluation, and monitoring. (Adapted from Westgard JO, Quam E, Barry T. *Basic QC Practices: Training in Statistical Quality Control for Healthcare Laboratories*. Madison, WI: Westgard Quality Corp.; 1998.)

METHOD VALIDATION: COVID-19 example



EVAg: European Virus Archive

PHEIC: public health emergency of international concern

The full genome of the novel coronavirus was published on January 10 of this year, just weeks after the disease was first identified in Wuhan, China. A week later, a group of researchers led by German scientists released the first diagnostic protocol for COVID-19 using swabbed samples from a patient's nose and throat; this PCR-based protocol has since been selected by the World Health Organization (WHO).

Not all countries have adopted the WHO's recommended diagnostic, including the US. The test detects the presence of SARS-CoV-2's E gene, which codes for the envelope that surrounds the viral shell, and the gene for the enzyme RNA-dependent RNA polymerase.

Reusken Chantal et al. Laboratory readiness and response for novel coronavirus (2019-nCoV) in expert laboratories in 30 EU/EEA countries, January 2020. Euro Surveill. 2020;25(6)

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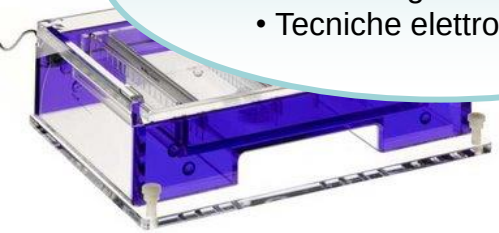
Metodi elettrochimici e sensori
- Elettrodi selettivi per pH/ioni
- Sensori per gas (O_2 e CO_2)

Metodi per la misura dell'attività enzimatica
- Metodi basati su substrati cromogenici, fluorogenici, chemiluminescenti

Tecniche di analisi

Tecniche separative
- Gascromatografia & cromatografia liquida
- Tecniche elettroforetiche



Metodi immunometrici
- Metodi immunochimici
- Metodi di immunodiffusione
- Metodi ELISA

Emocromocitometria
- "Coulter counters"
- Cito(fluori)metria a flusso
- Analisi d'immagine

Metodi di biologia molecolare e omiche
- PCR qualitativa e quantitativa, real time
- Proteomica

Strumentazione portatile
- Analizzatori portatili (es. glucometri)
- "Lateral Flow immunoassays"

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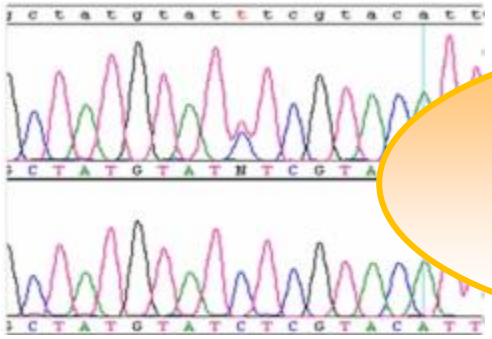
Analisi del sangue
Gas disciolti, elettroliti, esame emocromocitometrico, parametri di coagulazione, tipizzazione.

Analisi immunologiche
Antigeni, proteine, farmaci, ecc.

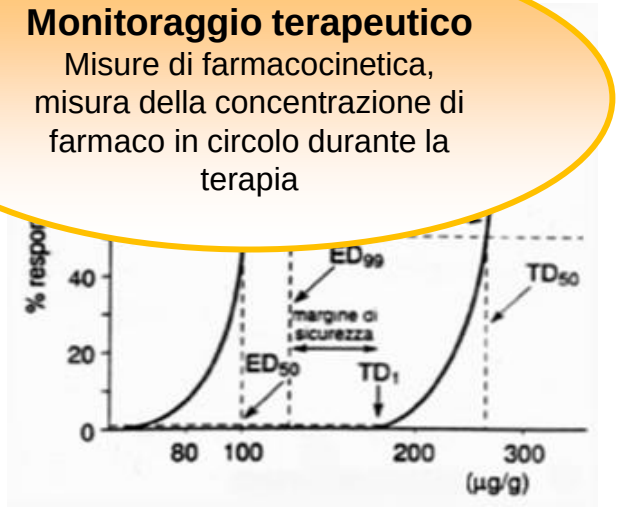
Analisi chimico-cliniche

Funzionalità di organi
Valutazione della funzionalità di organi (es. epatica) mediante determinazione di proteine ed enzimi nel sangue

Monitoraggio terapeutico
Misure di farmacocinetica, misura della concentrazione di farmaco in circolo durante la terapia



Diagnosi molecolare
Diagnosi di malattie infettive e genetiche, identificazione di mutazioni e di oncogeni



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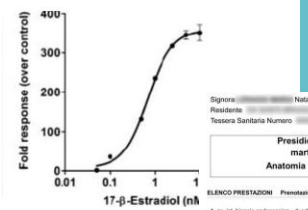
SIMULAZIONE «IN SILICO» DI UN METODO CHIMICO-CLINICO

	1	2	3	4	5	6
A	St_1	St_1	St_1	St_1	C_1	C_1
B	St_2	St_2	St_2	St_2	C_2	C_2
C	St_3	St_3	St_3	St_3	C_3	C_3
D	St_4	St_4				
E	St_5	St_5				
F	St_6	St_6				
G	St_7	St_7				
H	St_8	St_8				

Bianco	0,086	0,067	0,090	0,089
St_1	0,159	0,155	0,157	0,156
St_2	0,238	0,245	0,236	0,226
St_3	0,378	0,404	0,389	0,391
St_4	0,519	0,495	0,532	0,525
St_5	0,659	0,644	0,692	0,647
St_6	0,873	0,852	0,846	0,874
St_7	1,			
CQ	0,			



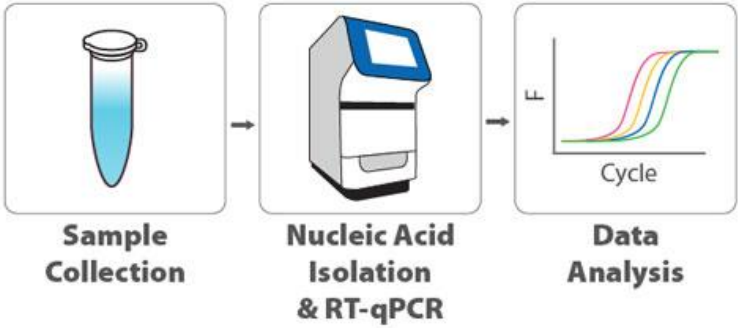
Diagnostics: COVID-19

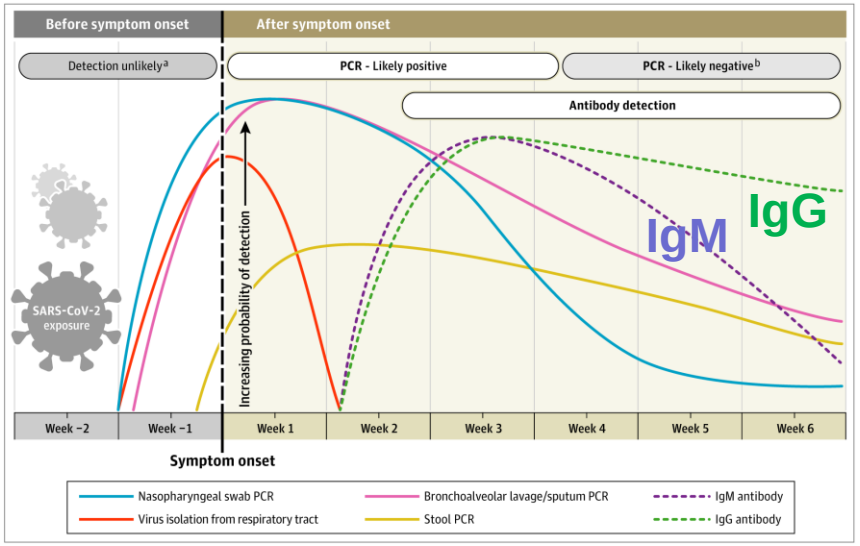
Two kinds of traditional methods for pathogen detection are **nucleic acid testing (NAT)** and **serological testing.**

Among all available testing methods, NAT plays a pivotal role in the public health response to SARS-CoV-2. It is the most sensitive method combined with high specificity and high efficiency.

Traditional serological testing for specific IgM, IgG, or viral antigens, such as ELISA, CLIA, and rapid serological testing should not be neglected.

Real-time RT-PCR assays for SARS-CoV-2 (Institut Pasteur)





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- *Introduzione*
- *Raccolta, trattamento e conservazione dei materiali biologici*
- *Il risultato nel laboratorio chimico-clinico (valori di riferimento, utilità di un test diagnostico e parametri che la definiscono, controllo di qualità)*
- *Analisi generiche (es. sangue e urine)*
- *Tecniche di analisi enzimatica*
- *Tecniche immunologiche*
- *Tecniche per la diagnosi molecolare*
- *Monitoraggio terapeutico*
- *Automazione nel laboratorio chimico-clinico*
- *Strumentazione portatile per analisi cliniche ("Point-of-Care Testing", POCT)*
- *Omiche per medicina di precisione*

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