Pro & Con on Molecular Microbiology Utilization In Clinical Practice

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Three laws of debate

#1 Every thing we're gonna talk today must be true

#2 We can skip some information,except those conflicting w/ the first law

#3 We must protect each other as long as such protection doesn't conflict w/ the first & second laws

What kind of audience are you?

A. Student

B. Resident

C. Fellow

D. Staff

E. Others

Which side are you regarding molecular microbiology utilization?

A. Pro

B. Con

Clinical utilization

1. Diagnosis: causative known & emerging pathogens
2. Susceptibility: genotypic resistance
3. Epidemiology: strain typing
4. Evaluation after treatment

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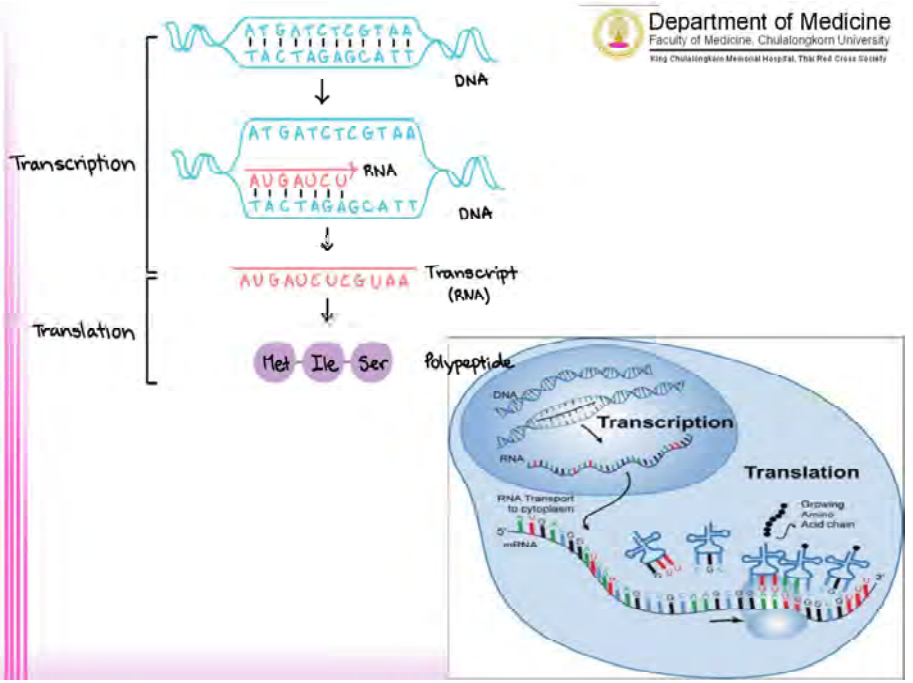

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Diagnosis

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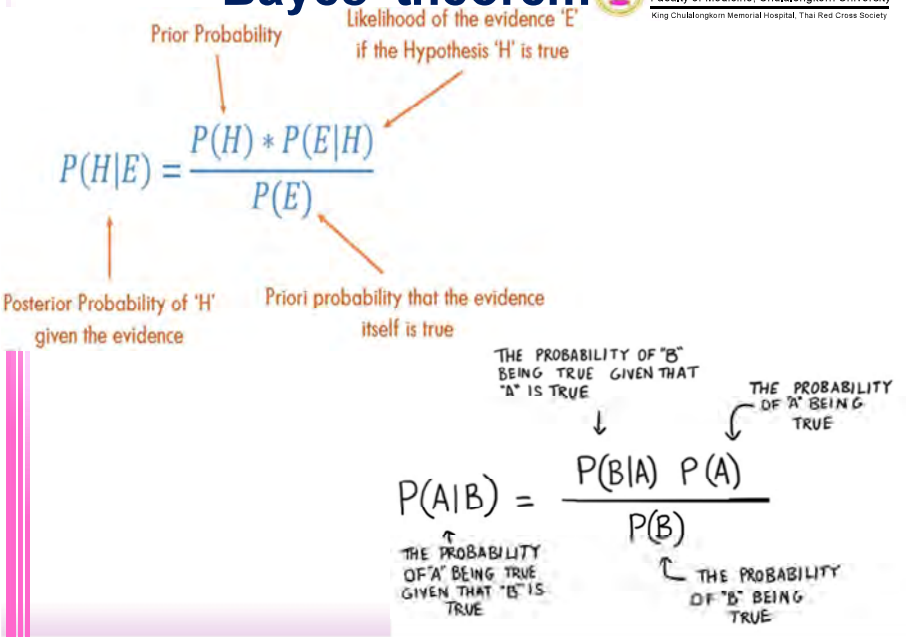
Bayes' theorem



$$PPV = \frac{(Sensitivity)(p)}{(Sensitivity)(p) + (1 - Specificity)(1 - p)}$$

$$NPV = \frac{(Specificity)(1 - p)}{(Specificity)(1 - p) + (1 - Sensitivity)(p)}$$

p = prevalence of the disease in the population being studied expressed as a fraction (ex. 0.20 for 20% prevalence)

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Pretest probability (%) of HSE	Posttest probability (%)	
	CSF PCR positive	CSF PCR negative
5 (low)	83.5	0.2
35 (medium)	98	2
60 (high)	99	6

Predictive use of HSV CSF PCR for Dx of herpes encephalitis

Tebas, et al. Am J Med 1993

การประชุมใหญ่วิชาการ ประจำปี ครั้งที่ 44
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Test performance for diagnosis

Too high sensitivity

Detection of

1. Not true causative pathogen, asymptomatic carriage
2. Pathogen of past infection, not current infection

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Not true causative pathogen, asymptomatic carriage

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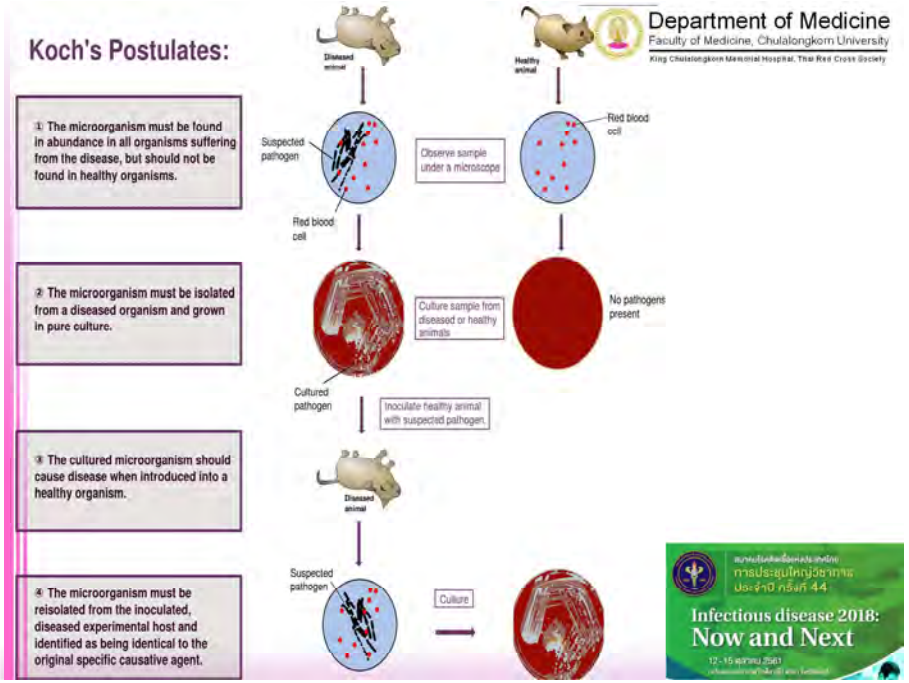
Koch's Postulates:



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Frequent Detection of Respiratory Viruses without Symptoms: Toward Defining Clinically Relevant Cutoff Values▽

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Highly sensitive techniques, such as PCR, have greatly improved the detection of respiratory viruses. However, the sensitivity of PCR tests also complicates clinical interpretation, as the presence of small amounts of viral targets may not necessarily have clinical relevance. We performed a prospective case-control study in asymptomatic and symptomatic young children. PCR detection of 14 respiratory viruses was performed in nasal washes, and results were quantified in copies per milliliter. A total of 141 cases and 157 controls were included. In 72% of the cases and 28% of the controls, at least one virus was identified. When stratified for age, at least one virus was identified in 47% of the controls younger than 1 year old. Rhinovirus (RV) was frequently detected in both symptomatic and asymptomatic individuals. Receiver operating characteristic analysis for quantitative rhinovirus detection showed that cutoff values for clinical relevance are feasible for RV. In contrast to rhinovirus, respiratory syncytial virus (RSV) was rarely detected in controls, suggesting that a positive RSV test result is almost always of clinical relevance, independent of viral quantity. In conclusion, our study shows that asymptomatic carriage of a respiratory virus occurs frequently in young children. However, significant differences in the amount of virus present were observed between cases and controls. This suggests that defining cutoff levels should be feasible and represents the next necessary step for diagnosing viral respiratory infections using molecular tests.

J Clin Microbiol 2011.

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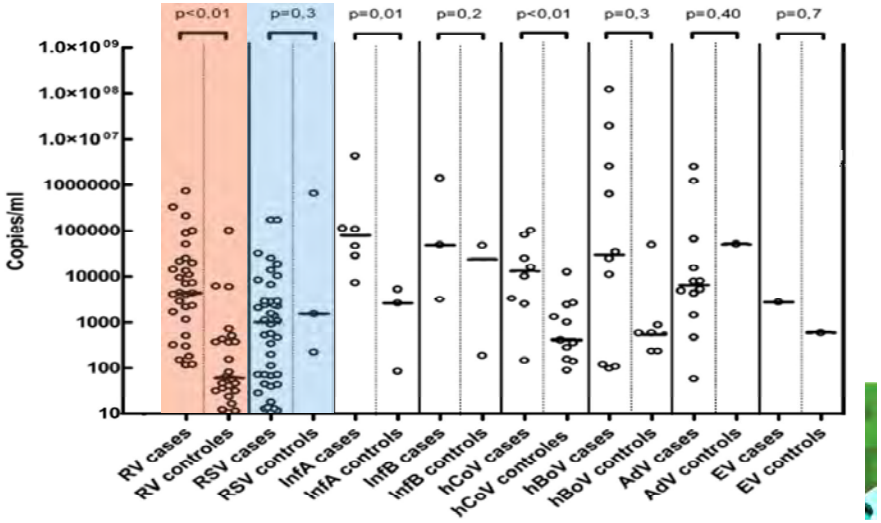
Case: IPD pts up to 6 y/o w/ suspected acute RTI
Control: OPD pts w/ same age w/o RTI or fever for >7 days



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Community Surveillance of Respiratory Viruses Among Families in the Utah Better Identification of Germs-Longitudinal Viral Epidemiology (BIG-LoVE) Study

Methods. Twenty-six households (108 individuals) provided concurrent symptom and nasal swab data for 4166 person-weeks. The FilmArray polymerase chain reaction (PCR) platform (BioFire Diagnostics, LLC) was used to detect 16 respiratory viruses. Viral illnesses were defined as ≥1 consecutive weeks with the same virus detected with symptoms reported in ≥1 week.

Results. Participants reported symptoms in 23% and a virus was detected in 26% of person-weeks. Children younger than 5 years reported symptoms more often and were more likely to have a virus detected than older participants (odds ratio [OR] 2.47, 95% confidence interval [CI], 2.08–2.94 and OR 3.96, 95% CI, 3.35–4.70, respectively). Compared with single person households, individuals living with children experienced 3 additional weeks of virus detection. There were 783 viral detection episodes; 440 (56%) associated with symptoms. Coronaviruses, human metapneumovirus, and influenza A detections were usually symptomatic; bocavirus and rhinovirus detections were often asymptomatic. The mean duration of PCR detection was ≤2 weeks for all viruses and detections of ≥3 weeks occurred in 16% of episodes. Younger children had longer durations of PCR detection.

Conclusions. Viral detection is often asymptomatic and occasionally prolonged, especially for bocavirus and rhinovirus. In clinical settings, the interpretation of positive PCR tests, particularly in young children and those who live with them, may be confounded.

Byington, et al. Clin Infect Dis 2015.