# RAPID ANTIGEN TESTING: ACCELERATING DIAGNOSIS AND ENHANCING RESPIRATORY DISEASE MANAGEMENT


- **DR. AMESH ADALJA MD FIDSA FACEP FACP**
- SENIOR SCHOLAR, JOHNS HOPKINS CENTER FOR HEALTH SECURITY
- **@AMESHAA**

# OUTLINE

Why diagnose



Biological
Dark Matter

The Impact of
Antibiotic Resistance

Integrating POC
diagnostic technology
into care

# DISCLAIMER

**01**

This presentation is on behalf of BD. Any discussion regarding BD products during the presentation today is limited to information that is consistent with the [FDA] approvals or clearances for those products. Please consult BD product labels and inserts for any indications, contraindications, hazards, warnings, cautions and instructions for use.

**02**

The opinions and clinical experiences presented herein are for informational purposes only. [The results from any study referenced herein may not be predictive for all patients. Individual results may vary depending on a variety of patient specific attributes.]

**03**

The speakers have been compensated by BD to give this presentation.

# WHY DIAGNOSE

"Rumpelstiltskin"

Know what is making people sick

Separate treatment pathways

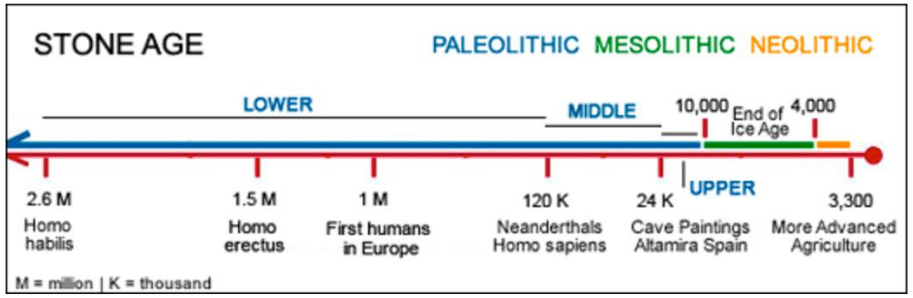
Epidemiology

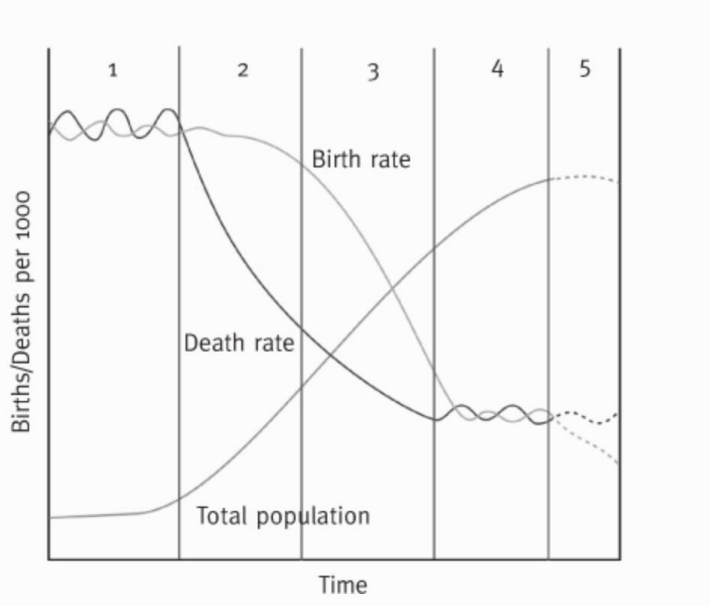
# BIOLOGICAL DARK MATTER

# EPIDEMIOLOGICAL TRANSITIONS AND AGES

## 3 major transitions from Neolithic to modern area

- **Nomadic → Agriculture 10,000 years ago**
  (Age of Pestilence and Famine)
- **Industrial Revolution**
  (Age of Receding Epidemics)
- **Globalization, Urbanization, Aging**
  (Age of Degenerative and Manmade diseases)

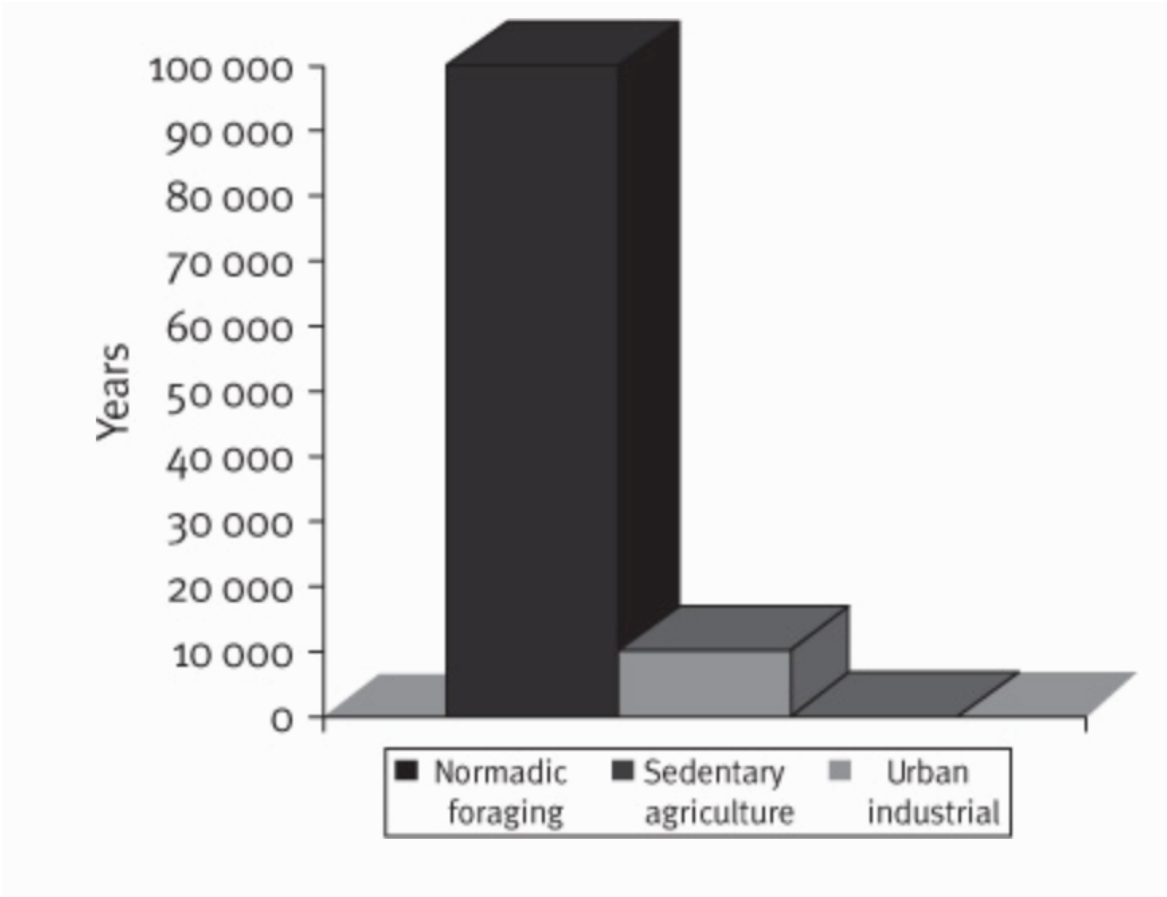



Omran AR. The epidemiologic transition: a theory of the epidemiology of population change. 1971. Milbank Q. 2005;83(4):731-57.

# NOMADIC → STATIONARY TRANSITION

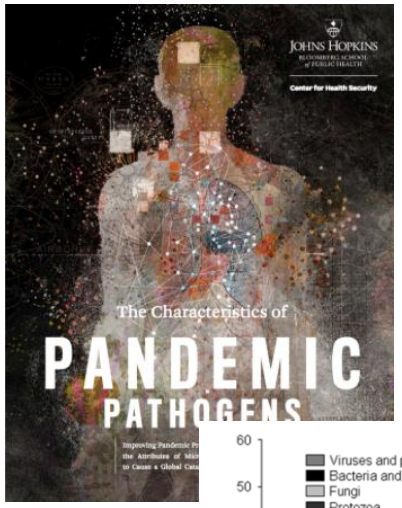
- Population density increases
- Human to human interaction increases
- Waste management
- Agriculture
- Lifestyle changes
- Evolution

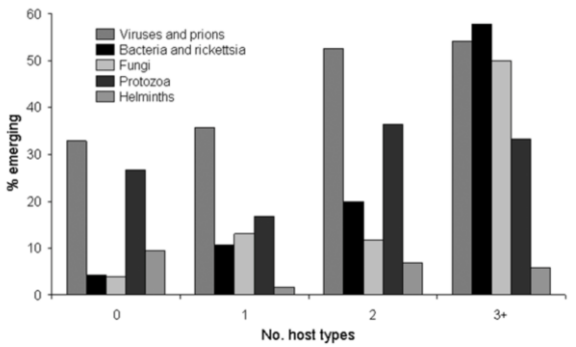



An unnatural history of emerging infections, Barrett & Armelagos

# THE ALCHEMY OF A PANDEMIC PATHOGEN

- Efficient transmissibility from human to human
- Moderate fatality rate
- **Contagious during incubation period**
- Mild illnesses with contagiousness
- Immunologically naïve population
- No vaccine or treatment
- Evasion of host immune response



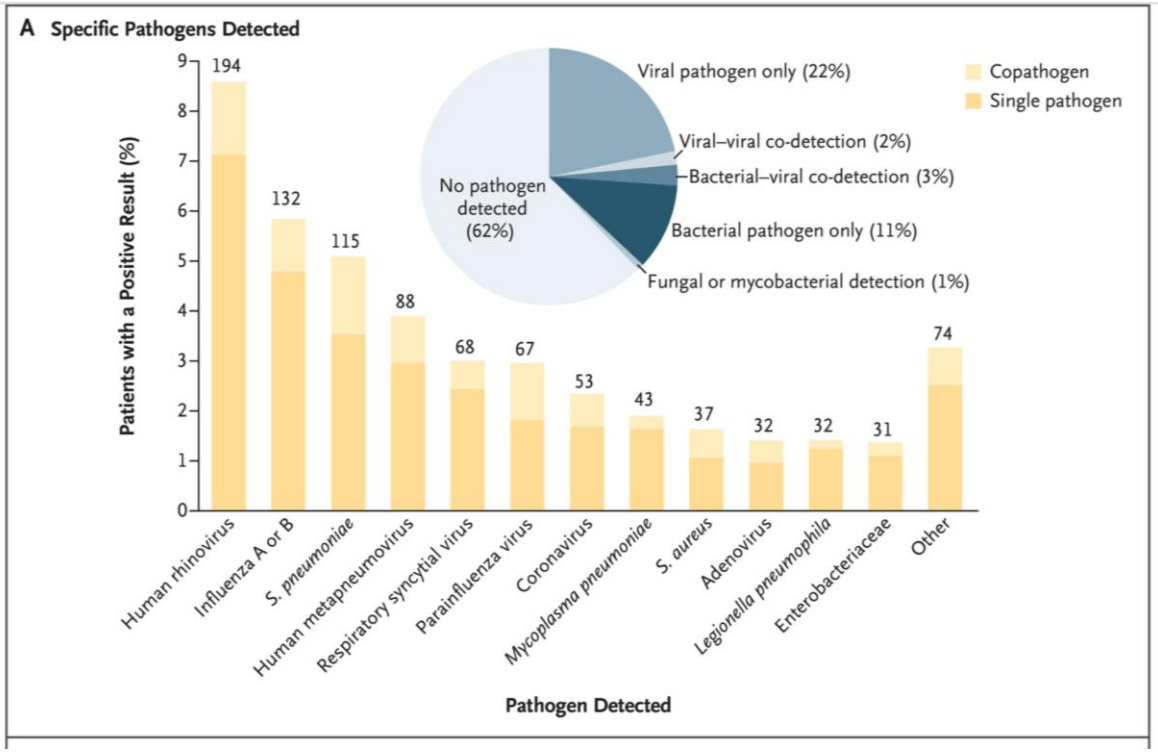




Woolhouse EID 2005

# What Does It Mean to Take Respiratory Viruses Seriously?

- ”You’ve got some virus”
- Biological dark matter
- Spectrum of illness

# SPECIFIC DIAGNOSIS
# → ANTIVIRAL THERAPY




*Clinical Infectious Diseases*

MAJOR ARTICLE

# Comprehensive Molecular Testing for Respiratory Pathogens in Community-Acquired Pneumonia

**Naomi J. Gadsby,[1] Clark D. Russell,[1,2] Martin P. McHugh,[1] Harriet Mark,[1] Andrew Conway Morris,[3] Ian F. Laurenson,[1] Adam T. Hill,[4] and Kate E. Templeton[1]**

[1]Medical Microbiology, Department of Laboratory Medicine, Royal Infirmary of Edinburgh, [2]College of Medicine and Veterinary Medicine, University of Edinburgh, [3]Department of Anaesthesia, University of Cambridge, and [4]Respiratory Medicine, Royal Infirmary of Edinburgh, United Kingdom

**(See the Editorial Commentaries by Musher on pages 824–5 and Jain and Pavia on pages 826–8.)**

***Background.*** The frequent lack of a microbiological diagnosis in community-acquired pneumonia (CAP) impairs pathogen-directed antimicrobial therapy. This study assessed the use of comprehensive multibacterial, multiviral molecular testing, including quantification, in adults hospitalized with CAP.

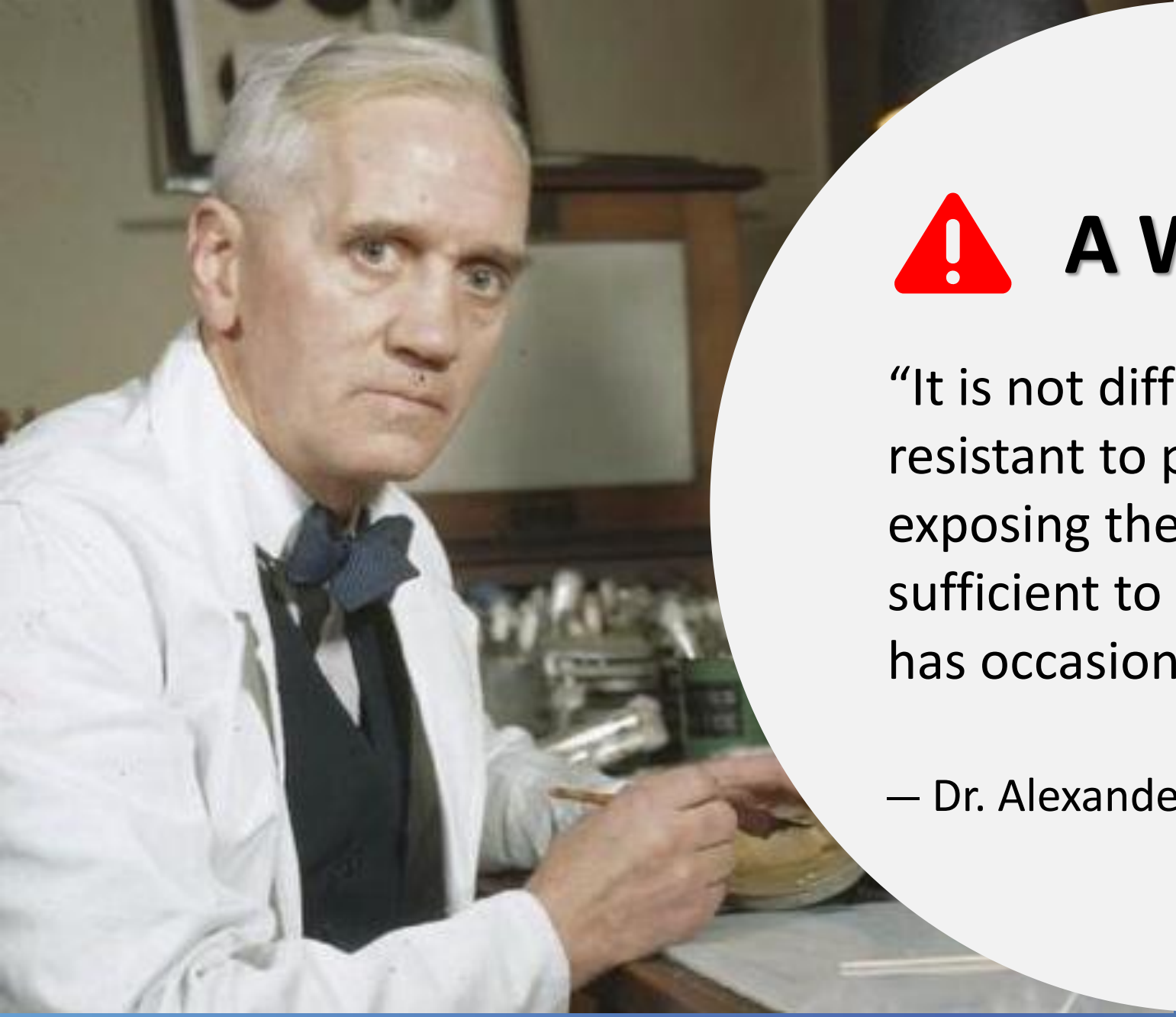
***Methods.*** Clinical and laboratory data were collected for 323 adults with radiologically-confirmed CAP admitted to 2 UK tertiary care hospitals. Sputum (96%) or endotracheal aspirate (4%) specimens were cultured as per routine practice and also tested with fast multiplex real-time polymerase-chain reaction (PCR) assays for 26 respiratory bacteria and viruses. Bacterial loads were also calculated for 8 bacterial pathogens. Appropriate pathogen-directed therapy was retrospectively assessed using national guidelines adapted for local antimicrobial susceptibility patterns.

***Results.*** Comprehensive molecular testing of single lower respiratory tract (LRT) specimens achieved pathogen detection in 87% of CAP patients compared with 39% with culture-based methods. *Haemophilus influenzae* and *Streptococcus pneumoniae* were the main agents detected, along with a wide variety of typical and atypical pathogens. Viruses were present in 30% of cases; 82% of these were codetections with bacteria. Most (85%) patients had received antimicrobials in the 72 hours before admission. Of these, 78% had a bacterial pathogen detected by PCR but only 32% were culture-positive ($P < .0001$). Molecular testing had the potential to enable de-escalation in number and/or spectrum of antimicrobials in 77% of patients.

***Conclusions.*** Comprehensive molecular testing significantly improves pathogen detection in CAP, particularly in antimicrobial-exposed patients, and requires only a single LRT specimen. It also has the potential to enable early de-escalation from broad-spectrum empirical antimicrobials to pathogen-directed therapy.

**Keywords.** community-acquired pneumonia; bacterial load; viral; molecular testing; PCR.

# ANTIBIOTIC RESISTANCE:
## THE WAR OF THE WORLDS



# A Warning

“It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body. “

— Dr. Alexander Fleming

NBC NEWS HEALTH

TOPICS Health care | Diet & Fitness | Aging | Body Odd | More

CRE-INFECTIONS More bad news about 'nightmare bacteria', CDC says

# More bad news about 'nightmare bacteria', CDC says

**JoNel Aleccia, Staff Writer, NBC News,**

BIRD-FLU

March 5, 2013 at 1:31 PM ET

# Superbug Drugs: Only 7 New Drugs In Development For Antibiotic-Resistant Bacteria

Reuters | Posted: 04/17/2013 11:59 pm EDT

*Published on Wednesday, March 6, 2013 by Common Dreams*

# CDC: Alarming Rise in Antibiotic-Resistant 'Nightmare Bacteria'

**"Our strongest antibiotics don't work and patients are left with potentially untreatable infections."**

**- Andrea Germanos, staff writer**


# Drug-Resistant Bacteria Pose Increasing Health Risks

YAHOO! CONTRIBUTOR NETWORK By L.L. Woodard | Yahoo! Contributor Network – Wed, Mar 6, 2013

Email | Share 8 | Tweet 19 | Share | +1 0 | Print

On Tuesday, the U.S. Centers for Disease Control and Prevention 's director, Tom Frieden, M.D., M.P.H. , sounded an alarm via telebriefing about an antibiotic-resistant strain of bacteria that pose a triple threat to health. The infections caused by these bacteria are acquired while patients are in the hospital or another type of medical care facility, referred to as nosocomial infections and most severely affect those people who are the most ill, have compromised immune systems and other risk factors.

**Carbapenem-Resistant Enterobacteriaceae: 'Nightmare Bacteria'**

# PHYSICIAN DISCOMFORT

## Not knowing if illness bacterial or viral

CRP, procalcitonin, other tools not always available in timely manner and have some degree of physician unfamiliarity

**Just playing it safe**

# STRIKING EXAMPLE

**2013 season: only 15% of PCR-confirmed flu cases got antivirals (outpatients)**

Twice as many got an antibacterial agent!

## Failing Our Patients by Suboptimally Treating Influenza Infections

**Michael G. Ison**[1,2]

Divisions of [1]Infectious Diseases and [2]Organ Transplantation, Northwestern University Feinberg School of Medicine, Chicago, Illinois

Havers, CID 2014 Ison, CID 2014

# Clinical practice of respiratory virus diagnostics in critically ill patients with a suspected pneumonia: A prospective observational study

Frank van Someren Gréve (MD)[a,b,*,1], David S.Y. Ong (MD, PharmD, PhD)[c,d,e,**,1], Olaf L. Cremer (MD, PhD)[c], Marc J.M. Bonten (MD, PhD)[d,e], Lieuwe D.J. Bos (PhD)[a], Menno D. de Jong (MD, PhD)[b], Marcus J. Schultz (MD, PhD)[a], Nicole P. Juffermans (MD, PhD)[a], on behalf of: the MARS consortium[2]

**Less than 50% of suspected pneumonia patients in the ICU are tested for respiratory viruses: 4 insights**

Journal of Clinical Virology 83 (2016) 37–42

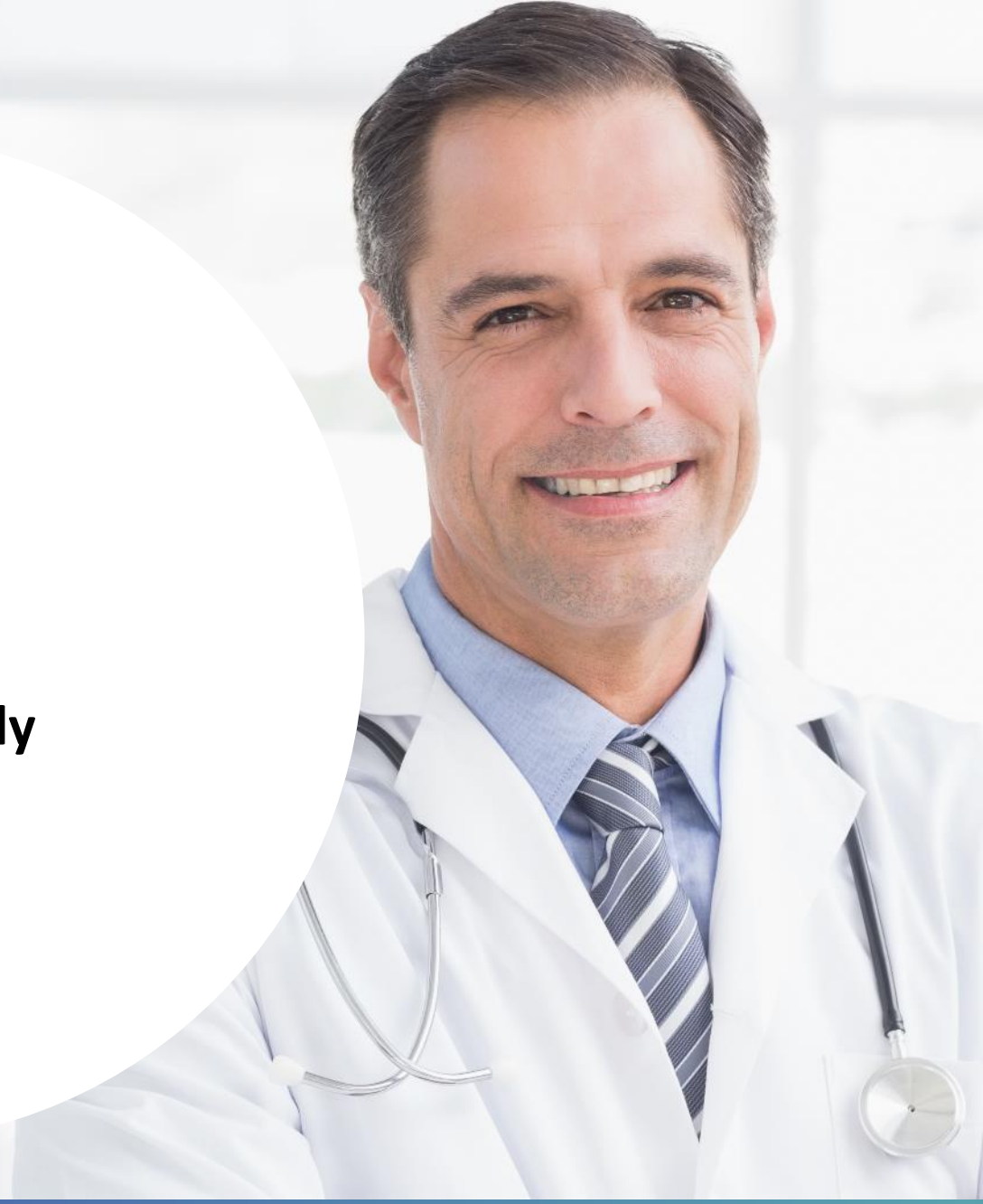
# Physician Empowerment

**Tools to better steward antibiotics**

---

**My approach: use all tools at hand (especially those that are CLIA-waived and/or provide rapid results)**

CRP, procalcitonin, rapid POC strep tests, mononucleosis, influenza, RSV, etc.



# BETTER ANTIVIRAL PRESCRIBING LESS ANTIBIOTIC USE

## Impact of Rapid Diagnosis on Management of Adults Hospitalized With Influenza

*Ann R. Falsey, MD; Yoshihiko Murata, MD, PhD; Edward E. Walsh, MD*

**Conclusions:** Rapid influenza testing leads to reductions in antibiotic use in hospitalized adults. Better tools to rule out concomitant bacterial infection are needed to optimize the impact of viral testing.

*Arch Intern Med. 2007;167:354-360*

# IMPACT ON ANTIBIOTIC PRESCRIPTION OF RAPID ANTIGEN DETECTION TESTING IN ACUTE PHARYNGITIS IN ADULTS:

## A RANDOMIZED CLINICAL TRIAL

## Conclusion

Even though more than 30% of negative RADT resulted in antibiotic prescribing, the study findings support the use of RADT in the consultation. This strategy has an important impact on reducing antibiotic prescription among adults with acute pharyngitis

The Pediatric Infectious Disease Journal

# Effect of rapid viral diagnosis on the management of children hospitalized with lower respiratory tract infection

ADCOCK, PENNY M. MD; STOUT, GORDON G.; HAUCK, MARY A.; MARSHALL, GARY S. MD

| Outcome | Median Days | | | | | |
|---|---|---|---|---|---|---|
| | All children | | Age ≤2 mo | | Age >2 mo | |
| | RSV-pos | RSV-neg | RSV-pos | RSV-neg | RSV-pos | RSV-neg |
| Length of stay | 4 (92)† | 4 (68) | 4 (33) | 4 (22) | 4 (59) | 4 (46) |
| Duration of parenteral antibiotic therapy | 2 (37)‡ | 3 (30) | 3 (14) | 3 (13) | 2 (23)§ | 3 (17) |

* Differences not significant unless indicated.
† Numbers in parentheses, number of patients.
‡ $P = 0.0387$; positive *vs.* negative.
§ $P = 0.0143$; positive *vs.* negative.
pos, positive; neg, negative.

**TABLE 2**. Outcomes in children tested for RSV

# Cost effectiveness of a point-of-care test for adenoviral conjunctivitis

Belina L. Udeh, PhD · John E. Schneider, PhD · Robert L. Ohsfeldt, PhD

## XVI. Should ASPs Advocate for Use of Rapid Viral Testing for Respiratory Pathogens to Reduce the Use of Inappropriate Antibiotics?

*Recommendation*

17. We suggest the use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics

# THE IMPACT OF POC TECHNOLOGY

# POC: 21ST CENTURY SOLUTION

## Now, near-patient testing available

- Including CLIA-waived forms
- Including home tests

## Multi-analyte syndromic testing

- Respiratory panels

# STEWARDSHIP

**Confident ability to not initiate inappropriate antibiotic use (as well as hedging use)**

**Example: pneumonia**

**Outpatient settings (rapid POC tests)**

**Clinical pathways incorporating testing use**

- Viral testing coupled to bacterial testing

- GAS, RSV, influenza, COVID, mono

# IN THE UPCOMING RESPIRATORY SEASON

**POC tests as critical component of rapidly triaging persons to the correct treatment pathway**

- Influenza antivirals
- COVID antivirals
- GAS antibiotics
- Antibiotic stewardship

**Patients are increasingly interested in the etiology**

- Behavior change

# POC IN URGENT CARE

**This a nexus where POC tests have a major impact**

- Diagnosis
- Triage
- Treatment
- Stewardship

**Epidemiology role**

# BARRIERS

CLIA-waived (and home) infectious disease tests are a major development

Tricorder

Balkanization and silo-based thinking have limited the impact thus far

The best way to empower physicians to make the correct clinical decision is to place tools in their hands

# REFERENCES


- Omran AR. The epidemiologic transition: a theory of the epidemiology of population change. 1971. Milbank Q. 2005;83(4):731-57.
- An unnatural history of emerging infections, Barrett & Armelagos
- Woolhouse EID 2005
- Adalja AA, Watson M, Toner ES, Cicero A, Inglesby TV. Characteristics of Microbes Most Likely to Cause Pandemics and Global Catastrophes. Curr Top Microbiol Immunol. 2019;424:1-20.
- Gadsby et al. CID
- Havers, CID
- Ison, CID
- Journal of Clinical Virology 83 (2016) 37-42
- Arch of Int Med 2007; 354-360
- Adcock, PIDJ
- Udeh. Am J Med Sci 2008Be
- IDSA/SHEA Stewardship Guidelines, CID 2016
- Llor, British Journal of General Practice 2011


# THANK YOU

**Amesh Adalja MD FIDSA FACEP FACP**

Adjunct Assistant Professor at Johns Hopkins University, Carnegie Mellon University and University of Pittsburgh

**@AmeshAA**