

Finding Rona

John A. Sellick, Jr., DO, MS, FACP, FIDSA, FSHEA

Professor of Medicine

Division of Infectious Diseases

Hospital Epidemiologist

KALEIDA Health

Veterans Affairs Western New York Healthcare System



Jacobs School of Medicine
and Biomedical Sciences

University at Buffalo



Kaleida Health



UB|MD

INTERNAL MEDICINE
PRIMARY & SPECIALTY CARE

Disclosure

- I have no actual or potential conflict(s) of interest in relation to this presentation.

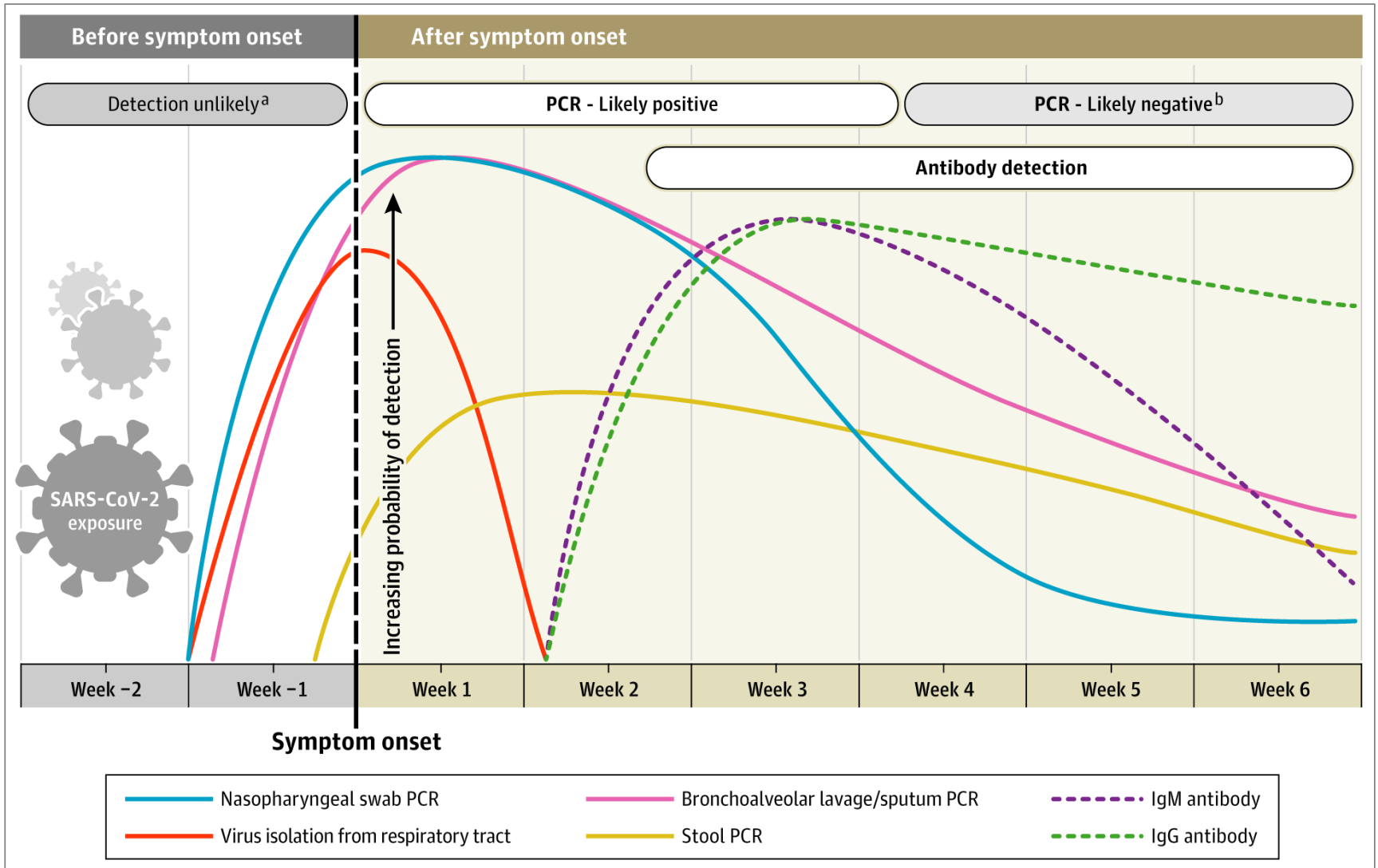
COVID-19

- SARS-CoV-2
 - Closely related to SARS-CoV
 - ~30k bases
 - 15 genes
- Spread primarily by respiratory droplets
- Some environmental persistence

Diagnosics

- Viral culture
- Antigen testing
- Molecular testing
 - Polymerase chain reaction (PCR)
 - Loop-mediated isothermal amplification (LAMP)
- Serology
 - Enzyme linked immunosorbent assay (ELISA)
 - Immunochemical (“lateral flow”)

Diagnostic Time Course



Major Caveats

- All current tests are available *via* FDA EUA (emergency use authorization) only
- ***Clinical*** sensitivity/specificity are unknown
 - Comparisons are done *in vitro*
 - PPV/NPV change with prevalence
 - (Other fully approved “microbe” PCR tests are generally 90–95% sensitive & specific)
- Tests used in studies are variable
 - Often homebrews, other unapproved tests

The Specimens

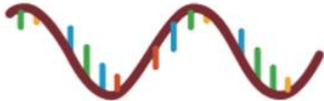
- Respiratory tract
 - NP, mid–turbinate; OP, expectorated
 - Bronchial or other “deep” lung
 - Proper technic, flocked swab & VTM
- Stool – ? Value, validation
- Blood
 - Serum for ELISA
 - Fingertstick for NYSDOH ELISA & lateral flow tests

Diagnostic qRT-PCR

a) sample collection



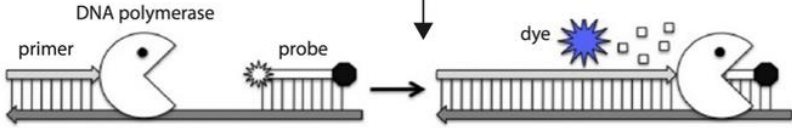
b) RNA extraction



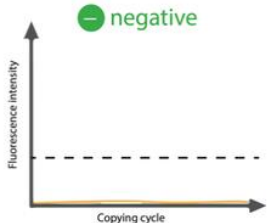
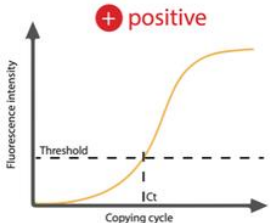
c) Reverse transcription



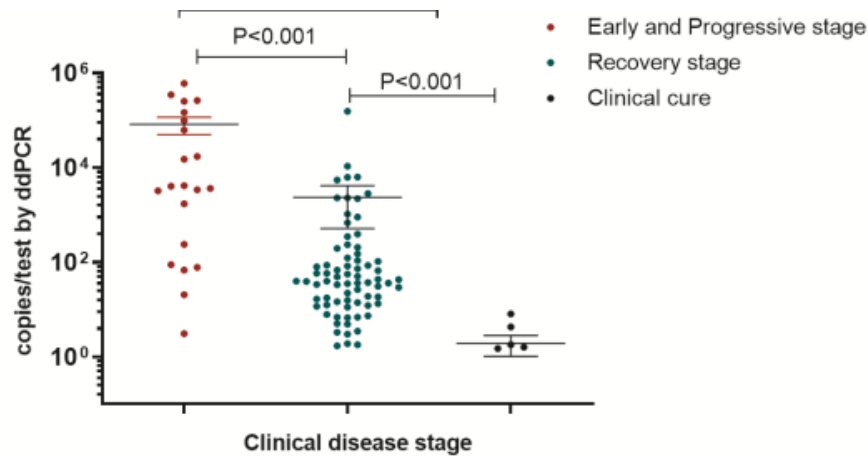
d) RT-PCR amplification



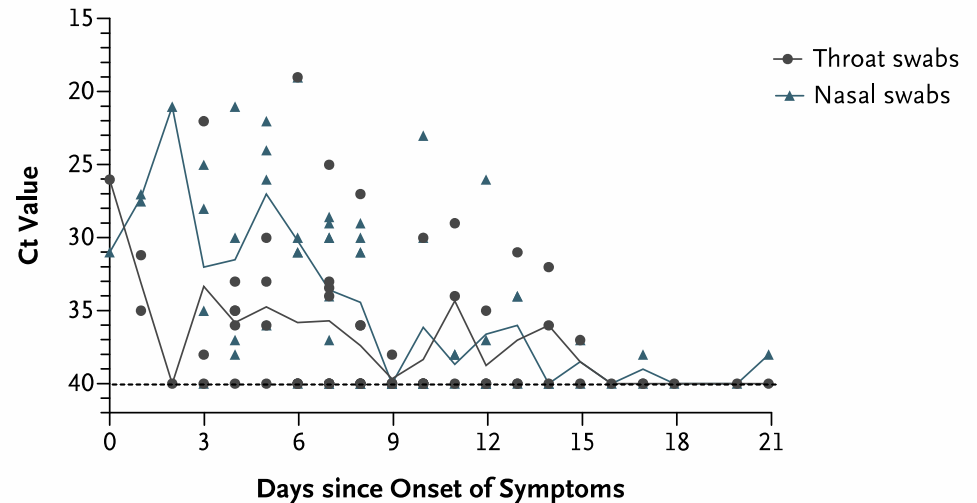
e) Results



What About the Y-axis?



C Aggregated Ct Values



The Tests

- Conventional PCR: hours
 - Limit of detection (LOD): ~100 copies/ml
 - Reliable if good quality swab early in illness
 - Later in illness, need bronchial/lung specimen
 - “Specificity” is high
- “Rapid” PCR (Cepheid/Biofire): <1 hr
 - LOD: ~250–300 copies/ml
- LAMP (Abbott/Alere ID NOW): ~15 minutes
 - LOD: ~125 copies/ml claimed
 - Worse performance if swab in VTM

Common Questions

- Repeats?
 - Yes, if suggestive history/symptoms/findings
 - How many??
 - Consider LRT specimen if possible
- Does (+) PCR = infectious?
 - No – PCR amplifies any matching RNA
 - Limited data suggest no infectious virus after 9 days or with high Ct values

More Questions

- Screening?
 - Hmm...complex...
 - Contacts of (likely) cases
 - 48–72 hrs before (all?) surgery/procedures
 - Return to college?
- Return to work for infected HCW?
 - 2 consecutive (–) >24 hrs apart
- Discontinue precautions for (+) cases?
 - 2 consecutive (–) >24 hrs apart

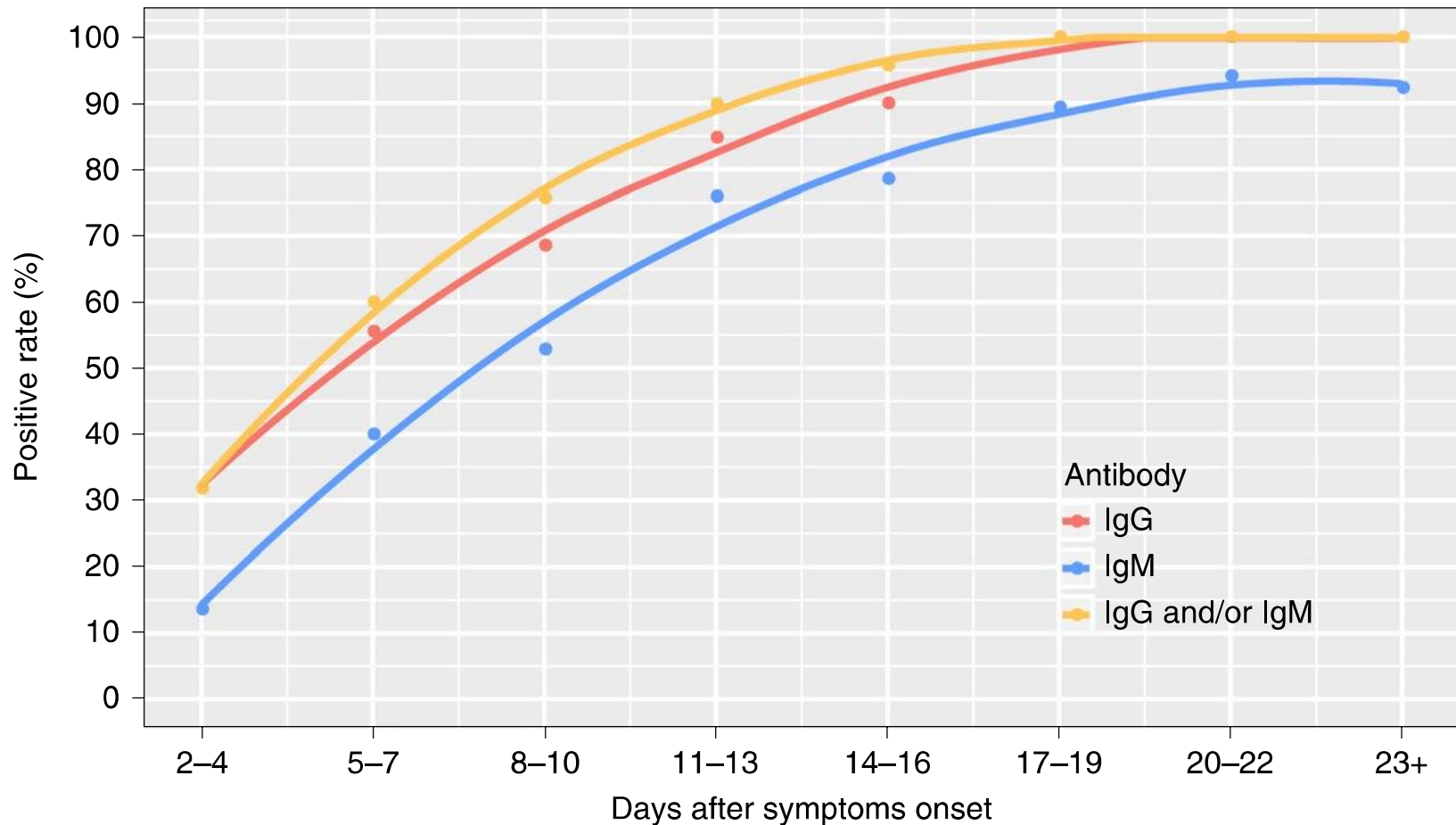
COVID Cliché

- I know where you're coming from and at the end of the day we have a really solid rapid test that is a real game changer.
- *The LAMP & rapid antigen tests have variable performance outside of early clinical cases (larger amount of virus.)*

Serology

- Properly validated IgG ELISA
 - Compared to pre-COVID-19 banked serum & known PCR (+) clinical cases
- Abbott Architect SARS-CoV-2 IgG EUA
 - >99% Sensitivity/Specificity >14 days of symptoms
 - Excludes other CoV Abs
 - Positive/negative – no “titer”

What About the Y-axis?

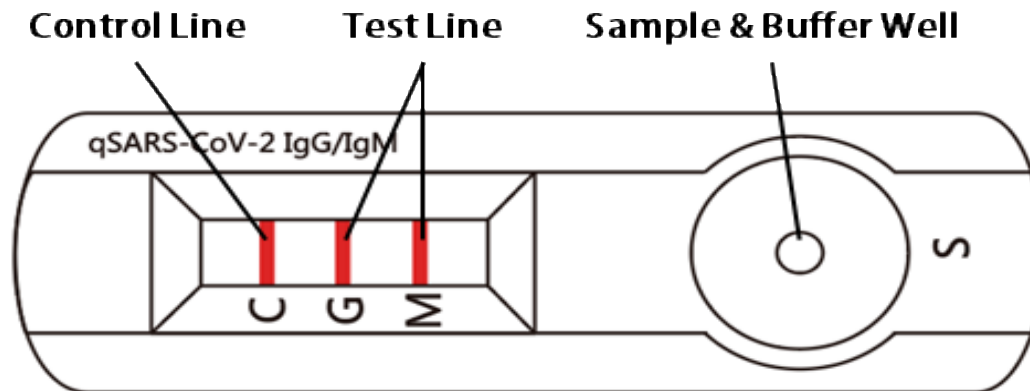


Use

- Reasonable
 - Determine seroprevalence in a population
 - PCR (–) clinical cases??
 - Screening for plasma donation
- Not Reasonable
 - Lack of infectivity
 - “Immunity Passport”
 - Level and/or duration of protection unknown!

Lateral Flow Ab Tests

- A few EUA & **MANY** non-EUA on market
 - POOR performance for most
 - Some with PPV $\leq 50\%$



References

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