Yale SCHOOL OF MEDICINE

As of September 16, 2020

Teacher Guide 3: Testing

NGSS In This Module:

Science and Engineering Practices:

Developing and Using Models

- Develop a model to describe unobservable mechanisms. (MS)

Constructing Explanations and Designing Solutions

- Apply scientific reasoning, theory, and/or models to link evidence to the claims to assess the extent to which the reasoning and data support the explanation or conclusion.

Engaging in Argument from Evidence

- Compare and evaluate competing arguments or design solutions in light of currently accepted explanations, new evidence, limitations (e.g., trade-offs).
- Evaluate competing design solutions to a real-world problem based on scientific ideas and principles, empirical evidence, and/or logical arguments regarding relevant factors (e.g., economic, societal, environmental, ethical considerations.)

Obtaining, Evaluating, and Communicating Information

- Compare, integrate, and evaluate scientific and/or technical information from multiple authoritative sources, assessing the evidence and usefulness of each source.

Disciplinary Core Ideas:

Life Science: From Molecules to Organisms: Structures and Processes -- Structure and Function (LS1.A)

- Systems of specialized cells within organisms help them perform the essential functions of life.
- All cells contain genetic information in the form of DNA molecules. Genes are regions in the DNA that contain the instructions that code for the formation of proteins, which carry out most of the work of the cells.

Crosscutting Concepts:

Scale, Proportion, and Quantity

- Some systems can only be studied indirectly because they are too small, too large, too fast, or too slow to observe directly.

Systems and System Models

- Systems can be designed to do specific tasks.
- When investigating or describing a system, the boundaries and initial conditions of the system need to be defined and their inputs and outputs analyzed and described using models.

Key Terms:

- **Symptomatic**
- **Asymptomatic**
- **RNA**
- **Base pairing**
- **Cells**
- **Coronavirus**
- **Amplification**
- **Reverse transcriptase**
- **DNA polymerase**
- **Protocols**
- **Molecular testing**
- **Antigen testing**
- **Antibody (Serological) testing**
- **Asymptomatic**
- **Presymptomatic**
- **Shed the virus**
- **SARS-CoV-2 (Severe Acute Respiratory Syndrome)**

<u>The Module: Testing</u>

The Story

As Tash's fever persists, Ray and June become increasingly concerned about their friend's health, especially after visiting the nurse's office and researching COVID-19 online. The trio

decides to seek care for Tash, but a debate breaks out about whether Tash should visit the Emergency Room, call a doctor by phone, or visit a walk-in clinic. Ultimately, the kids decide to call Tash's pediatrician, who sets up a telehealth visit. Upon seeing Tash, the pediatrician decides to have him tested. However, Tash, Ray, and June learn that they may have to wait days before the results will return! He will need to remain in isolation until the test results are back. Why is it so important to get a test? What kinds of tests are there? How does the testing for COVID-19 work?

Performance Expectations

- Provide evidence in support of the importance of widespread testing, even for asymptomatic people.
- Compare and contrast the differences between molecular, antigen, and antibody (serological) tests.
- Present an argument or counter-arguments based on data and evidence about the claim that detecting viruses in people is challenging.
- Use data as evidence to make a claim that detecting viruses in people is difficult to prove.
- Compare and integrate sources of information presented in different media in order to address the scientific question: What are the molecular differences between SARS-CoV-2 and human cells?
- Describe the molecular differences between SARS-CoV-2 and human cells.
- Develop and use a model to illustrate how specific features of SARS-CoV-2 RNA are detected.
- Draw and use a model to explain a process that amplifies SARS-CoV-2 genetic material to make detection more sensitive.
- Develop and use a model to illustrate how specific features of SARS-CoV-2 proteins are detected.

Challenges:

1. Why is testing so important?
2. How do we detect the virus?
3. How can we amplify our signal?
4. How can we detect COVID protein in our sample?

Challenge 1: Why is Testing So Important?

Learning Targets

- I can use evidence to support why testing is important for controlling the spread of coronavirus.
- I can use evidence to support why people who are asymptomatic should get tested.

Estimated Time:

1.1 Activity: Who Should Get Tested?

a. **Visit** the CDC website: "Test for Further Infection"

   https://www.cdc.gov/coronavirus/2019-ncov/testing/diagnostic-testing.html#who-should-get-tested

b. **Read:** "Considerations for who should get tested"
c. **Use:** Work through the "*Coronavirus Self-checker"* to learn about when it is appropriate to seek testing and appropriate medical care, according to the CDC.
d. **Answer:** Respond to the survey questions using the profile of this patient:
   - It's okay to **Agree** to disclosure
   - Lives in **Hartford, Connecticut**
   - Answer for **someone else**
   - No life-threatening symptoms
   - Age: 45
   - Feeling ill
   - Female
   - **Not sure** if this person had contact with another person who was diagnosed with COVID-19
   - Showing these symptoms: **feeling feverish**, **coughing, sore throat**
   - Live in a single family home

     They work as an **Emergency Medical Technician** (EMT)

e. **Reflect and Discuss**: What should this person do?

f. **Optional**: Complete the "*Coronavirus Self-checker" again, using a profile you create and share your results.*

1.2 Activity 2 - Why should you get tested for COVID-19 even if you do not have any symptoms?

a. Read:

It's the end of a long and really boring summer of social distancing. You haven't seen your friends in so long, rarely even been outside of your house, and you're even becoming tired of mindlessly scrolling through your phone. So, when you get a mass group text from one of your close friends, proposing an informal get together in the local park this weekend, you can feel yourself getting amped.

On Saturday after dinner, you kick your skateboard out the front door and shout to your parents, who are watching tv, that you will be home by nine and that you "just need some air."

At the park you can see a few of your friends and teammates hanging around the swings and you head over, noting how different everyone looks; some guys have longer hair, a few of the girls have new hairstyles and have obviously been to a hair salon. You note with relief that most of them are wearing a mask, and you pull yours back on too, feeling less awkward.

It's good to see everyone again and, after a few awkward fist and elbow bumps, you all begin laughing and catching up. As the sun sets, the crowd grows, it's so good to relax and see everyone looking almost the same as that weird week when school shut down and the whole world went virtual.

For about two and a half hours you laugh and joke, circulating around the informal party, occasionally taking off your mask for a quick selfie with your best friends, posting and sharing.

One week later your mom tells you that school won't be starting with in-person classes as they had hoped to do. She says the principal has based it on an uptick in students at the school testing positive for the Covid 19 virus, and she suggests you get a test also. You remind her you haven't left the house since mid-February and you think getting tested is useless.

b. **Watch and Reflect:** "What's the Difference Between Asymptomatic and Presymptomatic Spread of COVID-19?" [1:04] https://www.health.com/condition/infectious-diseases/coronavirus/asymptomatic-vs-presymptomatic
c. **Ask:** Write 3 questions for your classmates to answer based on the material.
d. **Discuss:** Use your questions to guide a whole-class discussion about the asymptomatic and presymptomatic spread of COVID-19.

1.3 Activity 3 - What conclusions can you draw from the data? What can we learn about testing from the data?

a. **Read and Analyze:** Read through the webpage and review the charts included in "Is Your State Doing Enough Coronavirus Testing?" **https://www.nytimes.com/interactive/2020/us/coronavirus-testing.html**
b. **Draw conclusions, Share and Discuss:**
    - Based on the series of charts, make 3-5 claims based on evidence from the data. (You may also cite other sources to support your claims.)
c. **Reflect and Discuss:** Analyze the data and answer these questions:
    - Make three claims based on evidence after reviewing these data.
    - Some have said that "if you test less, we'll have fewer cases." Do you agree or disagree? Use at least two sources to support your opinion.
d. **Reflect and Write:** *Should testing be limited to people with flu-like symptoms or should anyone be able to get a test even if they are asymptomatic?* Include at least 3 sources of evidence using data to support your claim.

Challenge 2: How Do We Detect the Virus?

Learning Targets:

- I can describe how to detect the coronavirus.
- I can describe the characteristics of SARS-CoV-2.
- I can identify different types of tests used to detect coronavirus and explain how they work.

Estimated Time:

2.1 Activity 1: Where would we expect to find the virus in someone who is infected?

a. **Watch:** "COVID-19: An Illustrated Scientific Summary." [8:17] https://covid.yale.edu/media-player/4989/
b. **Create and Share/Discuss:** Diagram the life-cycle of SARS-CoV-2.
c. **Write and Share/Discuss:** List the cells in humans that SARS-CoV-2 infects and where in the body those cells are located.

2.2 Activity 2: What are the different types of tests that can detect the presence of coronavirus?

a. **Watch**: "An Introduction to COVID-19 Tests" [2:48] -- the video introduction of the "Coronavirus Testing Basics" website: https://www.fda.gov/consumers/consumer-updates/coronavirus-testing-basics

b. **Read:** The text that follows the video in the website "Coronavirus Testing Basics".

c. **Read:** "The Latest in Coronavirus (COVID-19) Testing Methods and Availability" https://www.goodrx.com/blog/coronavirus-covid-19-testing-updates-methods-cost-availability/

d. **Reflect and Write/Discuss:**
   - What are the differences between molecular, antigen, and antibody (serological) tests?
   - According to the article, how accurate are molecular and antigen tests?

- How does “sample pooling” work?

2.3 Activity 3: “What is one way to collect a sample to test for SARS-CoV-2?”

a. **Watch:** “What is it like to be tested for COVID-19?” [2:56] https://youtu.be/HJsKFGUE-Ak
b. **Read: “Interim Guidelines for Clinical Specimens for COVID-19”** https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fguidelines-clinical-specimens.html
c. **Write:** List locations in the body where we might expect to find a lot of the virus.
d. **Create:** Find or diagram a tool that might allow us to obtain a sample from one of the locations you listed.
e. **Share** your results.

2.4 Activity 4: Can we see the virus that causes COVID-19 in our sample?

a. **Research**: Find the size of SARS-CoV-2.
b. **Investigate:** Check out this interactive website: “How Big? Interactive.” **https://www.cellsalive.com/howbig_js.htm**
c. **Write**:

- Which of these can we easily see with the naked eye?
- Rearrange the list of 10 items in the column from smallest to largest.
- Add SARS-CoV-2 to your sequenced list in the appropriate position.

d. **Discuss:** Compare your results with classmates.

2.5 Activity 5: How do different types of tests identify the virus?

a. **WATCH:** “Polymerase chain reaction (PCR)” [4:38] https://www.youtube.com/watch?v=aUBJtHwHASA [4:37]

b. **WATCH:** “Understanding COVID-19 testing” [6:14] https://www.youtube.com/watch?v=fMIy_2Oe9n8

c. **Reflect and Discuss:**
   - What parts of the virus does each test detect?
   - How do we measure the presence of the virus?
   - How can we be sure the interpretation of the test is correct?
   - What are false negatives and false positives and what are their implications?

2.6 Activity 6: What components of the virus could we detect in a sample?

a. **Watch 4 Videos**
   - **"**Coronavirus Anatomy Explained": Science, Simplified [2:01] https://www.youtube.com/watch?v=8hgc2iZflTI
   - "COVID-19 animation: Coronavirus and antibody testing explained" [1:57] https://www.youtube.com/watch?v=EGVPSdp4iLs
   - "Understanding COVID-19" [6:14] https://www.youtube.com/watch?v=fMIy_2Oe9n8
   - "How we test for SARS-CoV-2 - RT-PCR (Reverse Transcription PCR)" [3:54] **https://www.youtube.com/watch?v=j3ajN0DKaEw**

b. **Read**: "Coronavirus Genomic and Subgenomic RNA Architecture Mapped" https://www.genengnews.com/news/coronavirus-genomic-and-subgenomic-rna-architecture-mapped/

c. **Write and Discuss:**
   - List the major components of SARS-CoV-2 (i.e protein)?
   - Do our cells have these components? Which ones?
   - What, if any, are the differences between these components in our cells and those in coronavirus?
   - What is the difference between RNA in SARS-CoV-2 and RNA in our cells?

- **Draw:** the structure of a RNA molecule and label the components
- **Describe:** how RNA molecules differ from each other (e.g. structure, sequence)
- **Share:** your work with classmates.

2.7 Activity 7: How could we detect a specific RNA molecule?

a. **Research:** Use online resources to find molecules that would interact with the components of RNA.
b. **Model:** Draw an interaction between these molecules and the components of RNA.
c. **Identify:** List the types of interactions and strengths.
d. **Write and share:**
    - What type of bond is between the nucleotides and RNA?
    - What is the relative strength of those bonds?
    - What is the strength of the base pair interaction between a single nucleotide and a RNA?
    - What is an example of a strong bonding pair?
    - How can we create a stronger association with the SARS-CoV-2 RNA?
e. **Design and Share**: Create an oligomer of several nucleotides that base pair to SARS-CoV-2 RNA
    - How do we select which sequence of SARS-CoV-2 RNA to target?

2.8 Activity 8: How to detect viral protein in a sample?

a. **Research:** Use online resources to find answers.
    - Protein
        - Of what are proteins composed?
    - Amino acids
        - Describe amino acids: structure, charge, hydrophobicity, acidic/basic
        - Do the amino acids differ between SARS-CoV-2 and our cells?
    - How can you distinguish between SARS-CoV-2 proteins and our proteins?
        - Sequence?
        - Structure?
    - How does sequence determine structure?
    - How can we detect a protein with a specific 3-D structure?
    - How do proteins interact with each other?
        - 4˚ structure
        - Lock and key, induced fit

b. **Identify** the proteins in our bodies whose job is to bind to specific proteins in other organisms.

c. **Share and Discuss** your responses.

2.9 Activity 9: How do we obtain RNA or protein from our sample?

a. **Read:** Consult the instruction manual from a Viral RNA purification kit: "QIAamp DSP Viral RNA Mini Kit" that you can access at https://www.qiagen.com/us/products/diagnostics-and-clinical-research/solutions-for-laboratory-developed-tests/qiaamp-dsp-viral-rna-mini-kit/#orderinginformation
b. **Model:** Make a diagram that explains the procedure for purifying RNA from our samples
c. **Share and Discuss:** Provide and receive feedback on the models you and your class developed.
d. **Collaborate:** As a class, work together to incorporate ideas into the model that all can agree upon.

Challenge 3: How Can We Amplify Our Signal?

Learning Targets:

- I can explain and use amplification.
- I can model amplification.

3.1 Activity 1: How does amplification work?

a. **Answer** the following:
Our sample may contain very few viruses and our test may not be sensitive enough to detect the presence of the virus RNA or protein. How can we design a test that increases the signal? How can we increase the amount of viral nucleic acid?

- Is there a way to copy nucleic acids?
    - What do our cells need to do before dividing?
- Describe the process for how our cells copy their DNA.
- Could we use a similar process to copy viral RNA?
    - How can we convert viral RNA into DNA?
        - Reverse transcriptase (RT)
        - Oligomer that anneals to our RNA

- How can we make a copy of the DNA copy of the viral RNA?
  - DNA polymerase
  - Oligomers that anneal to our DNA copy and RNA
- Can we repeat the process to make several copies of the DNA?
  - Polymerase chain reaction (PCR)
- How many new DNA copies are produced after each round of PCR?

b. **Share and Discuss:** your responses.

3.2 Activity 2 - Design a RT-PCR Assay

a. **Design:** Using this sequence from the SARS-CoV-2 Nucleocapsid gene, design a set of primers to perform an RT-PCR assay:
   - 5'-GACCCCAAAATCAGCGAAATGCACCCCGCATTACGTTTGGTGGACCCTCAGATTCAA CTGGCAGTAACCAGA-3'
   - Primers should be 20 nucleotides in length
     - Forward primer: 5'-GAC CCC AAA ATC AGC GAA AT-3'
     - Reverse primer: 5'-TCT GGT TAC TGC CAG TTG AAT CTG-3'

b. **Outline a protocol** for performing RT-PCR
   - Reverse Transcription Step
     - Purified RNA from our sample
     - Reverse primer
     - Reverse transcriptase
     - Nucleotides
   - Polymerase Step
     - Sample from Reverse Transcription Step
     - Reverse primer
     - Forward primer
     - TAQ polymerase (A thermostable DNA polymerase)
     - Nucleotides

c. **Share and Discuss:** Examine each other's designs, offering helpful suggestions if needed.

3.3 Activity 3: Using PCR

a. **Calculate** the number of DNA molecules after 30 rounds of PCR. Assume our sample has 10 molecules of SARS-CoV-2 nucleocapsid RNA.

b. **Graph** the number of DNA molecules after each of the first 5 rounds of PCR.

- How would you characterize the line?

c. **Write** a formula that would allow you to estimate the number of DNA molecules for any number of PCR cycles.
d. **Share and Discuss** your results.

4.1 Challenge 4: How Can We Use Antibodies to Detect SARS-CoV-2?

Learning Targets:

- I can describe how antibodies function.
- I can explain the process of antibody production.
- I can illustrate the structure of an antibody and relate that to its function.
- I can explain how scientists generate and isolate antibodies to recognize SARS-CoV-2.

Activity: Using antibodies to detect SARS-CoV-2

a. **Research**: Look online to find out the roles of antibodies in the immune system. List them.
b. **Model:** Draw a diagram explaining how antibodies are produced.
c. **Draw:** Show the structure of an antibody and label the parts and their functions .
d. **Develop an Argument:** Use evidence to support which part of the antibody would help us identify SARS-CoV-2 in our sample.
e. **Diagram:** Outline a protocol to generate and isolate antibodies that recognize SARS-CoV-2.
f. **Share and Discuss:** your results.

Links to protocols and guides:
https://www.fda.gov/media/141570/download
https://www.abbott.com/corpnewsroom/product-and-innovation/upping-the-ante-on-COVID-19-antigen-testing.html

Professional Opportunities:

Molecular Biologist - https://www.careerexplorer.com/careers/molecular-biologist/
Pharmaceutical Scientist - https://explorehealthcareers.org/career/pharmacology/pharmaceutical-scientist/

Medical Lab Technician -
https://www.bls.gov/ooh/healthcare/clinical-laboratory-technologists-and-technicians.htm