Diagnostics

Miss: Why do they take my blood when I go to the doctor?

Photo by Kamaji Ogino: https://www.pexels.com/photo/crop-ethnic-daughter-injecting-mother-with-toy-syringe-5094090/

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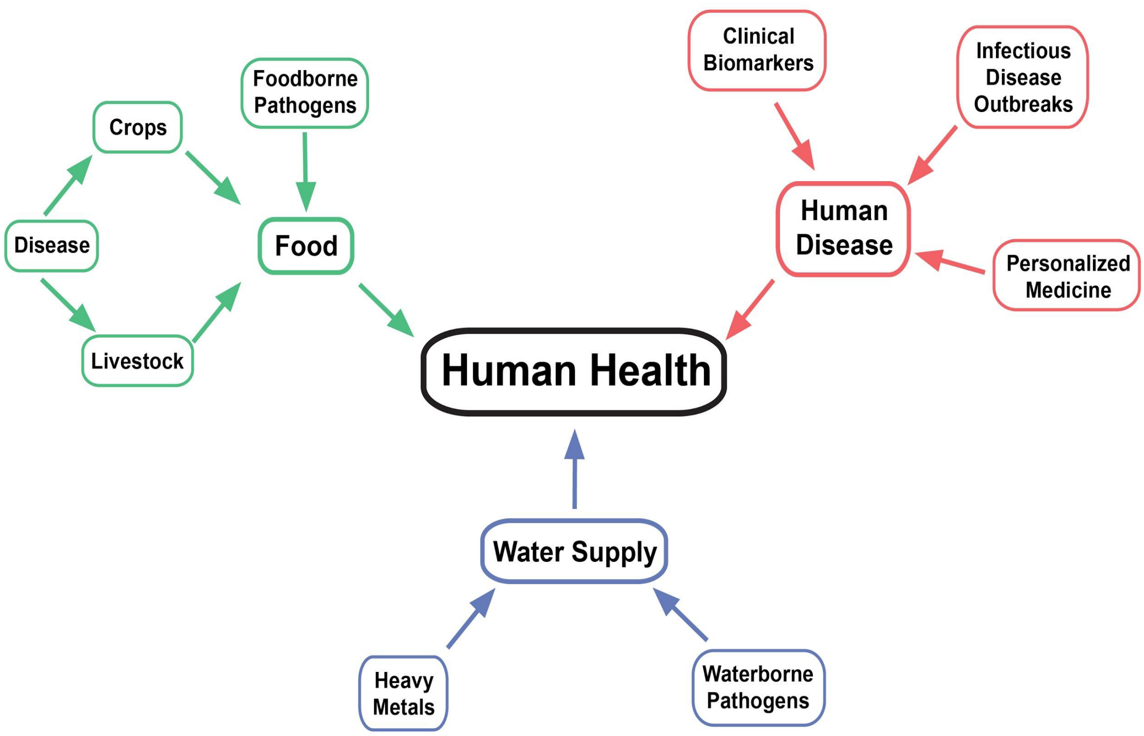
Diagnostics

Storyline

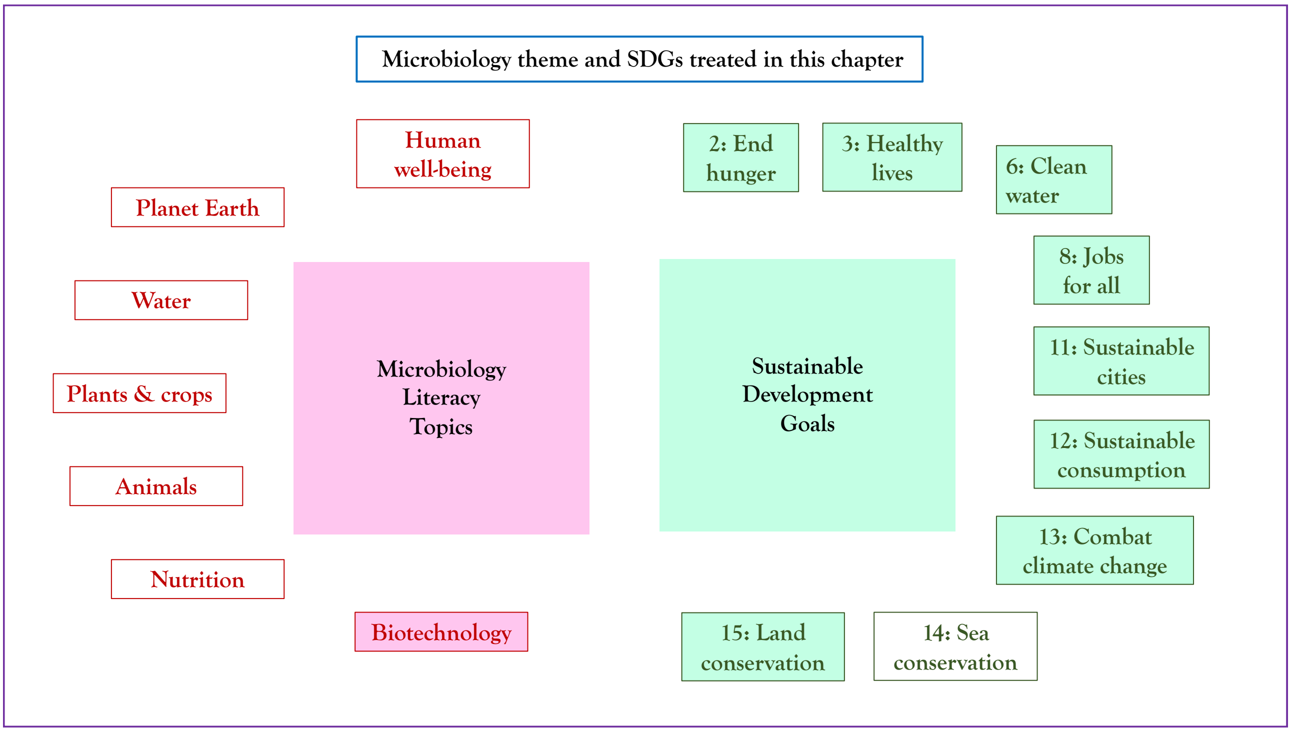
Our ability to respond to contamination of our food and water supply, and to disease, is only as good as our ability to detect those conditions. Diagnostics are the tools that we develop and use to test for analytes – specific molecules, nucleic acid sequences, and proteins, and non-biological toxic molecules – in the environment and in ourselves that provide information on a potential hazard or other issues of importance. Diagnostics use a wide variety of microbiological methods to transform the analyte in a sample into an easy-to-read output, such as a color change or digital number. Properly applied, diagnostics can help to ensure safe food and water supplies, detect and treat medical conditions, and stem the spread of infectious diseases like COVID-19. However, as 'point-of-care' diagnostics (i.e. at the time and place of patient's care) become more prevalent, we will need to be conscious of their disposal methods to avoid negative environmental impacts. The use of diagnostics thus has multiple consequences for Sustainable Development Goals.

Box 1: The Many Uses of Diagnostics



The Microbiology and Societal Context

The microbiology: detecting diseases in plants and animals; screening food for pathogenic microbes; heavy metals in water supply; pathogens in water supply; clinical biomarkers; containing infectious disease spread; DNA risk factors; personalized medicine. *Sustainability issues:* food supply; health; water security; economy and employment; pollution; land use.



Diagnostics: the Microbiology

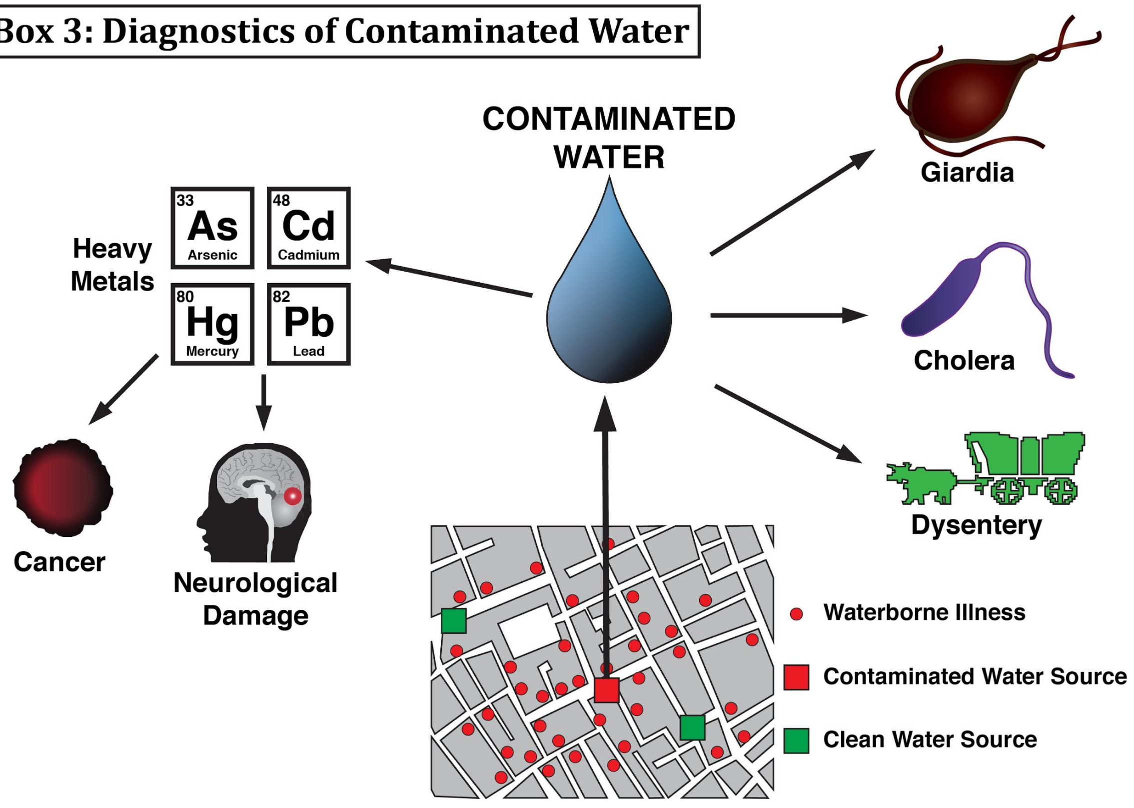
1. Diagnostics are important in detecting plant and animal diseases. As the population of humans living on the planet increases, the ability to grow enough food to sustain everyone is critical. While advances in fertilizers and other agricultural techniques have helped increase yields, it is also imperative that crops stay healthy and free of disease (*see microbial and viral diseases of plants topics for a more detailed treatment of this subject*). As many crop diseases can look alike, diagnostics help by responding to the unique DNA or protein signature of particular diseases, better helping farmers to determine what is affecting their crops. Similarly, disease can rapidly spread through a herd of livestock and rapidly diagnosing the cause can minimize its effect (*see 'The food animal plagues' topic for a more detailed treatment of this subject*). As climate change continues to increase the unpredictability of crop harvests, diagnostics will play an increasingly critical role in maintaining food security (*see 'Feeding the world' topic for a more detailed treatment of this subject*).

2. Diagnostics can detect pathogenic microbes in food, allowing it to be recalled before people get sick. "It must have been something I ate." This common expression, while sometimes related to allergic reactions or other conditions, is frequently a sign that the person is suffering from a foodborne pathogen (*see 'Foodborne microbial disease' topic for a more detailed treatment of this subject*). In severe cases, foodborne pathogens pose a great societal risk, requiring hospitalization or even resulting in death. Additionally, as commercial food systems become more centralized, contaminated food at one processing plant can proceed to be ingested by thousands or more. To help stem foodborne disease outbreaks, government organizations turn to diagnostics to determine which pathogen is responsible, such as *Salmonella*, *Trichinella*, or pathogenic *Escherichia coli*, and even track it back to the farm or factory of origin. Then, a recall can remove potentially contaminated food from the market supply, ensuring food safety from 'farm to fork'.

*3. **Diagnostics can detect levels of dangerous heavy metals, like lead and mercury, in our drinking water supply.*** Elevated levels of cadmium, lead, mercury, and inorganic arsenic pose potentially life-threatening risks. Even non-fatal doses, especially if repeated, can lead to serious complications like neurological diseases and cancer (*see 'Heavy metals' topic for a more detailed treatment of this subject*). Thus, ensuring that water supplies do not exceed a given threshold for these compounds is paramount. Diagnostics can help both by determining the cause, when there is suspected contamination, and catching potentially elevating levels through routine testing before they become a problem. On a community-level, this can be performed at drinking water treatment facilities before the water enters the municipal supply. In rural areas, field testing kits can be used to diagnose any problem on site.

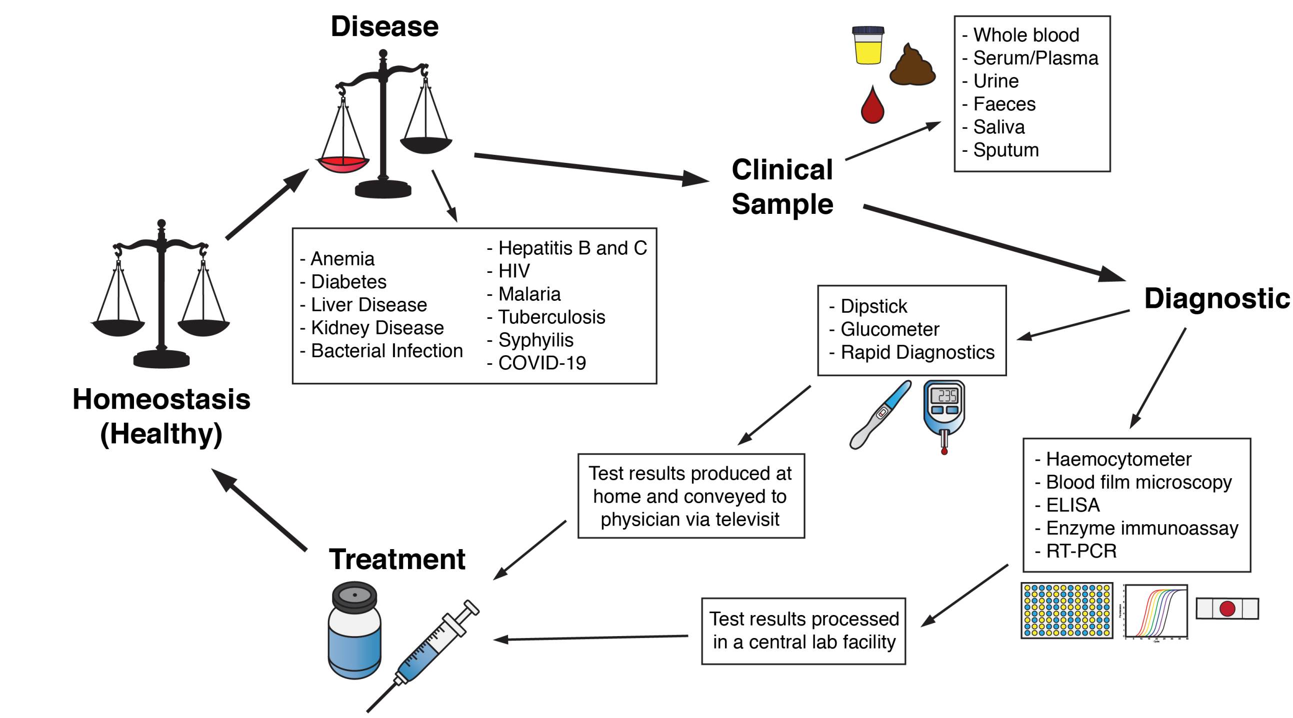
*4. **Diagnostics can detect pathogens, like Vibria cholerae or Giardia, in water supplies.*** Heavy metals and other dangerous chemical compounds are not the only threat to the drinking water supply. Bacterial and parasitic pathogens can also be present, causing a wide variety of diseases, like typhoid fever, cholera, and dysentery (*see 'Pathogens in water systems' topic for a more detailed treatment of this subject*). Testing water sources like wells can help determine the source of a waterborne disease outbreak so it can be stopped more quickly. Additionally, testing people who are ill with diagnostics can aid in better understanding the disease such that the source can more easily be found. This genre of pathogen sleuthing is called epidemiology and it was actually greatly advanced during the 19th century cholera epidemic to determine that the source of the outbreak was from a given well. For a more topical example: researchers are exploring the testing for SARS-CoV-2, the virus responsible for COVID-19, in sewage water to determine if this can help epidemiologists better understand the spread through the population.

Box 3: Diagnostics of Contaminated Water



5. ***Diagnostics can help us measure the levels of biomarkers in our bodies to detect and treat disease.*** When we are healthy, our bodies are in a state of homeostasis, with the different levels of salts, sugars, hormones, and other small molecules in balance. When we fall ill, the disease often causes changes in the levels of one of more of these compounds. There are a number of physical and chemical signs that we can use to detect that we are sick and determine what is causing it. At their most basic, physical measures like body temperature and blood pressure are biomarkers that can indicate the presence of a fever or cardiovascular risk. But diagnostics can also use sophisticated microbiology tools to measure the quantitative levels of particular biomarkers. Elevated glucose levels detected with a glucometer, for instance, may indicate the presence of diabetes. Additionally, clinical samples can be used to identify the unique nucleic acid or protein signatures of foreign pathogens. This can help you figure out if your sickness is caused by a bacterium, for instance, that can be treated with antibiotics, or a virus that won't be affected. (In fact, the antibiotics may make things worse by eliminating the natural microbiome that helps with your immune defense [*see 'Our Microbiomes' topic for a more detailed treatment of this subject*].) Diagnostics can detect biomarkers in a wide variety of clinical samples: including blood, urine, saliva, faeces, sputum (the mucus you cough up), or even sebum (the oily substance on the surface of your skin). Biomarker detection and quantification are also useful to follow the efficacy of a treatment. For example, in diabetes, blood glucose monitoring is key to evaluating the effect and dosage of insulin intake. While most diagnostics still require processing in a centralized laboratory, there is an increasing push for tests that can be performed at home or in the field where resources may be limited. Currently, the most common home tests are for pregnancy and blood glucose levels, but a push to develop rapid, at-home COVID-19 diagnostics may usher in a new wave of point-of-care diagnostics.

Box 4: Diagnostics in Treating Disease



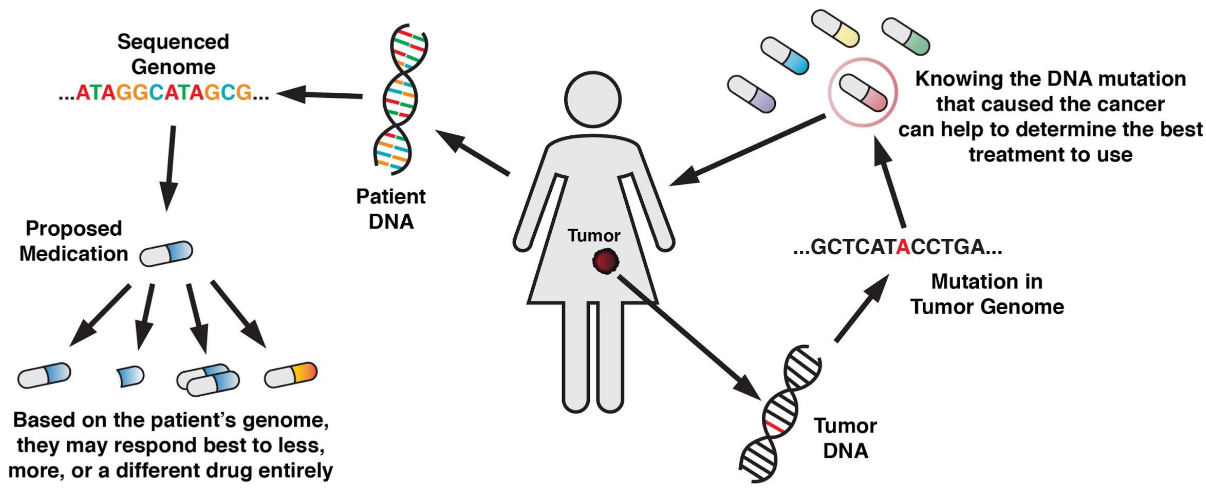
6. ***Diagnostics can screen for infectious diseases and help us prevent its spread.*** Diagnostics for long-term societal problems are important, but time becomes much more important for epidemics of infections that can rapidly be transmitted from person to person. From the plagues of the Middle Ages

to the current COVID-19 pandemic, rapidly transmissible infectious diseases have the ability to quickly devastate local, national, and even global populations. For diseases that transmit from person to person, the best way to stem the spread is to keep the sick people isolated away from the general population (*see 'Aerosol transmission of infections' topic for a more detailed treatment of this subject*). But what about diseases like COVID-19, where many people become contagious before they start showing symptoms or never show symptoms at all? This is where rapid access to diagnostics is critical. When someone is diagnosed positive, we can isolate them, treat them, and begin a process called 'contact tracing', or determining the other people with whom they had contact. Then, those individuals themselves can be tested, potentially diagnosing and isolating them before they have the ability to infect others. Otherwise, as we have seen, the situation can exponentially escalate into a global crisis.

7. Diagnostics that sequence our DNA can determine our risk factors for particular diseases and help lead to a revolution in 'personalized medicine'. At the turn of the century, the Human Genome Project was completed, giving us a DNA blueprint for the information coding our cells. While teasing out the phenotypic differences of height, personality, etc. from the genotypic difference in the individual nucleotides of the genetic code still remains complex, there have been major advances in certain fields of medicine to use our DNA makeup to help diagnose our risks for disease. Certain mutations in the BRCA1 and BRCA2 genes, for example, can affect one's risk of having breast or ovarian cancer. And the field of pharmacogenomics uses your DNA to know how your body will process particular medications so your doctor can prescribe the one most suited to you. Even DNA that isn't 'your own' inside your body can help inform medical decisions: tumors can be sequenced to know what mutations cause them to go haywire and how best to treat them, and developing fetuses can be screened *in utero* for genetic diseases. However, we need to remember that there is still a lot to learn and that many factors, be they environmental or socioeconomic, play important roles in determining disease risks.

8.

Box 5: Diagnostics for Personalized Medicine



Relevance for Sustainable Development Goals and Grand Challenges

The microbial dimension of diagnostics relates to several SDGs (*microbial aspects in italics*), including

- **Goal 2. End hunger, achieve food security and improved nutrition, and promote sustainable agriculture** (*end hunger and malnutrition, increase agricultural productivity*). Large quantities of the food produced globally goes to waste due to infection by animal or plant diseases. By increasing the use of diagnostics in the agricultural setting, we can help limit this waste and thus have more food to combat global hunger. Being able to better detect potentially devastating diseases also increases food security.
- **Goal 3. Ensure healthy lives and promote well-being for all at all ages** (*improve health, reduce preventable disease and premature deaths*). The ability to detect and diagnose potentially fatal diseases early is one of the most important factors in preventing premature deaths. This can involve diagnostics used on clinical samples in a doctor's office or hospital setting. However, an increasing trend of 'point-of-care' diagnostics allows detection in the home or in remote locations. Currently some of the most well known examples are glucometers to measure blood glucose in diabetic patients and pregnancy test strips for family planning. Other over-the-counter tests can measure cholesterol or test liver function or presence of illicit drugs. However, increased use of point-of-care diagnostics will continue to help improve health worldwide, particularly combined with teleconsultations with medical professionals, who can translate the test result into the best treatment option. Additionally, the current push of rapid, point-of-care diagnostics for COVID-19 may well create a new environment that facilitates a more rapid migration of tests from benchtop to bedside.
- **Goal 6. Ensure availability and sustainable management of water and sanitation for all** (*assure safe drinking water, protect water-related ecosystems, improve water and sanitation management*). Diagnostics that detect heavy metals and pathogens are vital in ensuring the safety of community drinking water supplies. This is particularly important in many parts of the world when water-borne pathogens are a major threat. By being able to test both locally (at small scale sites like a well) and more broadly (at water treatment and sanitation plants), we can ensure the safety of drinking water.
- **Goal 8. Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all** (*promote economic growth, productivity and innovation, enterprise and employment creation*). The development of diagnostics requires a large amount of research hours and funding to be invested. However, the overall economic benefit from investing in new and better diagnostics yields an overall positive effect for the community. Additionally, these sectors can help promote productive employment and sustainable economic growth.
- **Goal 11. Make cities and human settlements inclusive, safe, resilient, and sustainable** (*curb infectious disease outbreaks, ensure safe food and water supplies*). As an increasing portion of the global population becomes urbanized, the number of other humans with which one is in contact increases accordingly, making cities potential hotspots for infectious disease transmission. In order to ensure that they can be safe and resilient, adequate testing with diagnostics is crucial to help stem the progression of any disease outbreak.
- **Goal 12. Ensure sustainable consumption and production patterns** (*achieve sustainable production and use/consumption practices*). Part of the effort to achieve sustainable consumption and production is in reducing waste from what we produce. Diagnostics for disease in livestock and crops can help reduce overall production required. However, after use many diagnostics themselves become a waste product, so ecologically-friendly design that respects the principles and practices of the circular economy is important.
- **Goal 13. Take urgent action to combat climate change and its impacts by regulating emissions and promoting developments in renewable energy** (*reduce greenhouse gas emissions, mitigate consequences of global warming*). The ability to detect greenhouse gas emissions is vital in having an accurate

measurement of our total societal contribution. Additionally, efforts should be made in the research labs that create diagnostics to try to limit the energy they consume and thus their carbon footprint.

- **Goal 15. Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss** (*reduce overfarming and land degradation*). In order to protect the land used to grow crops and raise livestock, we need to ensure that the land being used is used in a way that minimizes waste. Employing diagnostics to regulate plant and animal health is key in this endeavor.

Potential Implications for Decisions

1. Individual

a. Determining what disease one may have and how to best treat it with one's doctor
b. Deciding whether or not to sequence one's DNA to better personalize one's medical plan
c. Getting tested for an infectious disease helps guide whether one can safely go out into society or needs to self-quarantine at home
d. Non-microbial parameters: the financial costs of doctor's visits and tests, access and availability of healthcare services, cost of medication

2. Community policies

a. Helping to stem the spread of infectious disease within the community
b. Maintaining overall health of citizens
c. *Non-microbial parameters: support local doctors and other health care workers*

3. National policies relating to diagnostics

a. Ensuring adequate testing during infectious disease outbreaks
b. Establishing health care policies to ensure testing is available
c. Testing food supplies for pathogenic microbes
d. Protecting safe drinking water supplies
e. Allocating research funding to develop new diagnostics
f. Stockpiling supplies of diagnostics for potential future outbreaks
g. *Non-microbial parameters: policies relating to health insurance regulations or socialized medicine*

Pupil Participation

1. Class discussion of the issues associated with diagnostics

a. Is it better to know you have a health problem or to remain unaware?
b. The deployment of diagnostics comes at a price. With a limited health budget, is it better to focus on the deployment of cheap diagnostics to improve health now, or to invest in the development of new but expensive ones that can only be used in the future, and initially for only a few people? Or should we compromise and do both, but on a smaller scale?

2. Pupil stakeholder awareness

a. Diagnostics have many positive consequences for the SDGs. Which of these are most important to you personally / as a class?
b. Can you think of anything that might be done to ensure that diagnostics are more readily available during an epidemic?
c. Can you think of anything you might personally do when you get sick?

3. Exercises

a. There is a mysterious outbreak of virus X spreading across the nation. Some people infected require immediate hospitalization while others appear to have no symptoms at all. How might diagnostics be used to help bring an end to this epidemic?

b. Sequencing our DNA has the potential to improve our health by better knowing our risks of certain diseases or which medicine we should take; however, many are concerned with privacy issues of having the information of our DNA in the hands of corporations and governments. What are some policies that can be put in place to ensure the safety of our personal medical data?

c. As diagnostics become cheaper and more available for use in the home, the amount of waste they produce will also increase. What are some ways that we could ensure sustainability such that diagnostics don't contribute to pollution?

The Evidence Base, Further Reading and Teaching Aids

1. Use of pesticides; Methods of plant diagnostics; Process for diagnosing plant disease; Plant disease resources for educators; Diagnosing animal diseases
2. OIE (World Organization for Animal Health) on food safety; US FDA 'Bad Bug Book' on commonly found foodborne pathogens; Diagnostic tools for foodborne illness; Time magazine article of food recalls; Fight BAC! campaign resources for school children; FDA CORE network foodborne pathogen response
3. Inside Flint's water crisis; US FDA regulations for chemical and microbial water contaminants; WHO chemicals of major public health concern; Two case studies of water quality assessment methods
4. Detecting COVID-19 in sewage water; John Snow - Father of Epidemiology; US FDA regulations for chemical and microbial water contaminants; WHO water sanitation hygiene; 7 most common waterborne diseases
5. Diagnostics biomarkers; WHO list of essential in vitro diagnostics; WHO TDR video resources; WHO guide for selecting a diagnostic test; Types of COVID-19 tests; The race is on for a covid-19 test you can take at home
6. US CDC COVID-19 contact tracing guidelines; Diagnostic testing and smart phone contact tracing for COVID-19; Vox video on COVID-19 infectiousness; US CDC teacher resources; Epidemiology education movement for middle and high schoolers; US CDC epidemiology classroom case studies; US CDC Body and Mind (BAM!) classroom resources; US CDC 'Solve the Outbreak' online game and app; Epidemiology: Solve the Outbreak lesson plan
7. Environmental and genetic risk factors lesson plan; Personalized Medicine Project teacher resources; Personalized medicine for cancer therapy; Limits of genomic medicine based on socioeconomic disparities

Glossary

19th century cholera epidemic - The 1854 Broad Street cholera outbreak was one of several outbreaks during the mid-19th century cholera pandemic when physician Jon Snow showed that the disease spread through contaminated water rather than through the air

analytes - Specific molecules of interest, nucleic acid sequences, and proteins, and non-biological toxic molecules in the human body or environment that can be measured to determine the presence of or prevent disease
BRCA1 and BRCA2 - Tumor suppressing genes for which certain mutations are known to significantly increase the risk of breast and ovarian cancer
cadmium - A soft metal historically used in batteries and paint that has numerous toxic effects on human health
cardiovascular risk - Risk level of having numerous cardiovascular diseases including stroke, heart attack, and hypertension
circular economy - An economic system designed to reduce waste through the reuse and recycling of materials
commercial food systems - The community, national, and international systems used to distribute crop and livestock products to stores in which they can be commercially purchased
contact tracing - The process of determining all of the individuals with whom an infected person may have recently come in contact in the hopes of isolating and testing them to prevent further spread of a disease
COVID-19 - The COronaVIrus Disease 2019, caused by the SARS-CoV-2 virus, that spread into a global pandemic beginning in early 2020
DNA - Deoxyribonucleic acid is a series of nucleotides that act as the instruction set for a cell
Diagnostics - The tools used by medical professionals and consumers to measure levels of biomarkers to detect, treat, or help prevent disease
dysentery - A gastroenteritis condition with several possible pathogen origins that results in diarrhea with blood
food security - The systems and laws in place to help mitigate against breaks or shortages in the food supply
foodborne pathogen - Pathogens that can be transmitted through contaminated foodstuffs
gene - A segment of DNA that codes for production of a given protein
genotypic - The makeup of one's genes that code for the expressed, or phenotypic, characteristics in an organism
Giardia - A microscopic parasite found in faecal-contaminated water that causes diarrhea
glucometer - An electronic device used to measure blood glucose levels
glucose levels - The concentration of glucose in the blood which must be routinely monitored by people with diabetes
homeostasis - The steady state of physical, biological, and chemical levels in an organism that are altered in states of disease
Human Genome Project - An international scientific research collaboration begun in 1990 which aimed to complete the first DNA sequence of a human genome (completed in 2003)
in utero - From the Latin for 'before birth', used to refer to a fetus during pregnancy
infectious disease - Disease that is transmitted between individuals by pathogenic microorganisms like bacteria, viruses, parasites, or fungi
inorganic arsenic - Highly toxic forms of arsenic that are not bound to carbon, like organic arsenic which is harmless
lead - Heavy metal that has high levels of toxicity and can cause neurological damage
mercury - Heavy metal that can leach into water supplies or accumulate in large fish and cause neurotoxicity in humans
molecules - Collections of bound atoms that form the basis of chemistry
microbiological methods - A broad range of techniques that are used both to study the functional mechanisms of biology and develop new diagnostics

microbiome - The assembly of different microorganisms found in the gut and on the surface of the body that influence the health of humans and other organisms
municipal water supply - The centralized network of water processing and recycling that provides drinking water to the citizens of a community
neurological diseases - Diseases that affect the nerves of the brain, spinal cord, or peripheral limbs
nucleic acid - One of either guanine, cytosine, adenine, thymine, or uracil (G, C, A, T, or U) that are the 'language' in which information is written in DNA or RNA
nucleic acid signature - The presence or absence of DNA or RNA that is characteristic or a given state or disease
output - The way in which a diagnostic is interpreted, be it a digital number output, color change, or appearance of a line on a pregnancy test
pandemic - An outbreak of disease that has expanded into a global crisis
pathogenic Escherichia coli *-* One of the strains of the *Escherichia coli* bacterium that leads to disease in humans
personalized medicine - A medical plan for a patient that is informed by their unique genetic makeup
phenotypic - The outward expression of the DNA-based, genotypic, coding of one's genes
plague - An infectious disease caused by the bacterium *Yersinia pestis* that has historically led to some of the deadliest epidemics in human history
point-of-care - A diagnostic that can be used outside of a hospital or doctor's office, such as at the home or in remote regions
protein - A folded series of amino acids that is produced by the cell according to the DNA code in a gene
protein signature - The presence, absence, or level of a particular protein in a clinical sample that can inform the diagnosis of a particular disease
Salmonella *-* One of two bacteria that cause a common and potentially deadly foodborne illness
SARS-CoV-2 - The coronavirus responsible for the COVID-19 pandemic
sebum - The oily residue secreted by human skin glands
sequencing - A microbiological method used to determine the order of nucleotides in a sequence of DNA
socioeconomic - Relating to one's social position on one's community and level of economic power
sputum - The mucus that is coughed up from the lower airways in the lungs that can be used to diagnosis pulmonary diseases
Sustainable Development Goals - A collection of 17 global goals set forth by the United Nations in 2015 to be a "blueprint to achieve a better and more sustainable future for all"
Trichinella *-* A group of parasitic roundworms that cause the foodborne illness trichinosis
typhoid fever - A potential fatal bacterial infection by a species of *Salmonella*
Vibrio cholerae - A waterborne bacterium that causes the disease cholera, resulting in potentially fatal diarrhea