Lecture 4.2

1. Principles of Infectious Disease Diagnostics

A. Clinical Presentation vs. Diagnostic Testing

- **Clinical Overlap:** Many infectious diseases (especially respiratory pathogens) share non-specific signs and symptoms (e.g., rhinorrhea, sore throat, fever, headache, malaise).
- **When to Test:**
  - Some illnesses have distinctive pathognomonic signs allowing rapid clinical diagnosis.
  - Mild, self-limiting infections (e.g., the common cold) generally do not warrant expensive diagnostic testing.
  - Severe, highly transmissible, or actionable diseases require confirmatory testing to guide clinical management, isolate patients, and direct public health interventions.
- **Diagnostic Inputs:** Geographic location/travel history, presence of local outbreaks, patient symptoms, and targeted specimen collection (e.g., blood, throat swab, sputum, feces, CSF).

B. Statistical Measures of Diagnostic Performance

- **Sensitivity:** The proportion of truly infected individuals (**true positives**) who are correctly identified by the test.

$$\text{Sensitivity} = \frac{\text{True Positives}}{\text{True Positives} + \text{False Negatives}}$$

  - *High sensitivity* minimizes false negatives (critical for screening and ruling out dangerous pathogens).
- **Specificity:** The proportion of uninfected individuals (**true negatives**) who are correctly identified as disease-free.

$$\text{Specificity} = \frac{\text{True Negatives}}{\text{True Negatives} + \text{False Positives}}$$

  - *High specificity* minimizes false positives (prevents inappropriate treatment, unnecessary isolation, or psychological harm).
- **Real-World Reality:** No diagnostic test is 100%sensitive and 100%specific; clinical tests must pass regulatory operational thresholds.

B. Host Range & Animal Modeling

- **Host Range:** The spectrum of biological species a microorganism is capable of infecting.
    - **Narrow Host Range:** Infects a single or very limited number of species (e.g., *Variola* virus / smallpox was restricted to humans, which enabled global eradication).
    - **Broad Host Range:** Capable of infecting diverse animal hosts (e.g., *Influenza A* virus infects humans, birds, pigs, horses, ferrets; *Coronaviruses* cross from bats/intermediate mammals to humans).
- **Significance of Broad Host Ranges:**
    - **Viral Reassortment / Genetic Shift:** Co-infection of a single animal host (e.g., a pig acting as a "mixing vessel") with distinct influenza strains allows genomic segments to recombine, creating novel pandemic variants.
    - **Experimental Animal Models:**
        - *HIV-1:* Narrow host range restricted to humans and chimpanzees. Transgenic rodents expressing human CD4 have largely failed as robust models.
        - *Influenza:* **Ferrets** serve as an ideal model because their airway distribution of sialic acid receptors and clinical manifestations (sneezing, rhinorrhea, fever, aerosol transmission) closely mirror human infection.

C. Toxin-Mediated Cellular Injury

Characteristic	Endotoxin	Exotoxin
Chemical Composition	**Lipopolysaccharide (LPS)** (Lipid A + core polysaccharide + O-antigen)	Soluble, secreted **Proteins / Polypeptides**
Bacterial Source	Integral component of outer membrane of **Gram-negative** bacteria	Synthesized and released by **both Gram-positive and Gram-negative** bacteria
Release Mechanism	Released during bacterial cell lysis or division	Actively secreted by living bacteria
Mechanism of Action	Triggers massive systemic release of pro-inflammatory cytokines (IL-1, TNF-α) → systemic inflammatory response, fever, vasodilation, **septic shock**	Binds specific host targets/receptors to disrupt defined biochemical pathways (locally or distally)

Practice Multiple-Choice Questions (MCQs)

Question 1

According to evolutionary psychology, why did the Behavioral Immune System develop alongside the physiological immune system?

A) The physiological immune system operates only after an infection occurs, consuming large amounts of energy and risking systemic tissue damage.

B) Primitive hominin ancestors lacked bone marrow, preventing the diversification of antigen-specific lymphocyte repertoires.

C) Cellular immune responses require several weeks of high-grade fever before synthesizing effective neutralizing antibodies.

D) The human central nervous system cannot process somatic inflammatory signals without specialized subcortical sensory receptors.

Question 2

What cognitive bias characterizes the Behavioral Immune System's detection of environmental pathogen cues under Error Management Theory?

A) Prioritizing false negatives over false positives to maximize social interaction

B) Biased toward detecting false positives, functioning like an oversensitive smoke detector

C) Setting detection thresholds exclusively based on analytical reasoning and empirical data

D) Eliminating emotional revulsion toward unfamiliar foreigners to broaden in-group trade

Question 3

Which of the following describes the relationship between an individual's Perceived Vulnerability to Disease (PVD) score and their demographic traits?

A) PVD increases linearly with advanced formal education and extensive scientific literacy.

B) PVD is significantly higher in older men compared to younger female cohorts across cultures.

C) PVD does not correlate with age, gender, or education, but tracks with negative emotionality.

D) PVD peaks during mid-adolescence and drops to undetectable levels in early adulthood.

Question 6

What ecological mechanism explains why the commercial pine siskin (*Spinus pinus*) transmits *Salmonella enterica* to humans in suburban backyards?

A) Siskins release bacterial endotoxins directly into groundwater via cutaneous shedding.

B) Ticks detached from dead birds crawl into household carpets to bite sleeping humans.

C) Direct or indirect human contact with bird feeders contaminated with avian fluids and feces transfers the bacteria to oral mucous membranes.

D) Siskins function as obligate intermediate hosts for mosquito-borne microfilariae.

Question 7

Following the Spanish conquest, how did environmental and infrastructural disruptions contribute to the collapse of the Aztec population in the Valley of Mexico?

A) The conquistadors introduced millions of European rabbits that consumed all staple maize crops.

B) Spanish destruction of indigenous lake-management dykes produced swampy bogs, while imported livestock introduced novel zoonoses into immunologically naive populations.

C) The indigenous population migrated into high-altitude alpine zones, developing fatal hypothermia.

D) Groundwater depletion caused immediate seismic liquefaction that buried all agricultural centers.

Question 8

In compartmental SIR epidemic modeling, what specific transition occurs when the effective reproduction number (R) falls below 1?

A) The number of new infectious cases decreases over time, leading toward epidemic decay.

B) All infected individuals immediately experience severe hemorrhagic symptoms.

C) The size of the susceptible population increases exponentially.

D) Pathogen transmission accelerates until 100% of the population is infected.

Answer Key & Detailed Explanations

1. **B** — The embryo protection hypothesis argues that pregnancy sickness is an evolved adaptation: aversions to strong smells, bitter tastes, and potential food contaminants shield the vulnerable embryo from toxins and foodborne pathogens during critical early organ development.
2. **C** — Tajfel's minimal groups paradigm demonstrated that arbitrary, explicit categorization into trivial groups (e.g., preference for abstract painters or a coin toss) is sufficient to rapidly induce in-group favoritism and out-group discrimination.
3. **D** — The universal disgust expression involves levator labii contraction, upper-lip raising, nose wrinkling, and lower-lip protrusion. Darwin noted these physical actions functionally narrow nasal passages against odors and facilitate the oral expulsion of distasteful matter.
4. **A** — Constructionist models (such as those championed by modern affective neuroscientists) argue against dedicated brain centers for each basic emotion; neuroimaging meta-analyses demonstrate that emotions are constructed through shared, distributed brain networks that also handle general cognitive and sensory tasks.
5. **B** — Animal-reminder disgust includes events that highlight our mortal, physical nature; breaches of the body envelope (open surgical wounds, exposed intestines, severe lacerations) serve as primary elicitors within this category.
6. **B** — Disgust sensitivity correlates with socially conservative attitudes, traditionalism, preference for social hierarchy, and behavioral avoidance of novel or foreign stimuli, likely reflecting an underlying behavioral immune system oriented toward norm preservation and contamination avoidance.
7. **B** — In contamination-related OCD, obsessions represent intrusive fears of pollution or disease, while compulsions (such as repetitive washing) serve as distress-reduction strategies to neutralize perceived contamination and disgust.
8. **C** — Longitudinal analyses using standardized instruments like the Kessler Psychological Distress Scale (K10) demonstrated that pandemic restrictions and social isolation led to documented increases in psychological distress, disproportionately affecting younger demographics.
9. **D** — Severe, unchecked health anxiety can trigger extreme avoidance behaviors, including historical accounts of community members neglecting bedridden neighbors during the 1918 influenza outbreak and abandoning domestic pets during the 2003 SARS crisis.
10. **B** — *Oscillococcinum* is manufactured by taking wild duck heart and liver autolysate and subjecting it to serial dilutions (200CK) that exceed Avogadro's number, leaving no active pharmacological molecules in the final commercial sugar pill.

4. The Psychology of Disgust

A. Evolutionary Origins: The "From Oral to Moral" Hypothesis

- **Primary Evolutionary Function:** Disgust originated as an adaptive food-rejection mechanism (distaste) designed to prevent the oral ingestion of pathogens, spoiled organic matter, and environmental toxins.
- **Facial Display:** Characterized by levator labii superioris contraction, causing upper-lip retraction, nose wrinkling, lower-lip protrusion, and slight mouth opening—biomechanically suited to expelling oral contents and restricting nasal airflow.
- **Exaptation to Moral Disgust:** Over evolutionary time, this pathogen-avoidance response expanded into social and abstract domains ("oral to moral"). Societal rule-breaking, taboo sexual behaviors, and severe transgressions against justice trigger emotional reactions that recruit the primitive physical disgust response.

B. Structural Typologies and Eliciting Domains

- **Core Disgust:** Elicited by direct contamination threats: spoiled food, bodily waste (feces, vomit), bodily fluids, purulence, and disease-carrying vectors (cockroaches, flies, rodents).
- **Animal-Reminder Disgust:** Triggered by events that expose human vulnerability, animal nature, and mortality: gore, breaches of the physical body envelope (exposed viscera), corpse contact, hygiene failures, and taboo sexual practices (e.g., incest, bestiality).
- **Action Tendencies and Physiology:** Disgust prompts behavioral withdrawal, tactile avoidance, and gastrointestinal rejection (nausea, emesis). Physiologically, it is often marked by transient drops in blood pressure and distinct autonomic fluctuations.

C. Disgust Sensitivity and Individual Differences

Disgust sensitivity varies across populations and correlates with specific clinical, social, and ideological markers:

- **Clinical Psychopathology:** Elevated disgust sensitivity correlates with obsessive-compulsive disorder (OCD; particularly contamination obsessions and washing rituals), blood-injection-injury phobias, specific animal phobias (where arachnophobia often tracks disgust more strongly than fear), and eating disorders.
- **Demographic Patterns:** Women consistently report higher disgust sensitivity than men, which aligns with evolutionary hypotheses regarding maternal pathogen protection during reproduction and infant care.
- **Sociopolitical Attitudes:** Heightened disgust sensitivity correlates with socially conservative ideology, strong preferences for social hierarchy, heightened threat sensitivity, out-group prejudice, and homophobia (frequently framed as aversion to perceived normative violations).
- **The Behavioral Immune System (BIS):** Acts as a proactive psychological defense network. While the physiological immune system fights pathogens post-infection at high metabolic cost, the BIS uses sensory detection (visual, olfactory), disgust, and avoidance behaviors to prevent pathogen entry.

2. Signal Detection Theory, Heuristics, and Threat Calibration

C. The Smoke Detector Principle (Error Management Theory)

- **Asymmetric Error Costs:** Evolution calibrates sensory detection thresholds according to the asymmetric survival costs of errors:
    - **False Positive (Type I Error):** Mistaking an innocuous physical irregularity (e.g., a birthmark, facial asymmetry, physical disability, or novelty) for an infectious disease. The fitness cost is negligible (e.g., unnecessary avoidance, lost social interaction).
    - **False Negative (Type II Error):** Failing to identify an authentic, lethal pathogen. The fitness cost is severe (systemic infection, incapacitation, or death).
- **The "Smoke Detector" Bias:** Because a false negative can be lethal while a false positive is merely inconvenient, natural selection favors an oversensitive detection system. The BIS functions like an overly reactive smoke detector that sounds an alarm for burnt toast rather than risking an undetected fire.
- **Cognitive Heuristics:** The mind operates under heavy cognitive load, utilizing fast, frugal perceptual heuristics rather than exhaustive analytical scrutiny. Consequently, harmless superficial deviations from morphological normality trigger automatic visceral revulsion.

D. Psychological Measurement Scales of Disease Vulnerability

- **The Culpepper Disgust Image Set:**
    - An experimental visual instrument comprising 20 pathogen-salient images paired with matched, pathogen-free controls.
    - Evaluates four empirical factors (F1–F4) underlying pathogen disgust:
        1. *F1: Hygiene issues*
        2. *F2: Parasite exposure*
        3. *F3: Spoiled or contaminated food*
        4. *F4: Physical injury and body envelope violations*
- **Perceived Vulnerability to Disease (PVD) Scale:**
    - A psychometrically validated 15-item instrument measuring trait-level differences in individual vulnerability.
    - Unrelated to age, gender, or formal educational attainment, but correlates with neuroticism/negative emotionality and health anxiety.
    - Divided into two distinct subscales:
        1. *Perceived Infectability:* An individual's subjective assessment of their physiological susceptibility to contracting infectious illnesses.
        2. *Germ Aversion:* The subjective emotional and behavioral discomfort experienced in contexts involving potential pathogen transmission.
- **Trait vs. State Dynamics:**
    - Baseline disgust sensitivity and PVD operate as stable personal traits, but they exhibit situational flexibility.
    - During periods of objective environmental threat (e.g., COVID-19 lockdown), measured germ aversion and core disgust sensitivity rise, demonstrating that baseline detection thresholds adapt dynamically to immediate context.

Lecture 10.2

1. The Continuum of Infectious Disease Intervention

Public health approaches to infectious disease management operate along a hierarchical continuum defined by three distinct operational thresholds:

- **Disease Control:**
  - Involves reducing disease circulation, incidence, prevalence, morbidity, or mortality to a locally acceptable background level.
  - Targets vary across geographic jurisdictions depending on local healthcare infrastructure, resource availability, and baseline disease burdens.
  - Requires ongoing public health interventions (e.g., seasonal vaccination, food safety monitoring, vector abatement) to maintain incidence within the defined target range.
- **Disease Elimination:**
  - Defined as reducing the incidence of locally acquired (endemic) transmission of a specific disease to zero within a defined geographical area (such as a state, country, or continental region).
  - Requires continuous public health measures and active surveillance to prevent the re-establishment of transmission following imported cases (**relocation diffusion**).
  - When importations occur, rapid surveillance and intervention are required to extinguish secondary spread and return local transmission to zero.
- **Disease Eradication:**
  - Defined as the permanent worldwide reduction of an infectious pathogen's incidence to zero, resulting in its complete global removal from existence in nature.
  - Represents an absolute global endpoint where active intervention efforts (such as routine community vaccination programs) can safely cease.
  - Achieved historically in only two instances: smallpox in humans (certified by the WHO in 1979/1980) and rinderpest in cattle and domestic ungulates (certified in 2011).

2. Public Health Actions for Elimination and Eradication

Achieving disease elimination or eradication requires coordinated multi-sectoral strategies:

- **Systematic Screening and Surveillance:**
  - Routine testing and screening programs identify active symptomatic and asymptomatic cases to link them to curative treatment.
  - Clarifies population-level disease distribution, distinguishing between isolated sporadic infections and concentrated hotspots.
- **Targeted and Mass Vaccination:**
  - Deploys vaccines toward high-risk demographic groups or geographical zones with heavy disease burdens.
  - Aims to establish population-level herd immunity thresholds to interrupt transmission chains.

7. Global Polio Eradication Initiative (GPEI)

- **Transmission Dynamics and Pathophysiology:**
  - Poliovirus is an enterovirus transmitted via the **fecal-oral route** through unwashed hands or sewage-contaminated water and food supplies.
  - Enters via the gastrointestinal mucosa, replicates within local lymphoid tissue, and can invade the central nervous system.
  - Destroys lower motor neurons in the anterior horns of the spinal cord, causing **acute flaccid paralysis (AFP)** characterized by asymmetrical, flaccid weakness, muscle wasting, and potential respiratory failure if diaphragmatic motor neurons are affected.
- **The Asymptomatic Transmission Barrier:**
  - Approximately **1 out of every 200 infected children** develops overt, recognizable paralytic symptoms.
  - The remaining roughly 199 out of 200 infections are subclinical or present as mild transient gastrointestinal illnesses.
  - Asymptomatic individuals shed poliovirus in their feces for weeks, facilitating silent transmission through communal water systems without raising clinical alerts.
- **The Global Polio Eradication Initiative:**
  - Established in 1988 by the World Health Assembly; spearheaded by a coalition including Rotary International, the WHO, the CDC, UNICEF, the Bill & Melinda Gates Foundation, and donor governments.
  - Widely recognized as one of the largest internationally coordinated global health initiatives in history.
  - Prevented an estimated 16 million individuals from developing lifelong paralytic disability since 1988.
- **Field Challenges in Conflict and Fragile Environments:**
  - *Vaccine Cold-Chain Maintenance:* The live-attenuated oral poliovirus vaccine (OPV) is heat-sensitive, requiring continuous cold-chain refrigeration. In post-conflict or rural settings (e.g., post-civil-war Angola in the early 2000s), teams relied on scarce diesel generators subject to mechanical failure and fuel competition with transport vehicles.
  - *Unexploded Ordnance and Infrastructure Collapse:* Destruction of roadways, damaged landing strips, and extensive landmine fields necessitate military air transport to reach remote villages.
  - *Competing Health Priorities:* In settings with high child mortality from malaria or acute diarrheal illness, engaging communities and local health workers around an asymptomatic or low-visibility disease like polio poses communication challenges.
  - *Targeted Violence and Misinformation:* Conspiratorial narratives—such as false rumors that oral vaccine drops cause sterilization—have generated social resistance and resulted in physical attacks on community health workers in lingering endemic regions (e.g., Pakistan and Afghanistan).