
HIOX
Good
Afternoon

Fascinating **F**eatures and **M**ysterious **M**anifestations of Disease

OLLI @ University of Illinois

Fall 2022 Semester

Néstor A. Ramírez, MD, MPH

Session 2
Diseases with an Odor or a Taste

September 23, 2022

Plan for the Course

- Session 1: Diseases with a color
- Session 2: Diseases with an odor or a taste
- Session 3: Diseases with a texture or a sound
- Session 4: Diseases with unusual appearance
- Session 5: Flying, crawling & burrowing critters
- Session 6: Forgotten or ignored epidemics
- Session 7:
- Session 8:

} Medical detectives solve mysterious cases

Plan for the Session

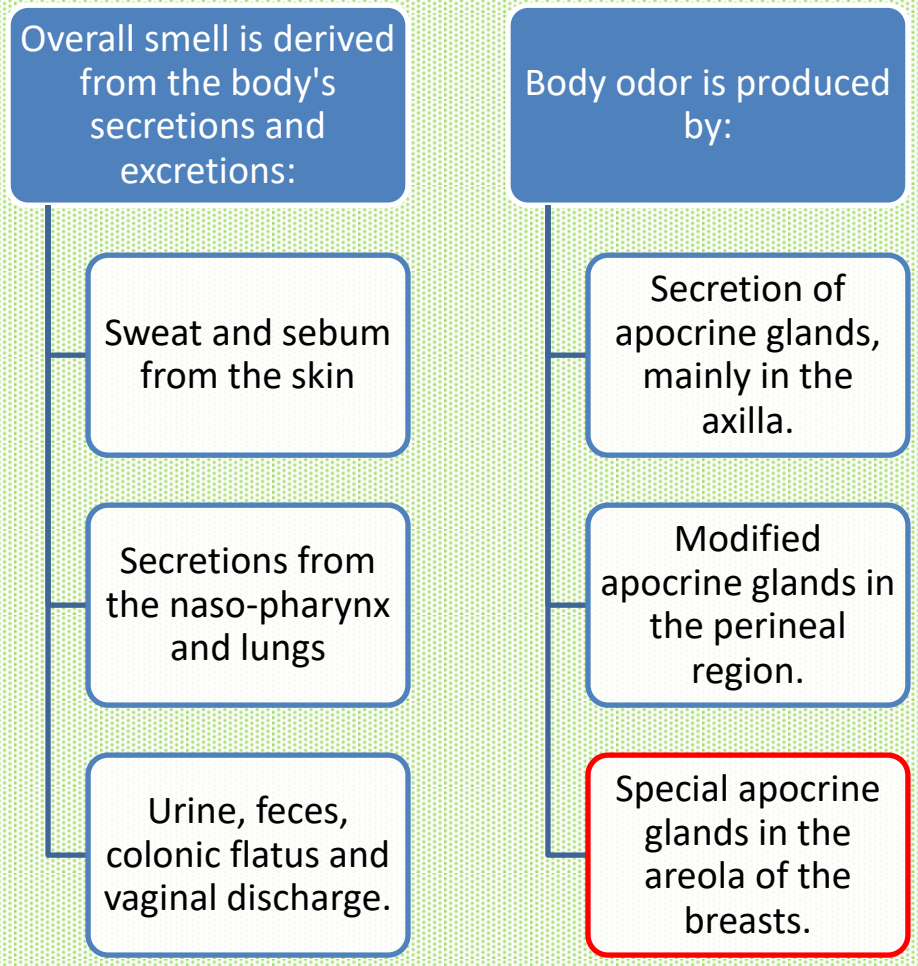
- General thoughts on smells and odors.
- Odors of certain diseases or infections.
- Smell diagnosis by dogs.
  - Diabetes and Ketoacidosis
  - Narcolepsy, Parkinson's, Migraines, Autism
  - Cancer
- Maple Syrup Disease and Phenylketonuria.
- Arsenic and Cyanide.
- Taste of diseases.
- Infections: Smallpox, Typhoid, Monkeypox.

One passage in the Sushruta Samhita – a Sanskrit text written long before the birth of Christ – says:

"By the sense of smell we can recognize the peculiar perspiration of many diseases, which helps in their identification."

SMELLS and ODORS

Smells and Odors (1)



Smells and Odors (2)

- Body smells are unique to an individual and vary with age, gender, diet, and health.
- Some diseases produce a characteristic odor coming from the body of a sick person.
- Subtle differences in a person's smell come from their skin, breath, blood and urine and can reveal just how healthy or ill they are.

Smells and Odors (3)

- Let's face it: Sick people stink.
- That's not just an insult, but a scientific reality.
- Different diseases release a range of smells.
- People have various responses, some more compassionate and some more self-protective than others.

Smells and Odors (4)

Kuna albino Indians can't sweat normally and emit a repulsive odor likened by their non-albino fellow tribe members to the smell of a swamp.

Smells and Odors (5)

- Syphilis and some Sexually Transmitted Diseases (STD's) have a fishy smell.

- In a study of 34 women, about 50% of samples of sweat and body odor of men infected with gonorrhea were judged to be to be off-putting and foul-smelling.

Smells and Odors (6)

- Studies show that the disgust felt by people when smelling unpleasant odors activates an immune reaction that protects them further from disease.
- People exposed to disgusting smells, like spoiled cheese, fermented fish and rotten yeast show slight increase in immune activity.

The body gears up for an attack!

Smells and Odors (7)

Remedies for the Plague

- John Colle, an English physician (~1345) said that the best way to counteract bad air that carried infection was with more bad air: “One foul smell drives out another”.
- He prescribed sniffing a latrine every morning, so people gathered around public latrines inhaling deeply.
- Belief was that smelling a bigger stink would ward off contagion from the bad smell that carried the plague!

Smell Disorders

People may have a decreased ability to smell or changes in the way they perceive odors:

Hyposmia: a reduced ability to detect odors.

Anosmia: the complete inability to detect odors.

Congenital anosmia: born without a sense of smell.

Parosmia: A normally pleasant smell now smells foul.

Phantosmia: the sensation of an odor that isn't there.

DISEASES and THEIR ODORS

Disease Odors

Scrofula: stale beer	Typhoid fever: freshly baked bread	Yellow fever: a butcher's shop
Diphtheria: cloying sweetness	Diabetic ketoacidosis: decomposing apples, nail polish remover	Hypermethioninemia: boiled cabbage
Hyperaminoaciduria: dried malt or hops	Cyanide poisoning: bitter almonds	Smallpox: rotting flesh
Arsenic poisoning: garlic	Phenylketonuria: mousy odor	Migraines: burning trash

Other Smelly Conditions

Trimethylaminuria (TMAU): rotten fish/rotten eggs

Proteus spp: smells rancid, like rotten chicken soup or broth; some say this smells like chocolate cake or brownies.

Actinomycetes, Streptomyces, Nocardia spp: (Fungi) smell like a rich, earthy, musty dirt scent after fresh rain.

Gram (-) anaerobes: bad breath, morning breath, disgusting.

Infectious Disease Odors

Pseudomonas aeruginosa: grape,tortilla, taco chips

Eikenella corrodens: bleach

Escherichia coli: flowers

Moraxella catarrhalis: pungent, semen-like

Staphylococcus ludgenensis: Sweet, earthy, hay

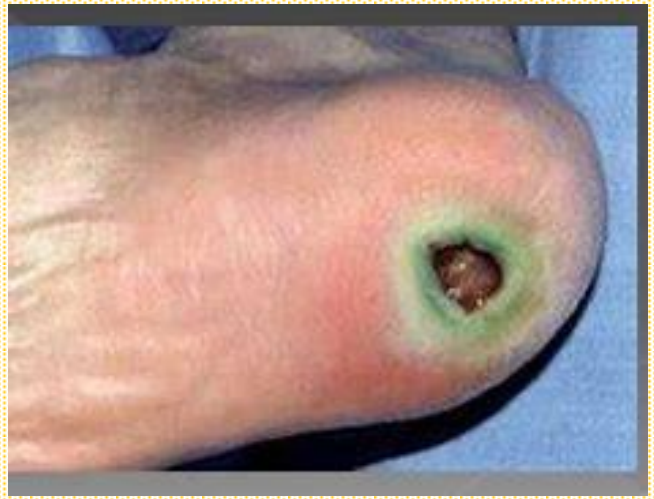
Streptococcus anginosus: sweet caramel

Haemophilus influenza: fresh flowers

Acinetobacter baumannii: dirty gym socks

Candida, yeast: Beer, bread baking

Pseudomonas Infections



- *Pseudomonas aeruginosa* is an opportunistic bacteria that can cause many types of infections in humans.
- It produces a characteristic blue-green color and is a common infection in those with diabetes, cystic fibrosis, burn patients, drug users and in post-operatory.
- It can cause extremely dangerous infections if not treated quickly, and it frequently wreaks havoc in hospitals.
- A non-pathogenic strain produces hot tub f*olliculitis*.

SMELL DIAGNOSIS BY DOGS

Smell Diagnosis by Dogs (1)

- If your dog acts worried towards a part of your body, Go Get It Checked!
- If you notice that your dog is paying more attention to a certain part of your body than others, it might be a good idea to see a doctor.
- Because dogs have such a strong sense of smell they can apparently sniff out signs of cancer.

Smell Diagnosis by Dogs (2)

- VOC's (Volatile Organic Compounds) are by-products of many biological processes.
- Studies have shown that dogs can smell VOC's, which humans generally can not detect.
- Infection, inflammation, and even cancer, can produce VOC's, which can be sensed by dogs in the breath, sweat, or urine.

Animal Noses (1)

- A family dog has a sense of smell 10 thousand to 100 thousand times more sensitive than any human.
- They have 300 million olfactory receptors to our measly 6 million.
- Scientists say this allows them to detect “the whiff of one rotten apple in two million barrels.”

Animal Noses (2)

Humans have about 1.6 sq. in. of olfactory epithelium; some dogs have 26 sq. in.

Dog's olfactory epithelium has 100X more receptors per sq. in. than humans.

Bloodhounds have noses 10 - to 100 - **million** times more sensitive than a human's.

They can detect a trail of scent a few days old.

Animal Noses (3)

Animals have a much better sense of smell than humans:

- Humans 1
- Macaque 2 times
- Cows 7 times
- Most mammals 12 times
- Mice 50 times
- Dogs 200 times
- Pigs 700 times

Grizzlies have a sense of smell 7 times stronger than the bloodhound.

- Bears' sense of smell is ~2500 times better than humans'
- Detect the scent of food from up to 18 miles away
- Detect smell of food up to 48 hours after animal left its scent

Smell Diagnosis by Dogs (3)
(Cancer)

In one study, dogs were given urine and breath samples:

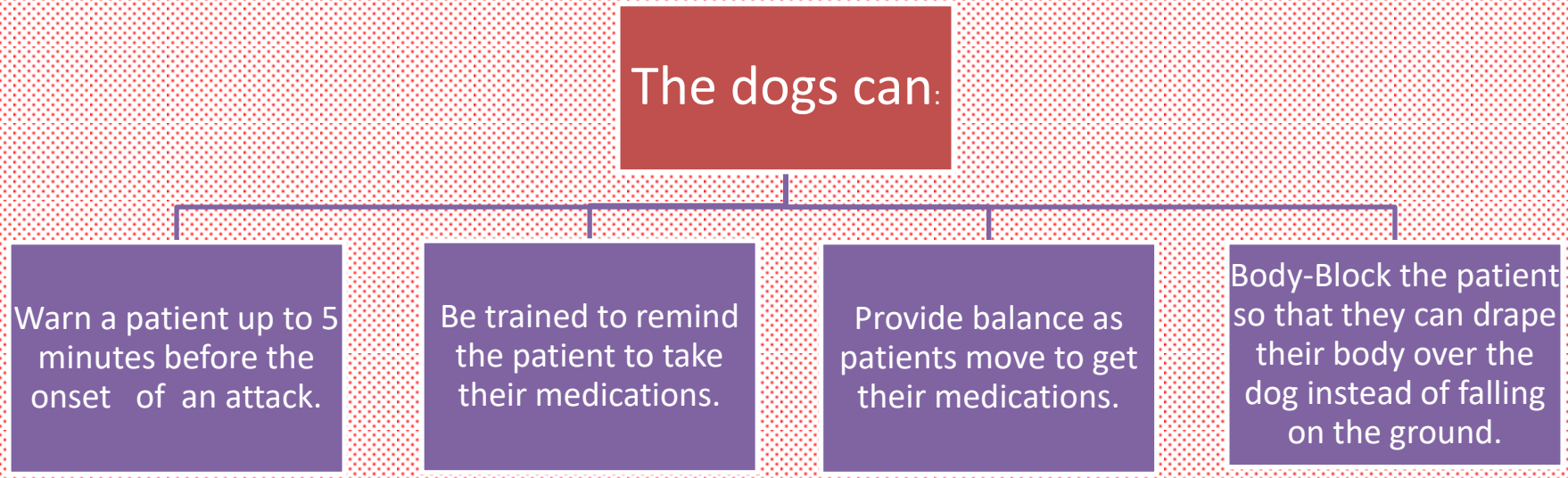
- Dogs with both <u>urine and breath</u> samples = **98%** correct.
- Dogs with just <u>urine</u> samples = **87%** correct.
- Dogs with just <u>breath</u> samples = **78%** correct.

VOC's were present at different levels for many cancers:

- Breast
- Prostate
- Lung
- Bladder

Smell Diagnosis by Dogs (4)
(Narcolepsy)

Sweat samples from patients with narcolepsy and healthy controls were presented to two trained dogs who were able to correctly identify the samples from the narcoleptics.



Questions?

DIABETIC KETOACIDOSIS (DKA)

Diabetic Ketoacidosis (DKA)

- In diabetes the body cannot make enough insulin to store glucose in the tissues.
- Unable to create energy from sugar, the body switches to fats break-down to make energy.
- Broken-down fats are blood acids known as ketone bodies.

Diabetic Ketoacidosis (DKA)

- When diabetics' insulin gets extremely low and their sugar extremely high, they can go into *diabetic ketoacidosis*.
- Ketone bodies levels then rise to an extremely unsafe and potentially harmful level.
- Diabetic ketoacidosis produces a certain fruity smell on the patient's breath.

Those Smelly Ketones

- People on ketogenic diets purposefully want to enter a ketotic state.
- They consume little or no carbohydrates, so their body burns fats and produces ketones.
- The acetone component gives off the fruity smell.
- If they eat excessive protein, they will also give off an ammonia smell.

Diabetic Ketoacidosis (DKA)

Smell Diagnosis by Dogs

- The smell produced by acetones can be detected by dogs trained to alert patients to their high blood sugar.
- The fruity smell of ketone bodies can help trained dogs to alert patients of imminent falls or other serious complications.

HYPOGLYCEMIA

Hypo- and Hyperglycemia

Dogs are trained to react in different ways to an owner who is having a high or low blood sugar episode.

- Holding a particular toy in their mouth as a signal.
- Jumping on the owner
- Sitting and staring at the owner.
- Touching owner with its nose.

Also perform other activities besides warning their owners about changes in blood sugar.

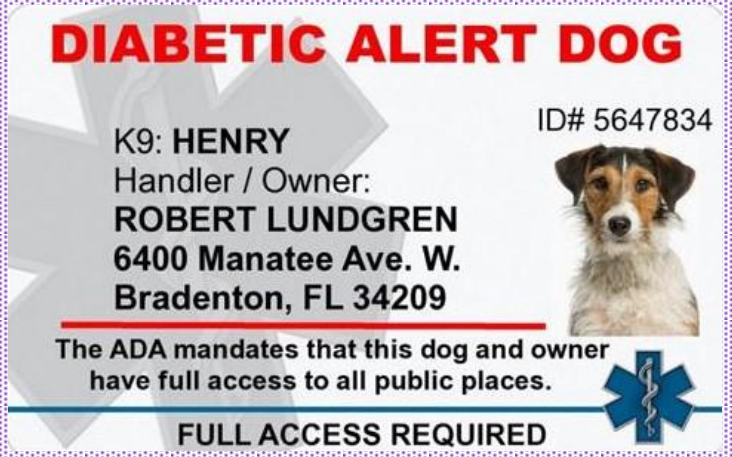
- Alerting family members.
- Bringing medications or needed objects.
- Retrieving a cell phone.
- In some instances, dial 911 using a special device, if assistance is needed.

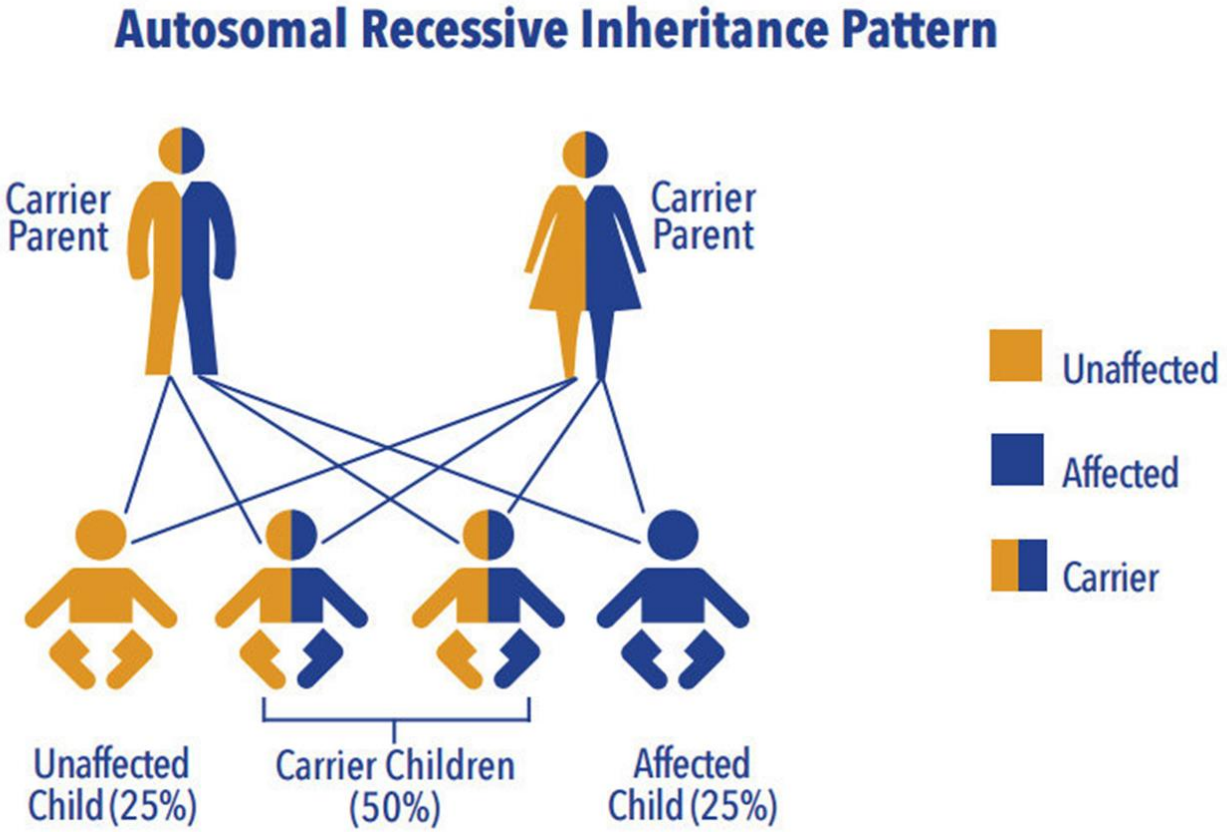
Dogs and Low Blood Sugar

- Dogs have the ability to sense spikes and also drops in human blood sugar ("hypo-alert dogs").
- In hypoglycemia dogs detect *isoprene*, a natural chemical in human breath that rises significantly as blood sugar drops.
- Hypoglycemia can cause disorientation, unconsciousness, coma or even death in an insulin-dependent diabetic.
- Many diabetes service dogs are also trained to retrieve a sugar source in cases of hypoglycemia.

Diabetic Support Dogs

ID Tags





AUTOSOMAL RECESSIVE INHERITANCE

MAPLE SYRUP URINE DISEASE (MSUD)

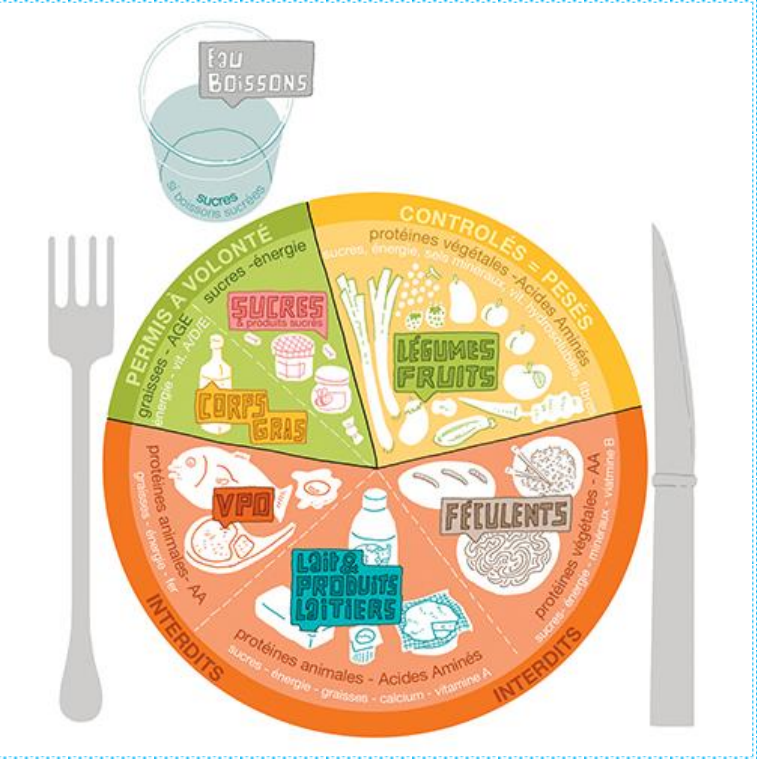
Maple Syrup Urine Disease

- Autosomal recessive metabolic disorder that affects the way patients can break down certain amino acids.
  - Inability to correctly break down branched amino acids, including valine, leucine and isoleucine.
  - These amino acids must exit the body through the urine, causing a distinct odor.
- Affected infants seem healthy at birth but rapidly deteriorate, eventually suffering from brain damage and death if left untreated.

Maple Syrup Urine Disease (MSUD)

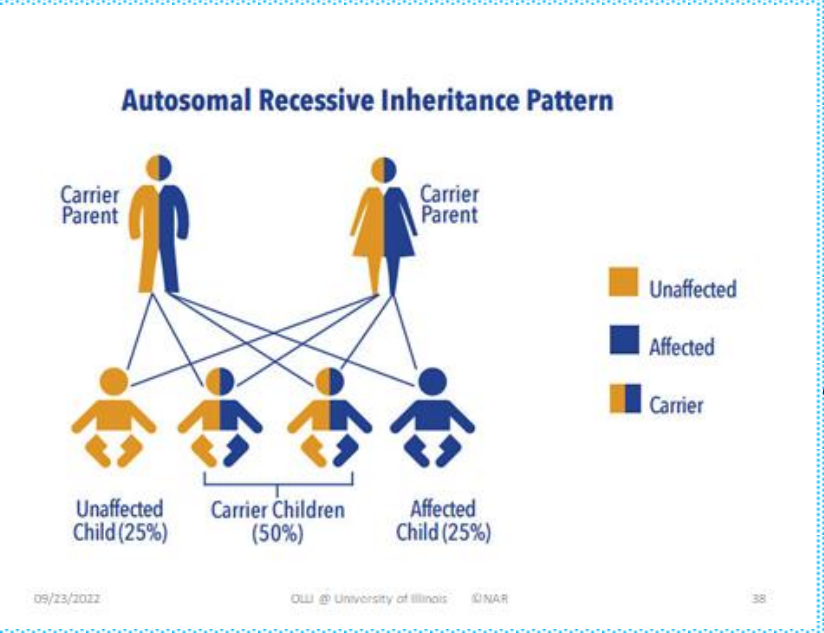
Branched chain ketoaciduria

- Later onset leads to symptoms like weight loss, diarrhea, uninhibited behavior and hallucinations.
- *Sweet syrup-smelling* urine warns of the onset of symptoms.
- Patients must control their intake of branched amino acids which are found in many foods.
- There is currently no cure for the disease, but dietary steps can be taken to control the severity of symptoms.



PHENYLKETONURIA (PKU)

Phenylketonuria (PKU)



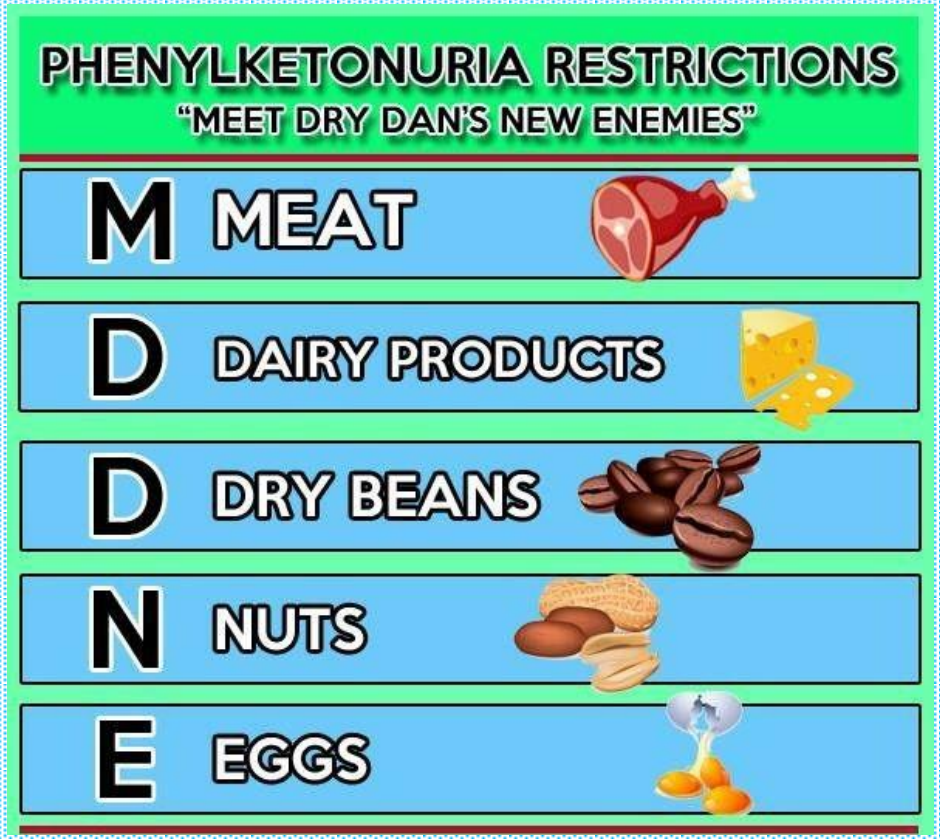
- Autosomal recessive inherited disorder in which patients are unable to break down the amino acid *phenylalanine.*
- Dietary *phenylalanine* builds up of to potentially toxic levels.
- *Phenylalanine* buildup produces a musty odor described as *"like a wet mouse".*

Phenylketonuria (PKU)

- The disease was actually first described in 1934, thanks to this odor.
- A mother of two intellectually impaired children asked her doctor about a strange odor being emitted from her kids.
- Urine samples were taken and studied, leading to the description of the disease.

Phenylketonuria (PKU)

- People with PKU must avoid foods that contain phenylalanine (diet soda contains aspartame).
- PKU can lead to intellectual disability, seizures, and behavioral problems.



Phenylketonuria (PKU)

- Those with one copy of a mutated gene typically do not have symptoms (= carrier state).
- Babies born to a mother who has poorly treated PKU may have heart problems, a small head, and low birth weight. (small head = small brain)
- Newborn screens for this disorder allow parents to start early treatment: IDPH screens for PKU, MSUD and 38 other conditions.

Phenylketonuria (PKU)

- It produces a musty, mouse-like smell and lighter skin and hair coloration.
- The compound in urine is *phenylpiruvic* acid.
- Untreated PKU can lead to intellectual disability, seizures, behavioral problems, and mental disorders.

Phenylketonuria (PKU)

- **Clinical Manifestations of Untreated PKU**
- Eczema.
- Hypopigmentation.
- Seizures.
- Limb spasticity.
- Mousy odor.
- Severe mental retardation.

ARSENIC POISONING

Arsenic Poisoning

- Over the centuries, arsenic has been used to poison kings, emperors, and prize-winning racehorses.
- Humans may come into contact with high levels of arsenic through contamination of groundwater.
- People in a remote village in Chile appear to have developed a tolerance to arsenic levels 20 times the safe limit.

Arsenic Poisoning

- Arsenic has been called the "poison of kings" and the "king of poisons“ because of its use by the ruling class to murder one another.

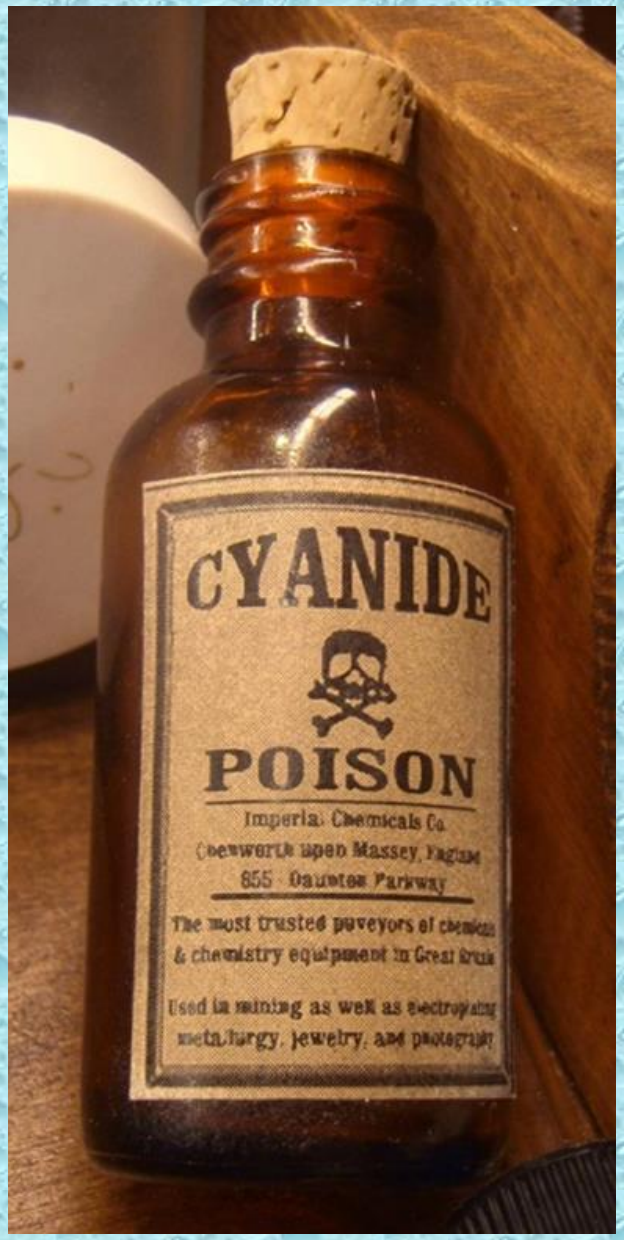
- Arsenic is very potent and very discreet.

- In the Renaissance, arsenic was known as “inheritance powder” due to its use in killing family members.

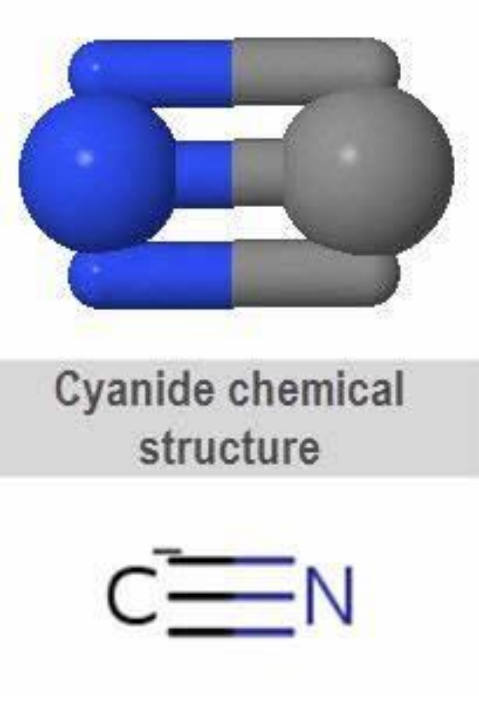
Arsenic Poisoning

- Arsenic works by blocking enzymes that are essential for creating energy in the body.
- Symptoms include vomiting, abdominal pain, encephalopathy, bloody diarrhea, and eventually, death.
- One unique symptom is that of a *garlic odor* emanating from the body of the victim.
- Ironically, scientists have found that garlic may be able to combat the effects of arsenic poisoning!

CYANIDE POISONING



Cyanide



- Chemical compound that has a C≡N *cyano* group, a carbon atom triple-bonded to a nitrogen atom.
- Ingestion of cyanide solution of as little as 200 mg, or exposure to airborne cyanide of 270 ppm, is sufficient to cause death within minutes.
- An antidote, *hydroxocobalamin* reacts with cyanide to form *cyanocobalamin*, which can be safely eliminated by the kidneys.
- This method has the advantage of avoiding the formation of **nitrites** in older regimens which cause methemoglobin.

Questions?

TYPHOID FEVER

Typhoid Fever

- Bacterial infection caused by *Salmonella Typhi*.
- Symptoms include a gradual onset of high fever, weakness, abdominal pain, constipation, and a rose-colored skin rash.
- Is still common in areas with poor sanitation and hygiene.

Typhoid Fever

- Treatable with antibiotics.
- Vaccine available
- Not contagious
- People with typhoid fever reportedly smell like *freshly baked bread.*

SMALLPOX

Smallpox

- Historically, 30 % of cases died.
- The end was often painful as the skin lesions spread into every bodily opening, including the mouth, nose and eyes.
- When these lesions blacken and peel off, they emit an odor that is characteristically sweet and pungent and is known as the "smallpox smell."

Smallpox

- Description of the death of Queen Mary II from smallpox in December 1694, was compiled from contemporary sources:
  - The queen's blisters…appeared to be ripening into plump and mellow pustules.
  - The *rotten garden* and the *malodorous orchard* produced foully abundant crops of clear blisters.
  - Such putrid fruit smelled like death.

- She died of late hemorrhagic smallpox.

MONKEYPOX

Monkeypox

- In 2003, an outbreak of 71 cases in 6 states was investigated by the CDC.
- 35 cases were laboratory confirmed
- Prior to this cluster of cases, monkeypox had not been previously found in the Western hemisphere.

Monkeypox

- A fever with pustular rash developed in patients who had recently purchased or had contact with pet prairie dogs.
- The prairie dogs got the virus from African rodents from Ghana when the two species were housed at a distribution center in Illinois.
- The CDC and the FDA then issued a ban on importing pets of diverse classes from Africa.

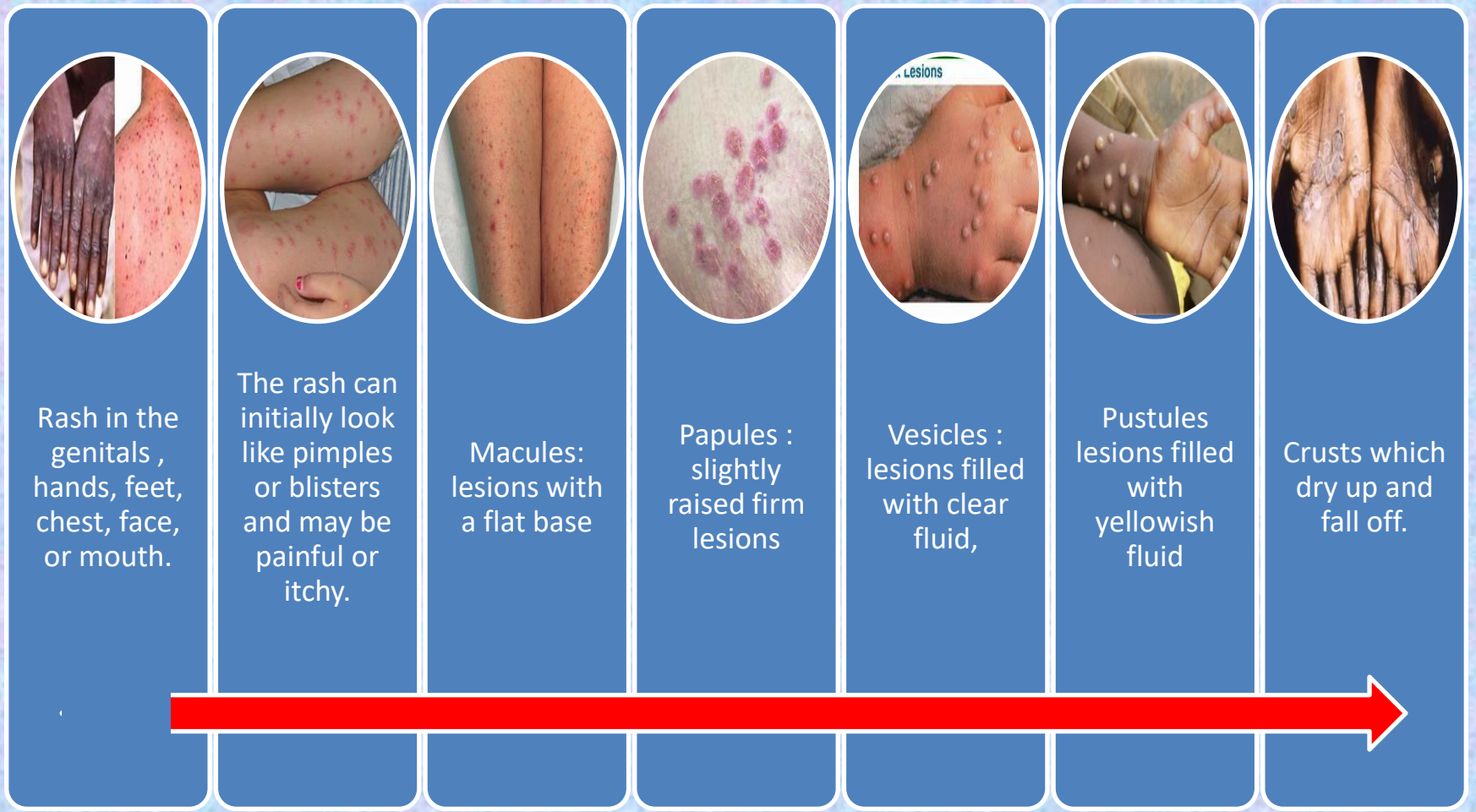
Monkeypox

- Transportation, sale, or release into the wild of prairie dogs and animals from Africa (including tree and rope squirrels, dormice, brush-tailed porcupines, striped mice, and Gambian giant rats) was prohibited by the CDC and the FDA.

- There have been no other United States outbreaks related to imported animals since the time of this prohibition.

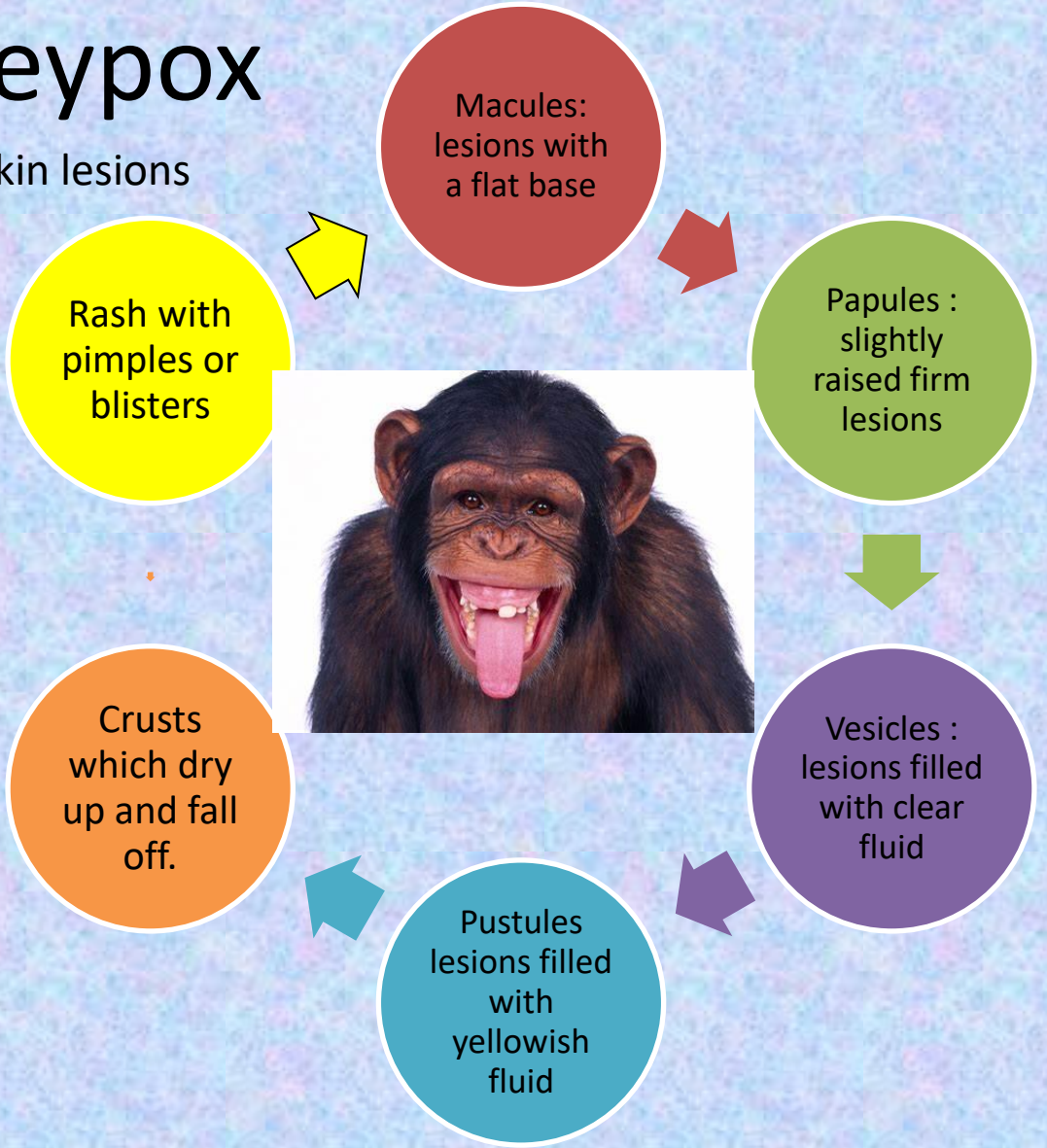
Monkeypox

Sequential evolution of skin lesions



Monkeypox

Sequence of skin lesions



Monkeypox

Sequential evolution of skin lesions

- Pimply, blistery rash in genitals , hands, feet, face, chest, or mouth.
- Rash initially may be painful or itchy.
- Description of a “monkeypox smell” is scarce and sketchy, so there is no comparing it with the famous “smallpox smell”.

SCHIZOPHRENIA

Schizophrenia

- In the 1960s, nurses began noticing an odd odor emanating from patients in mental hospitals, described as *"skunk-like",* despite bathing, especially in those with schizophrenia and catatonia.

- A study showed that human odor testers and trained rats could reliably sense this unknown odor in the sweat of patients with schizophrenia.

- A few years later, the compound responsible was identified as trans-3-methyl-2-hexenoic acid (TMHA).

MIGRAINES

Migraines

- Migraine sufferers who owned dogs were recruited and completed a survey to see how their pets reacted to their migraines.
- Survey found that 1 in 4 migraine sufferers are able to recognize a noticeable change in their dog's behavior up to 2 hours before the onset of their migraine.
- Some patients who suffer from migraines experience an *aura* that occurs prior to the onset (visual changes, yawning, frequent urination, or neurologic symptoms).

Migraines

- Some dogs can sense and/or smell the *aura* and allow the person to take preventive measures.
- Their dog can alert them to an impending headache an hour or two in advance.
- Some severe migraine sufferers have service dogs specifically trained to detect serotonin spikes in the blood.
- They are able to warn patients of the brutal stroke-like symptoms up to 2 hours in advance.

NARCOLEPSY

Narcolepsy

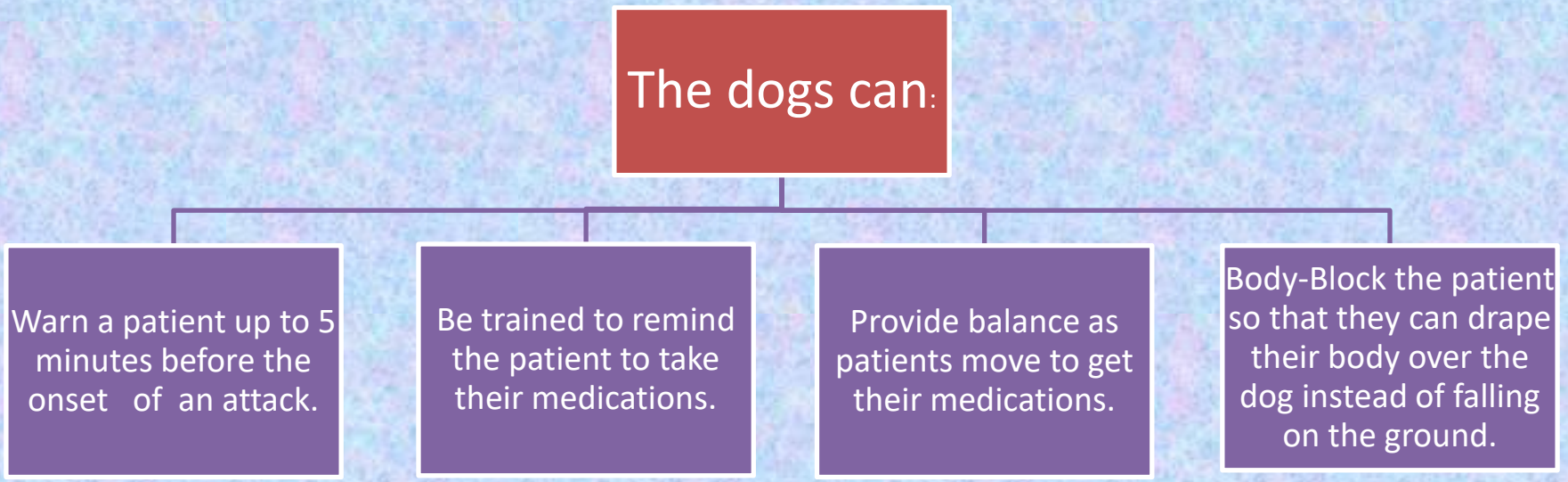
- A debilitating disease that causes patients to fall asleep at extremely inopportune times.
- They may experience excessive sleepiness, hallucinations, sleep paralysis, or *cataplexy.*
- Many people can go years without receiving the correct diagnosis.

Narcolepsy

- Narcolepsy is caused by the loss of a brain chemical called *hypocretin -1 (orexyn A).*
- *Hypocretin* comes from the hypothalamus and works as an alert system that maintains wake/sleep cycles.
- Narcolepsy is another disease that causes patients to emit a special odor usually only detected by canines.

Smell Diagnosis by Dogs (4)
(Narcolepsy)

Sweat samples from patients with narcolepsy and healthy controls were presented to two trained dogs who were able to correctly identify the samples from the narcoleptics.



Narcolepsy Support Dogs

- A person could fall asleep walking down a flight of stairs or crossing a busy street.
- Narcolepsy service dogs detect a subtle odor when an attack is coming on.
- With a 5 minute warning before an attack, the masters can seek safety.
- They are trained to “body block” the owner allowing them to drape over the dog and not fall.

AUTISM

Dogs and Autism

- Dogs can most certainly read human emotions.
- They can “smell fear” when hormones like adrenalin and cortisol are released in response to stressful situations.
- Service dogs are especially important for people on the Autism spectrum and for those suffering from PTSD, who experience higher levels of the “stress hormone” (cortisol).

Autism and PTSD

- PTSD in autism spectrum patients is characterized by hyperarousal.
- They have greater difficulty concentrating than other forms of PTSD.
- Patients on the spectrum are more easily startled, more likely to have insomnia, and are predisposed to anger and anxiety.
- ⇧ Anger/anxiety = ⇧ cortisol + adrenalin

PARKINSON'S DISEASE

Parkinson's

- A neurodegenerative disorder resulting from a loss of the neurons that produce dopamine.
- This leads to tremor, slow movement, rigidity, and problems walking in patients.
- There is no cure for Parkinson's, but there are treatments available to reduce the severity of symptoms.
- There is also no current definitive test for the disease other than observing patients with symptoms.

Parkinson's

- Joy Milne, a retired nurse, began noticing a very interesting smell that her husband Les was emitting.
- She was convinced that he smelled differently, but he became upset at her constant nagging.
- In 1985, after meeting patients with Parkinson's at a support group, Joy realized what the musty smell meant.

Parkinson's

- Joy was given 6 T-shirts from patients with the disease and 6 without.
  - She correctly identified all 6 of the patients with Parkinson's.
  - She incorrectly identified one of the controls as having Parkinson's.
  - The patient that she "incorrectly identified" actually ended up being diagnosed with Parkinson's 3 months later.

- Joy is currently in studies that are trying to find the compound causing the odd odor that she picks up on.

- Mass spectrometry is being used to identify 10 molecules that are unique to patients with Parkinson's, which could eventually create a new diagnostic test for Parkinson's.


CANCER

Cancer

- The owners of Lucy, a mix of Labrador Retriever and Irish Water Spaniel used her remarkable sense of smell by training her to smell cancer.
- Over 7 years, Lucy was able to find bladder, kidney, and prostate cancers.
- Now Lucy is part of one of the largest canine cancer detection clinical trials in UK.
- Medical Detection Dogs is an organization that uses human urine to figure out if humans have cancer through scent.

Cancer

- The founder started the group after her Labrador, Daisy, picked up on a very deep cancer in her breast.
- In 1989, King's College, reported about a woman whose dog persistently kept sniffing a mole on her leg, which turned out the be a very-early-stage malignancy.
- It is thought that the dogs are picking up on *alkanes* or aromatic compounds that are synthesized by malignancies.
- These volatile compounds can then be sensed by dogs in human urine or breath.

Cancer

- The dogs of the In Situ Foundation are able to sense early stage cancer in small samples of human urine, saliva or expelled breath more accurately than any modern equipment.

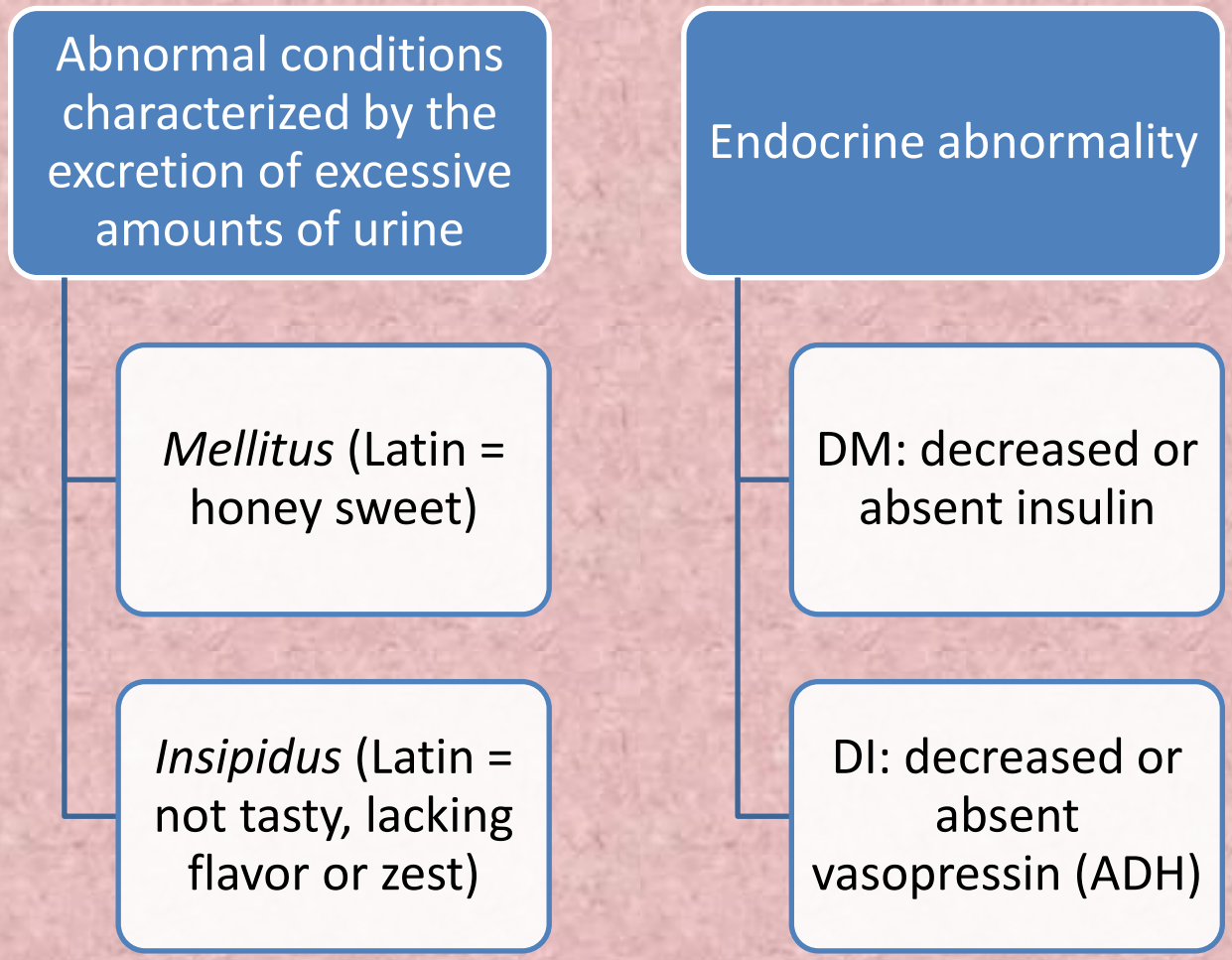
- The 50+ dogs trained by In Situ founder, Dina Zaphiris can sense multiple types of cancer in parts per trillion – similar to sensing a single drop of blood in an Olympic-sized swimming pool.

Diabetes Mellitus

Cystic Fibrosis

THE TASTES of DISEASE

Diabetes


Abnormal conditions characterized by the excretion of excessive amounts of urine
Mellitus (Latin = honey sweet)
Insipidus (Latin = not tasty, lacking flavor or zest)
Endocrine abnormality
DM: decreased or absent insulin
DI: decreased or absent vasopressin (ADH)

Cystic Fibrosis (CF)

- Autosomal recessive transmission of a faulty gene that affects the movement of sodium chloride (NaCl, salt) in and out of certain cells.

- This produces thick, heavy, sticky mucus and thickened digestive juices, which cause inadequate nutrient absorption, malnutrition and failure to thrive.

- The thick mucus can clog the lungs, cause breathing difficulties, lung infections, and severe lung damage.

Cystic Fibrosis (CF)

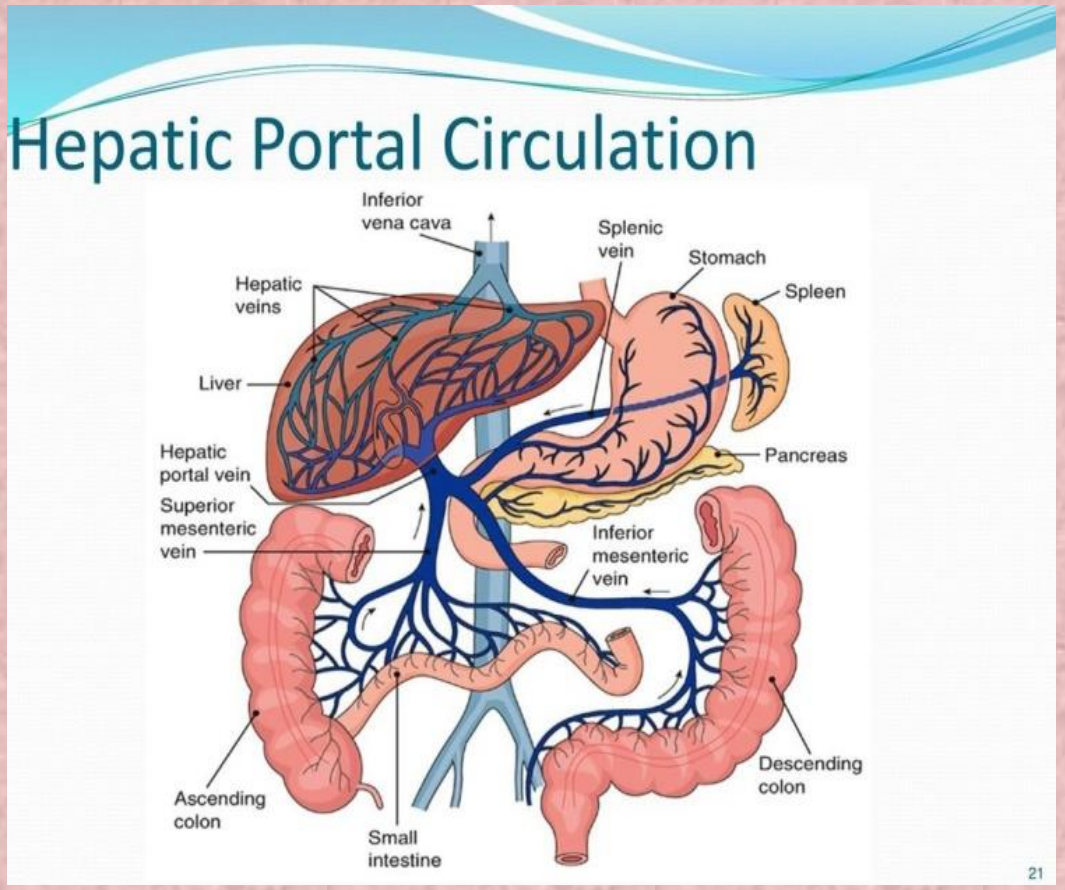
- Babies with CF can have salty skin and sweat.
- There is increased sodium and chloride loss through the skin.
- An ancient folk saying from Northern Europe is: “Woe to that child which when kissed on the forehead tastes salty. He is bewitched and soon must die.”

Fetor Hepaticus

Fetor Uraemicus

SEVERE ORGAN FAILURE

Hepatic Portal Venous System



- A portal venous system occurs when a capillary bed pools into another capillary bed through veins, without first going through the heart.
- The hepatic portal system delivers about 3/4 of the blood going to the liver.

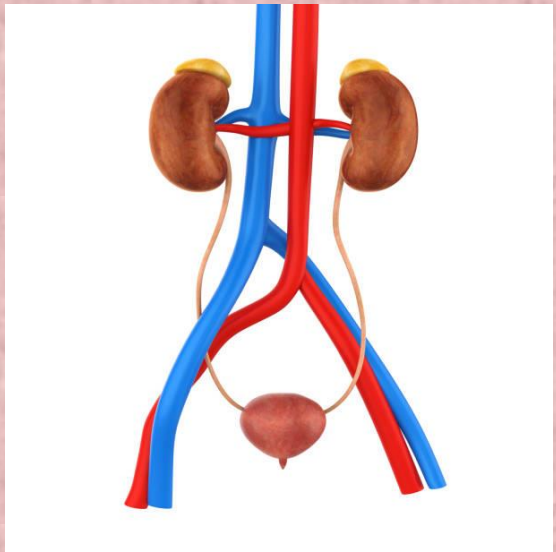
Liver Failure

Fetor Hepaticus

- Portal hypertension increases the blood pressure in the veins of the liver, making it hard for blood to flow through the organ.
- Blood backs up in the veins around the liver, so sulfur substances end up in the bloodstream and make their way to the lungs.
- These substances (e.g. Dimethyl sulfide) give the person's breath a *distinct smell of rotten eggs, garlic or a slightly sweet smell.*
- *Fetor hepaticus (hepatic stench) is* often called *breath of the dead*, due to its association with severe liver disease, often fatal.

Renal Failure

Fetor Uraemicus



- An early symptom of uremic coma is an ammonia (urine-like) odor in the mouth when the urea in saliva breaks down to ammonia.

As the blood urea nitrogen (BUN) level increases, patient might develop:

- Skin itching
- Uremic stomatitis and digestive disorders
- Encephalopathy
- Pericarditis.
- Anemia.

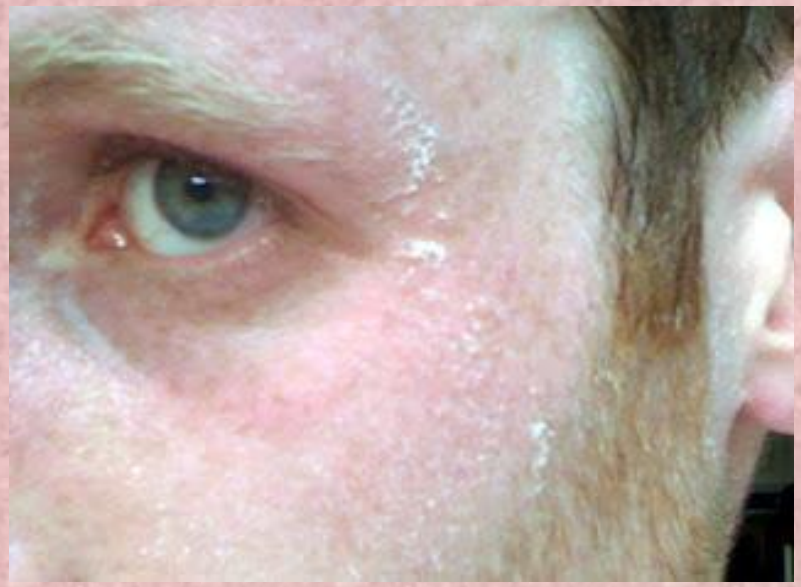
- These levels happen with high BUN level >150 mg/dl and disappear spontaneously when the BUN level is reduced with medical treatment.

Renal Failure

Fetor Uraemicus

- *Uremic fetor* is associated with an unpleasant metallic taste (*dysgeusia*), a symptom of chronic kidney disease.

- Uremic frost, a white plaque found on the skin or in the mouth is caused by residual urea crystals on the skin epithelium after evaporation of perspiration and saliva.



Final Questions?


Thanks


RED
Warm, Dry, Hot
PINK
Luscious, Sweet
YELLOW
Warm, Sour Bitter
GREEN
Damp, Sour, Fresh
BLUE
Cold, Wet Fresh
BROWN
Useful, Nutritious, Sweet
BLACK
Dry, Firm, Bitter
GRAY
Dry, Soft, Tasteless
WHITE
Dry, Pure, Salty
VIOLET
Tasteless, Empty
Colors and their Flavors