



MICROBIOLOGY

Lecture : 3

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Viral skin infection

Viral Warts

- Caused by Human Papilloma Virus (HPV)
- Non enveloped DNA viruses
- Infect human epithelial cells there are different type of HPV which categorize according to which epithelial cell they prefer effect
 - Cutaneous epithelial cells like face, hand, feet
 - Mucous membrane like respiratory track(pharynx, nasal, oral cavity), genital region
- 150+ subtypes of HPV identified: 6,8,16,18
- Some types can cause benign tumor called papilloma (Warts)
 - Benign proliferations of the skin and mucosa
- Several subtypes associated with cancer

بعض ال HPV بسبب benign tumor الي هي warts or papilloma الي هي low risk بتكون من نوع 6,11

pathogenesis – Squamous Cell Carcinoma (SCC) of skin, mucosa, cervix, etc

ولكن بعض الانواع ممكن تسبب cancer الي بتكون high risk ووهي من نوع 16,18

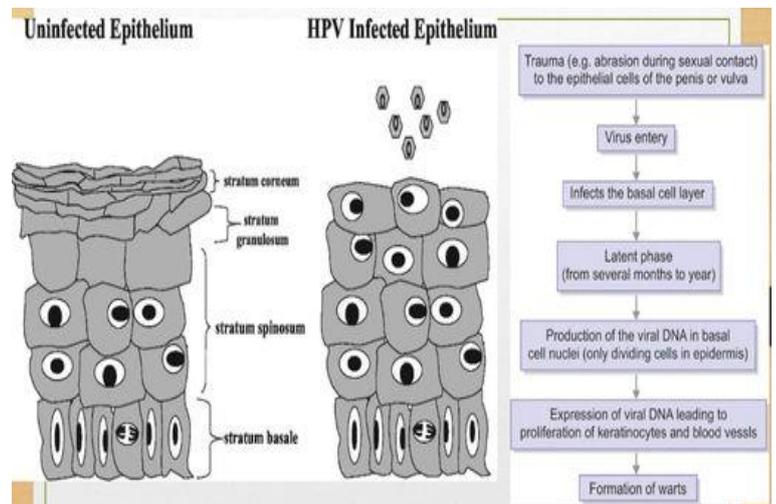
-epithelial line outer surface of organ and blood vessel

-and spread the interior of the body from external world

-they primarily serve as protective to invade the bacteria, virus, fungal and parasite

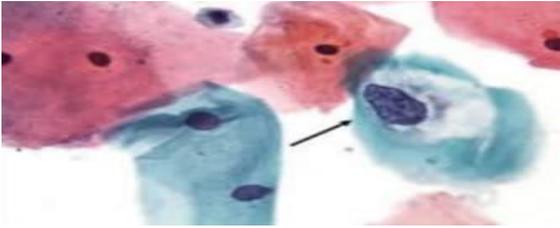
-stratum basale will be protected under all layers because these are deep layers but if there is a cut in the epithelium so HPV can access to infect basal cells

-HPV can replicate within basal cells which produce viral DNA in basal nuclei and expression of viral DNA leads to dysregulation of the replication of epithelial cells and blood vessels and these cause warts



-In some types of HPV infections

- koilocyte, or a cells with an irregular shape, enlarged and dark staining nucleus, and a clear area around the nucleus that's called a perinuclear halo.



- precancerous lesions that can transform into carcinomas

فبصير epithelial cell بالchange فتؤدي الى uncontrol regulation ممكن تعمل HPV بعض انواع irregular shape و enlarge and dark stain of nucleus في وكمان في clear area around nucleus called perinuclear halo وهي عبارة عن koilocyte وهاي اسمها precancerous lesion cancer الي ممكن تتحول ل

- HPV types 6 and 11 low-risk HPVs because they don't tend to progress beyond warts. This responsible to laryngeal papillomatosis which is warts in respiratory track and these consider low risk because they do not tend to progress beyond warts these mean this make warts lesion but not transfer to cancer

- High-risk HPV types like types 16 and 18 have a high risk of transforming into cancers of the cervix, vagina, vulva, penis, anus, or upper respiratory tract over one or two decades. These high risk HPV which can transfer to cancer from 10-20 year especially genital area

بس هون بكون في cofactor زي smoking, low immunity and radiation

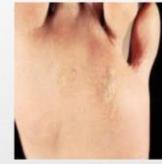
-Many HPV infections are asymptomatic, but when symptom present depend on type of HPV so symptom of nongenital cutaneous infection can involve some benign warts if these low risk type

هسا حسب المكان بنسمي ال warts :

- **Common skin warts** of the hands or nails is mainly painless and dome shape projection that give skin rough appearance



Common wart



Cauliflower wart



- **Plantar warts** on the soles of the feet many painful and scaly



- **Flat warts** of the face and extremities mainly in pediatric population, is painless, smooth, small, flat and numerous

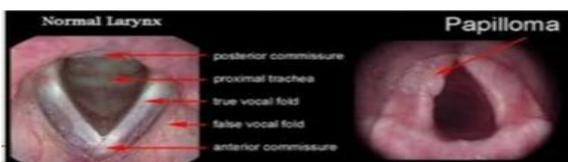


- **Filiform warts** of the face it is finger projection around eyelids and lips



Filiform wart

In mucous membrane of respiratory track called respiratory papillomatosis and can lead to voice changes and high pitched breath sound like in vocal cord and give hoarseness voice



Genital Warts (Condyloma Acuminata)

- Anal and genital infections like in female vulva, cervix, vagina, male penis and scrotum
- painless, they can cause itching, burning, local pain, or bleeding.
- Generally an STD, but not always
- When seen in children, may or may not indicate sexual abuse

هو غالبا بكون sexual transmitted بس مش دائما يعني مثلا ممكن نلاقي اطفال مصابين وهذول اكيد مش sexual

- When seen around orifices (anus;vagina) important to investigate further as infection in rectum/vagina more likely to lead to squamous dysplasia and SCC



Transmission

- The cause of an HPV infection is contact with infected epithelial cells

لازم يكون في contact مع ال epithelial cell الي فيها الwarts فبتنتقل من شخص لآخر عن طريق الcontact

Some can increase risk of exposure:

- Sex: having multiple or new infected sexual partners
- Child birth: delivery a baby through an infected birth canal
- Sharing clothes
- Auto-inoculate if individual have papule and they scratch them they can spread the virus around other area

Diagnosis

- Warts are diagnosed clinically.
- It may be helpful to pare the surface to reveal **small black dots**, which are thrombosed capillaries.



- Dermoscopy



- Endoscopy,

اذا كانت مثلا بال GI, Respiratory track

- a definitive diagnosis of HPV can not be made without molecular testing of biopsied cells for viral DNA or RNA.

ممکن نوحذ biopsy حتى نتأكد انو هاي HPV و نوديهها عالمختبر

Treatment of Warts

- Most cases resolve spontaneously in 1-3 years. self limited
- Patient expectations prior to treatment extremely important – cutting, burning and freezing of warts does not guarantee a cure – visible warts can disappear and reappear as infection becomes subclinical

هون لازم نوضح للمريض شو بنتوقع من العلاج مثلا اعملت cut, burn, freezing of warts ولكن هاي ممكن تختفي لفترة ولكن هاي راح ترد ترجع as infection subclinical فلزام توضح للمريض لو شو ما عملنا ممكن ترجع

- never treat warts without discussing appropriate expectations first – warts can be one of the most stubborn diseases to treat!
- treatments often center around removal of warts and precancerous lesions
- Destructive treatment: Aim is to destroy skin cells occupied by virus in hopes of stimulation an immune response:
- Daily application of paints or gels containing keratolytics such as 15 to 60% salicylic acid.

Salic acid مادة كاوية بحطوها عالجلد اسبوع لشهر وبعدين بتروح وممكن ترجع

- Cryotherapy with liquid nitrogen which freezing cell to destruction
 - Electrosurgery (curettage and cautery), used for particularly large and annoying warts.
- Surgery to remove warts or laser

Human papillomavirus is a DNA virus spread through contact that infects human epithelial cells of the skin and mucous membranes.

Symptoms can range from warts, to precancerous lesions and carcinomas.

Definitive diagnosis can be made molecularly and treatment can range from allowing the immune system to clear the infection, to mechanical or chemical removal of infected cells.

Molluscum Contagiosum

- localized skin infection with vesicular shaped papules
- Molluscum Contagiosum virus
- Pox virus
- worldwide phenomenon
- it is one of the most common childhood skin conditions but can infect adult

-some of the risk factors for

- immunodeficiency like infection with HIV or steroid use
- being sexually active
- having other skin conditions like atopic dermatitis, eczema

transmission

- direct skin-to-skin contact
- sexually transmitted
- Autoinoculation
- fomites
- swimming pool

the incubation period for developing the papules is generally between two to six weeks

-diagnosis is mostly clinical: dome-shaped papules that have characteristic

- belly button or umbilicus and is very small, smooth, round, flesh color



But patient with immunodeficiency can get giant molluscum contagiosum



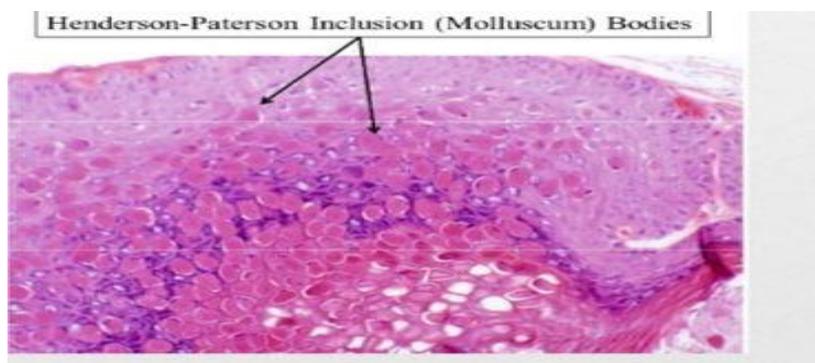
-can be distributed anywhere on the body except for the palms of the hands and the soles of the feet so if you see vesicular in the palm or the hand or sole of the feet is not molluscum contagiosum

often asymptomatic

- but pruritus can occur these papules become itching and distribution and these help to auto-inoculation and these lead to molluscum dermatitis
- molluscum dermatitis reaction in skin from itching

diagnosis of

- clinical which is dome shape by central umbilicus
- histology
 - molluscum bodies or Henderson Patterson bodies

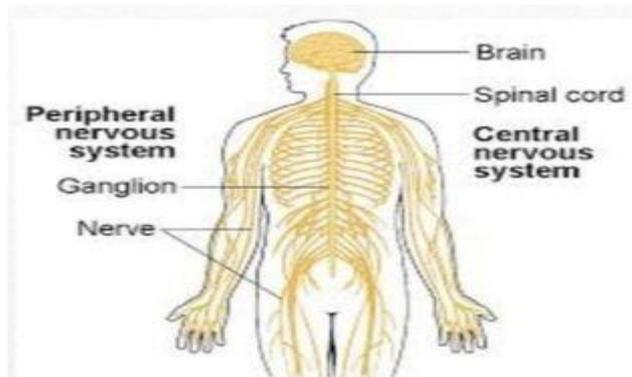


Varicella Zoster Virus

- VZV – Varicella Zoster Virus, What is it?
- Common herpes virus infecting ~98% of human populations by adulthood
- As primary infection resolves (chicken pox,) virus retreats to sensory nerve ganglia and enters period of latency.
- VZV immunity declines with age, concurrent disease/malignancy, immune compromise – this allows VZV to re-activate as localized dermatomal infection called “shingles” or herpes zoster

Nervous system

- Central: brain and spinal cord
- Peripheral
 - Cranial nerves come from brain and these motor and sensation innervation to head and neck
 - Trigeminal nerve (v) is 5 cranial nerve sensation of the face
 - Spinal nerves come from spinal cord



Each nerve comibnt with ventral root and dorsal root

Ventral root have neuron carry motor innervation from spinal cord to muscle

But sensory information like touch, tempressure, pain come from skin and other tissue travel by sensory neuron to dorsal root of spinal cord and there dorsal root ganglia near to spinal cord which is convergence two nerve



Every spinal nerve is charge of sensation of specific area of skin called dermatome

So dermatome is area of skin that is supply by single spinal nerve

مثلا اذا دعست على اشي الpain ينتقل S1nerve بس مثلا اذا خبطت Big toe لتنتقل عن طريق L5

Varicella – “Chicken Pox”

- ~90% of cases occur in children 10 y/o or younger.
- Unusual in adults
- Transmitted by respiratory contact with airborne droplets and direct skin-to-skin contact – highly contagious!

- Replicate in epithelial cells
- Incubation period 10-23 days
- Epidemics in schools usually winter/spring

When an infected person sneezing or cough transmitted to lung and get infection into air

Can also transmitted by oral or skin lesion

When it contacted with skin then start replication in epithelial cell then picked up by immune cell then transferred to near lymph node then start cause primary infection called varicella "chicken box"

These have two stages: primary viremia and secondary viremia

In primary viremia the virus infected liver and spleen (reticuloendothelial system) which is made phagocytosis cell

About two week after entry the body, the virus start infected immune cell especially T cell and these consider secondary viremia

Infected T cell start express protein that bind to receptor on the skin cell

Once T cell reach the skin start release the virus which start infected the skin

The infection spread through the skin going directly from cell to cell sometimes the infection keratinocyte start fuse to gather and create giant multinucleated called Tzanck cell

And uninfected cell start release IFa and IFB which inhibit virus protein synthesis and protect these cell from getting infection

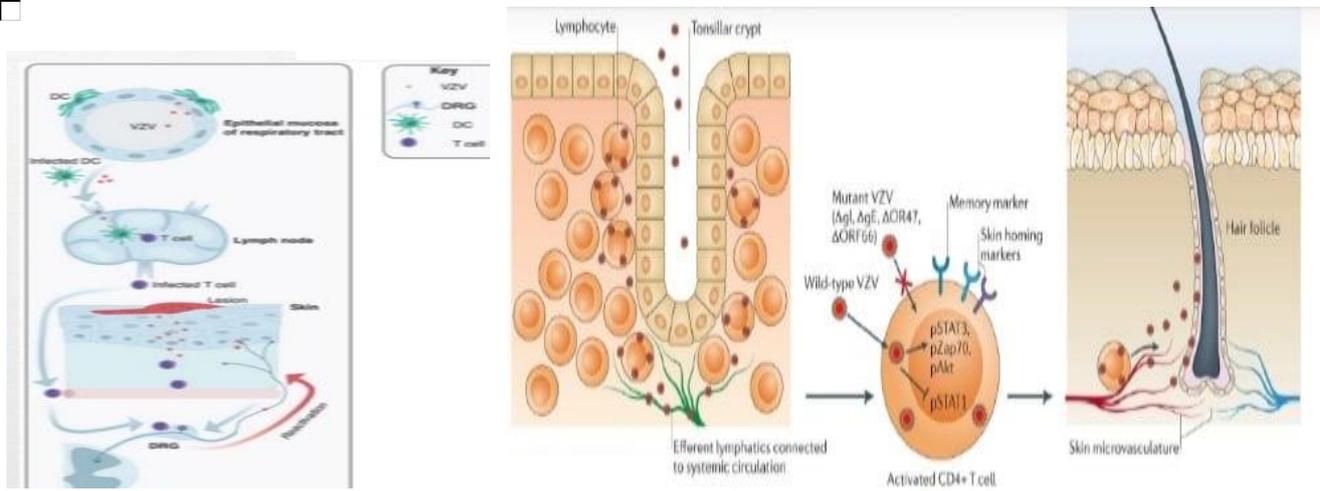
As result, we get tiny lesion on skin separate by normal area of skin

In addition to infected keratinocyte the virus also infected sensory neuron on the skin and those neuron travel retrograde, meaning backward the neuron to the dorsal ganglia or if it is on the face to trigeminal ganglia

Overtime, when the adaptive immune response reaction kicks in, most of the virus in the body are elimination but once the ganglions are spread, they can remain for many years

So virus establish latent period in the trigeminal ganglia and the dorsal ganglia

Later on, if the immune system weak due to aging, stress, immunosuppressive therapy the virus can activated and can travel up through the sensory nerve, anterogradely to the skin and cause infection in the innervated dermatome that's called herpes zoster "shingle"



• **Distribution:** Rash usually starts on face/scalp, then progress downwards to trunk/extremities.

- Flat red itchy spots (macules)
- Elevated (papules)
- Small fluid filled vesicles
- Crust over and form scabs
- Scab fall off without scar

Chicken box start after 2 week , start appear fever, headache, general weakening after a couple days. Skin lesion appear on the scalp, face and trunk

at first, there are flat, red, itchy, spots called macules over time, become elevated and develop into papules and then into small fluid filled vesicles

and within 1 to 2 day these vesicles begin to crust over and form scabs

after 5 days the scabs fall off usually without scar

new crops of lesion are continuously forming in different place in the body every 3 to 5day so it is possible to see lesion in different stage at the same time

-in addition to itchy lesion, painful sores can appear on mucosal surface in the mouth



- Often accompanied by mild fever and malaise
- Infection can be more severe in adults, with potential severe prodrome and complication by Varicella pneumonia
- Extremely pruritic = scratching = secondary bacterial infection (most common complication)
- Greater age of patient = greater severity of primary infection

VSV – Treatment

- **VSV vaccine**: ~80% effective. Should be used in VSV negative adults, patients with immune compromise, childhood cancers.
- In healthy children, symptomatic **treatment with antipruritics and rest appropriate**
- Topical **antipruritic medication**
- **Analgic anti inflammatory**
- **Aspirin should not be used** (Reye syndrome): liver affected by varicella and aspirin **lead to toxic build up of ammonia** because virus infect liver and spleen so aspirin metabolic in liver so become toxic
- In select cases: Oral/IV antivirals
- Occasionally VSV secondarily infected with bacteria – treat accordingly

Herpes Zoster

- Infect sensory neuron
 - Dorsal root ganglion
 - Trigeminal ganglion
- Commonly known as “shingles”
- Reactivation of latent VSV in dorsal root or cranial nerve ganglion cells
- Lesions appear over several days, **usually resolve in 2-4 weeks**
- Disease more severe/longer duration in immunocompromised patients

HZ - Presentation

- Lesions appear posteriorly, the progress in anterior direction, then to peripheral locations
- Presents as grouped papules, vesicles, pustules and crusts on erythematous base
- **Single stripe of vesicles around left or right side of body**
- **One side of face**

• Pain itching tingling

- Lesions spontaneously heal in 1-2 weeks



- 50% of cases involve thoracic nerves
- 15-20% cervical or lumbar nerves
- Remainder involve sacral and cranial nerve roots

PHN – Post Herpetic Neuralgia

- Syndrome defined by pain and/or other neurologic symptoms within affected dermatome persisting beyond 4 of onset of skin lesions of HZ
- Can last months to years beyond the illness itself
- Severe pain during prodrome/onset of skin lesions highly predictive for PHN

هنا احنا حكينا انو ال shingle بتروح خلال 4 اسابيع بس هون بهاض ال syndrome ال pain بضل موجود لاكثر من 90 يوم

HZ - Diagnosis

- Usually a clinical diagnosis based on characteristic prodromal symptoms and appearance
- When it's Zoster it usually looks/acts like zoster.....but when in doubt....
- Usually do viral culture for VSV
- Can also do skin biopsy for histopathology, Tzanck smear, Antibody studies, etc.

نهاية التلخيص سامحونا على اي اخطاء