Micro sheet #17

Refer to slides#7

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**Human Papilloma viruses**

* About **10%** of Jordanians have experienced an infection by HPV.
* HPV generally isn’t so dangerous especially in relation to skin and often causes **asymptomatic infections**.
* HPV: has a **Double stranded DNA**, and a capsid composed of a large number of capsomeres, **non-enveloped;** so it can survive more in the environment and more associated with infections.
* HPV, especially the genome can survive in the damaged dry skin, so it remains active and can easily spread
* HPV in general is considered “non-pathogenic” under normal conditions, rarely associated with true damage to epithelial cells, but under certain conditions it might cause true damage in association with other viruses.
* Infection by HPV usually persist in the basal layer of epithelial cells, and rarely the genome of the virus integrated in the host chromosomes, due to the fact that it multiplies and replicates in the nucleus, and might under certain conditions produce **episomes**: "extrachromosomal –viral or bacterial- part of genome which can be integrated in the genome of the host cells” and this prevents the lyses of the cells, it’s a form of some cell-damage not considered as a whole lyses “the dr said even that you may find in some text books that HPV causes cell lyses, but it’s really not true”
* Epidermis and mucous membranes, once infected, might be associated with the eruption of the wall, but it’s not necessary to be always recognized
* You might recognize some lesions that appear similar to **warts**, to make sure if they are true warts or not: you should ask for some pieces of the damaged skin to look for the presence of HPV, because sometimes there are **wart-like** structures associated with other viruses not HPV, but if the warts persist for a long period you can say 100% it’s an HPV infection.
* The majority of Human Papilloma Viruses’ clinical infections are benign and less than 0.1% might be associated with a form of malignancy, especially in HPV related to the genital tract.
* HPV infections are generally divided into : **1)skin and mucosal infections** ,**2)genital infections**
* There are about **200** types of HPVs, but **15-20** types are associated with the majority of HPV infections.
* Often, It’s easy to get the infection by HPV, especially during childhood; **children** are more susceptible than adults
* In adults and elderly, patients with **immunodeficiency** are also susceptible to HPV infection.
* **Close contact** “by hands or any means” usually causes transmission of HPV
* **Cutaneous warts**; widely distributed and the most important …associated with few types of HPV (1 to 8 , and 10)
* **Type 9** is not involved in any skin infections
* Cutaneous warts contain: **1)common skin warts:** caused mainly by types 2,4,7

**, 2) deep planter warts:** associated mainly with soles of feet, during walking any contamination with HPV can get into the skin through any damaged part of skin of the soles, the majority of the population worldwide are associated with this type, there’s no human being not affected by this type, but it’s normally not so significant and usually not associated with any malignancies

**, 3) flat warts:** recognized in any part of our bodies, fingers, face, neck. And the majority of us has 1 or 2 or 3 flat warts on their skin, and these warts often only not well pigmented areas and have a change in the pigmentation; pink or light brown, not significant and not important and may appear and disappear without noticing.

* ***Verruca***is a Latin word means “warts”
* Warts with Intensive coloration in the skin or crusting or more granulate form, we don’t say they are more dangerous but they may persist for a longer time, and require treatment; at least due to dissatisfaction, especially if these warts were in the face or fingers… easily removed by surgical means like **cold applications** or by available simple methods like rubbing the warts by the inner side of a **banana peel** for at least 2-4 weeks.
* The “banana peels” method is useful according to the doctor’s experience, and it’s not recommended to use any type of acids for treatment because they damage the skin.
* Banana peels contain some antioxidants that aid in elimination of the infected skin.
* There are recommendations that eating a lot of fresh **green** “contains high levels of antioxidants” fruit and vegetables can decrease the incidence of HPV infections.
* Regarding pictures, slide 4 : what you see here is not the typical form of warts that develop usually, these are more associated with damage of the skin (granular form) and often require treatment, not easily eliminated because they often make clusters ,"تتفرع" which means that they disseminate from one finger to other or from face to other part of the body**, this form is associated with certain immunodeficiencies of skin**
* In general, about immunity against HPVs, following contact with the virus, whether symptomatic or asymptomatic; our body responds by production of specific antibodies-**humeral** **immunity**, and **cell mediated immunity**, humeral immunity is not important for this issue and the cell mediated immunity is more important.
* Cell mediated immunity; control -to some extent- the proliferation of the warts and inhibits latent recurrence of the infection.
* Cell mediated immunity differs between populations, always there’s less than 0.1% of any community or population who have some deficiency in immunity against HPVs, infected more by HPVs and develop more warts than others, and these persons that have this susceptibility to HPVs infections may present within a family that has other normal individuals.
* **Genital HPVs**; more dangerous especially for women, very common in western countries due to sexual liberation.
* Genital HPVs and other sexually transmitted diseases are less common in Muslim countries due to cultural and religious aspects.
* Genital HPV infections may affect any part of the genital organs, in women, the infection may be not recognized in extra genital, it present mainly inside the genitalia, and it might be even not noticed if there’s no clinical symptoms.
* Only by examination by colposcopy the physician can recognize warts in the cervix or vagina, but normally warts can be present without feeling of the infection.
* In general there are specific types of HPVs that produce genital infections, mainly type 16 and type 18 (there are other types but with less importance)
* These 2 types are associated with 70% of all types of anogenital warts.
* Infection by HPVs type 16 or 18 not necessarily to develop to adenocarcinoma or malignancy.
* Adenocarcinoma can be developed with type 16 and 18 infections but not necessarily, depends on the status of immunity, especially cell mediated immunity.
* There are types of cervical warts: Flat Condyloma and squamous intraepithelial neoplasia, these might be associated with certain malignancies and can be easily transmitted to the oral cavity
* To prove the risk of malignancy we depend on two factors: 1-the type of HPV and 2-the amount of the DNA of that type of HPV in the infected tissue, if virus DNA amount increase, this increase the possibility of the risk.
* Generally genital HPVs infections may persist for few months to few years without developing any malignancy, but still in some persons may develop, therefore it’s not easy to know in clinical practice that the presence of these warts should be considered as dangerous or not, so we have to remove them by surgical means because according the statistics from different sources including WHO; there’s at least every year 1 million cases of infection with genital HPVs and 25% of these cases dies because of developing cervical carcinoma (high fatality).
* There’re certain factors that contribute for increasing risk for developing genital HPVs infections in women : **marriage at young age under 18 years old, using of contraceptive pills ,smoking, drinking of alcohol , continuous stress conditions , using of immunosuppressant drugs**.
* Precancerous HPV lesions in cervix usually takes 15–20 years to develop to cancerous lesions, so it’s very important to detect the presence of the infection then to cure the infection and not to wait later; and this is done easily using surgical means to remove the warts/infected areas, and this procedure can reduce the potential of developing malignancy from 100% to less than 10%.
* so there’s less than 10% possibility for recurrence ,which means it’s not easy to eradicate the genome of the virus (DNA) from the infected site , it will remain and therefore there’s a possibility of recurrence of the warts and developing of endocervical adenocarcinoma.
* Screening for these warts can be done easily by **Colposcopy,** also by taking biopsy and this biopsy should be later examined by **pap-smear** by a pathologist in order to see the differentiation of the cells, to determine whether that proliferation is benign or malignant.
* **Human respiratory papilloma** infections are related to genital HPVs infections; associated with the same genital HPV types (16 and18), as well as it might be associated with the same types of skin HPVs (6 and 11)
* In general the genital HPVs (types 16 and 18) are more associated with respiratory papilloma ( this is contrary to what written in the slides and wiki that types 6 and 11 are more associated with respiratory papilloma)
* Respiratory papilloma can be easily recognized during our future practice as a dentists because it firstly appear as warts at any part of the oral cavity , tongue or lips… and later the infection may spread to reach the larynx and rarely it may produce obstruction of the airways that may result in suffocation and death, therefore the infected mucosa should be removed quickly because within a short period it can increase in size and disseminate to produce damage to the respiratory system.
* **Squamous oral papillomas** are very common, it’s form of an oral hyperplasia , and often affect the surface of vermillion mucosa, it might be harmless at the beginning but if persist for a long period then some complications can be observed ,especially increasing the size of the warts to the limit that interfere with eating and speaking, so any wart of this type must be removed and not left for a long time, despite the fact that mild oral papilloma like a small infections may usually disappear without treatment.
* **Lab diagnosis;** the best way to diagnose genital HPV infections is to collect a biopsy from the mucosa of the cervix and to look for the presence of HPVs by the **pap-smear.**
* Pap-smear test is very simple, and should be done to every married woman at least every 2-3 years, in order to be sure that she is not infected by type 16 or 18 of HPVs.
* Recently they have introduce PCR, which is more important to detect asymptomatic infections without presence of warts as well as to know exactly the quantity/real amount of viral DNA within the biopsy and this help to know if there is a risk for a malignancy. (this is done by **NEAR-PCR**)
* **PCR technique** is more important than pap-smear in some countries, but in our country pap-smear still used as the best method.
* **Treatment** : there’s no available antiviral drug against HPVs, although some physicians claimed that there’re certain drugs can help, but according the scientific literature there’s no antiviral drug against HPVs.
* The only way for treatment is surgical removal; usually **by Cryotherapy/ Cryosurgery** (cold applications) , laser is not recommended and still not effective as Cryotherapy
* The eradication of the virus may require more than one treatment session ,recurrence is common so it’s recommended to repeat the surgery if necessary after 1-2 years
* Recently , a **new vaccine** has been developed ,available in Jordan ,save vaccine and reduce the incidence of infection by HPVs up to **90%**, it’s expensive but it’s recommended in certain cases especially for ladies with immunodeficiency.
* A **study** has been done In UJ hospital 3 years ago, to know the common HPVs skin types which infect our population, they have collected a samples from 200 patients who have warts, by simple methods ;rubbing the surface of the wart by a cotton swap then place it in a tube containing physiological saline, later in the laboratory the viral DNA is extracted ,and using especial kits they do isolation for the DNA groups and using a specific primer (complement nucleotide sequences) for the common types of the virus in order to detect which type is present.
* The study resulted that there’re 3 common types associated with skin warts in the general population in jordan.
* Those types are **(2 , 27 , 57) ..** known to be benign ,not associated with skin malignancies.

 , and they are also common in most of middle east countries, but they are different from the common types in western Europe and north America …Each region or country has certain specific common types.

* In Spain they have an Alpha HPV type which associated with skin malignancy especially in certain patients.
* But these types in our countries are rarely to be associated with malignancies.
* If somebody lives here and moved to other country for years, they may get an infection with new types other than common here, and the infection will be more severe.
* Keep in mind that children are more susceptible than adults , and the majority of young adults are immune- to some extent- against types other than that common in their community (that they may have infected by them in the past) .
* This is called **herd immunity** ; in Jordan for example , we are immune-to some extent-against that common 3 types , but if we move to other country we might be infected by more aggressive distributed types that causes skin malignancies.