HPV INFECTION IN RENAL TRANSPLANT RECIPIENTS

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OUTLINES

- Introduction
- Epidemiology
- Pathogenesis
- Vaccination
- Screening
- Case report

frontiers | Frontiers in Immunology

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SPECIALTY SECTION

Human papillomavirus in the setting of immunodeficiency: Pathogenesis and the emergence of next-generation therapies to reduce the high associated cancer risk

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INTRODUCTION

- ~ 15-20% of global cancers are associated with oncogenic viral infections.
- Only a small proportion of chronically-infected cells develop cancer.
- Viruses such as HPV, EBV, HBV, & HCV…
- The virus 'reprograms' host cellular signaling

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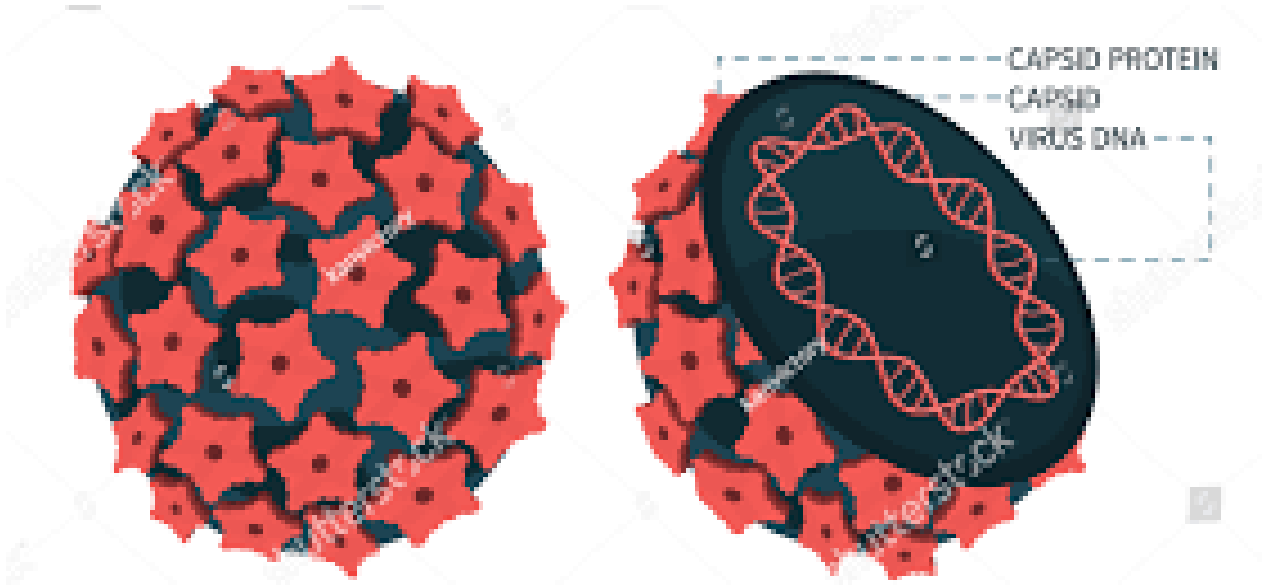
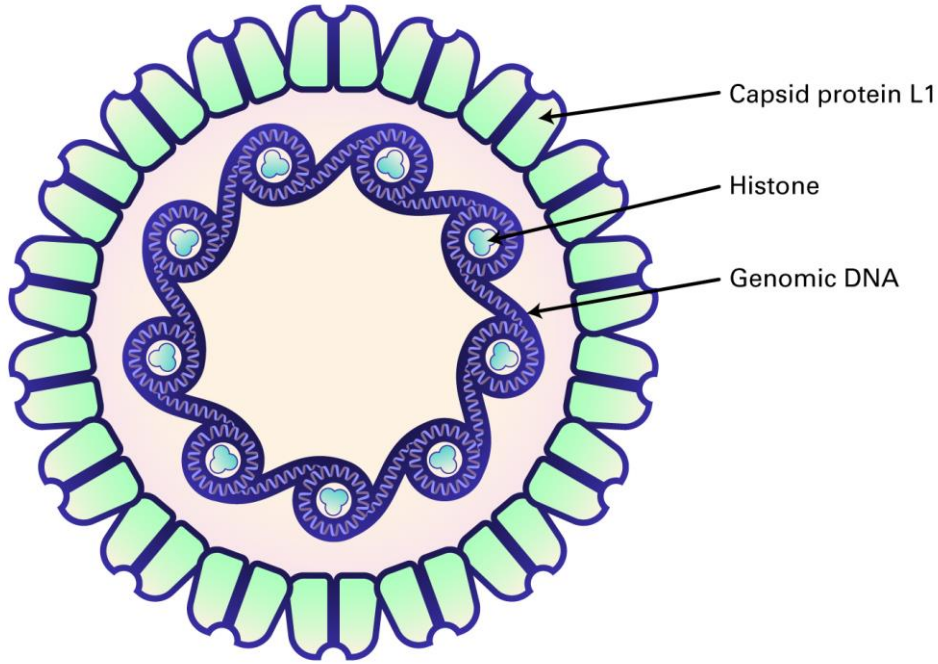
INTRODUCTION

- **HPV is a double-stranded DNA virus associated with cancers of the squamous epithelia of the cervix, oropharynx, & anogenital regions.**





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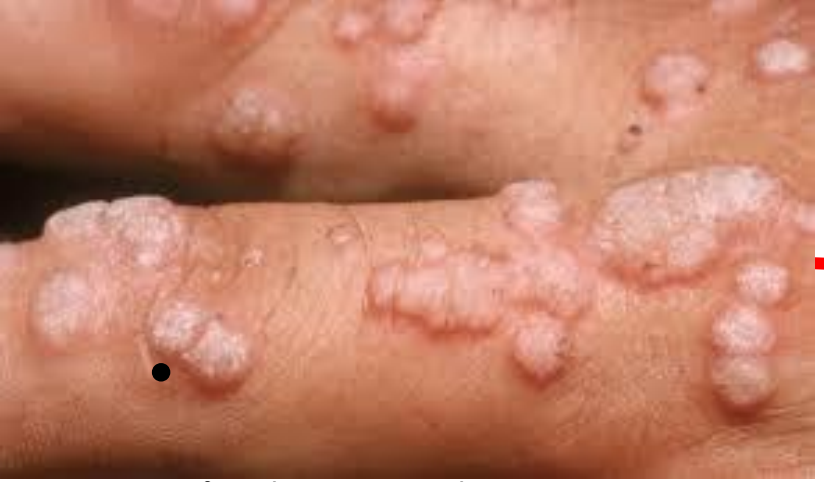
HPV



- It is an important cause of cervical, vaginal, vulvar, penile, anal & head & neck cancers in RTRs.
- There are ~ 200 distinct HPV subtypes:
  - High-risk Types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, & 82
  - Low-risk types, such as 6 & 11
- Types 16 & 18 are the most common HPV types found in cervical cancer, accounting for 70% of these malignancies.

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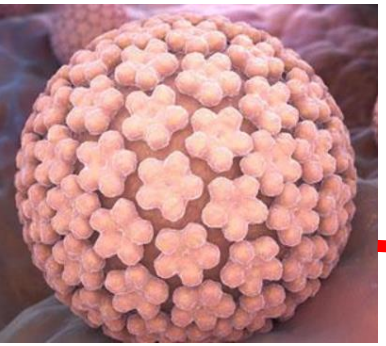

HPV

- HPV-associated cancer affects many mucosal sites:
  - 99% of cervical cancer
  - 64–91% of vaginal
  - 40–50% of vulvar
  - 88–94% of anal
  - 40–50% of penile

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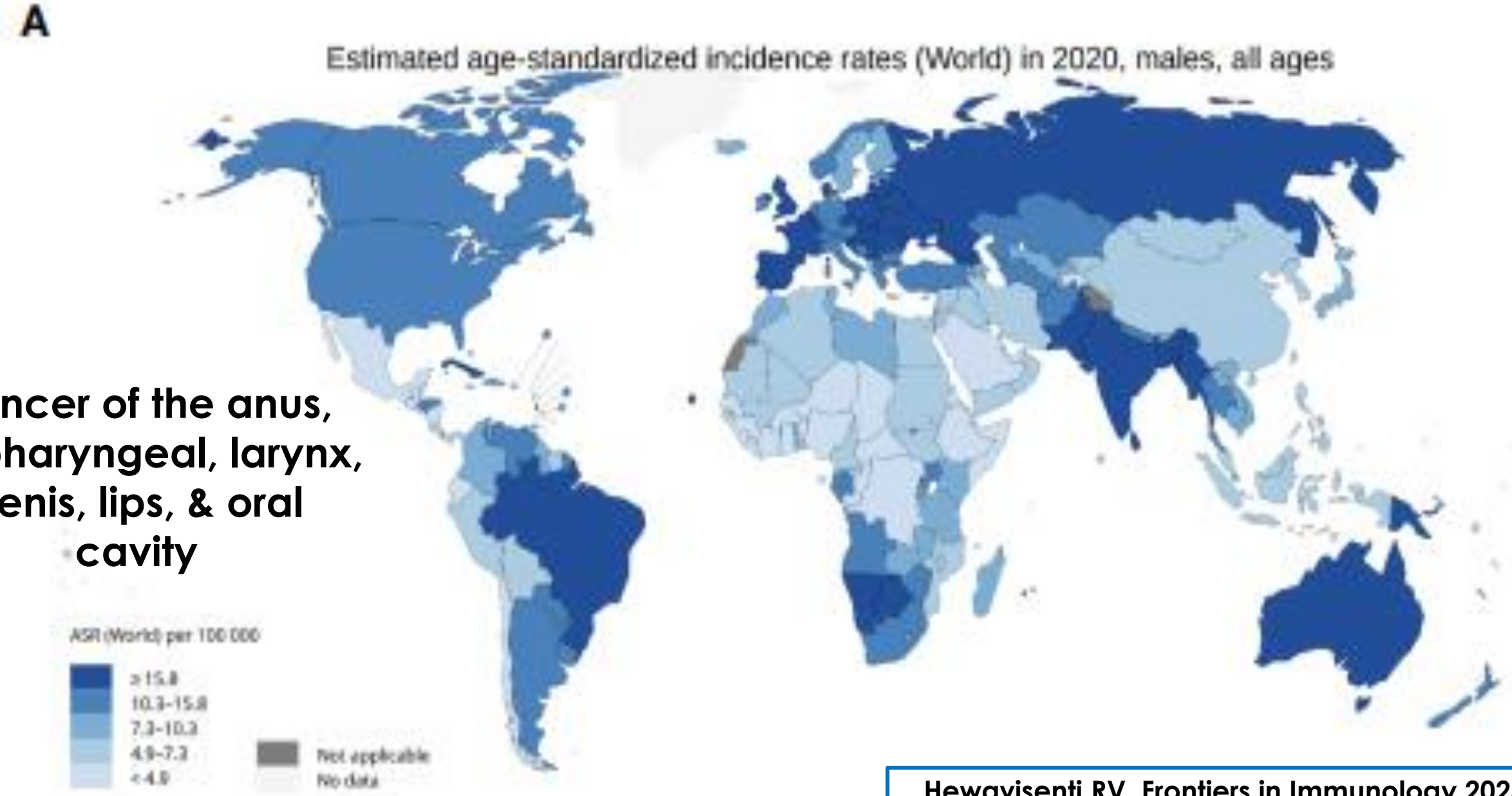
Incidence of HPV associated malignancies in 2020



Cancer of the anus, oropharyngeal, larynx, penis, lips, & oral cavity

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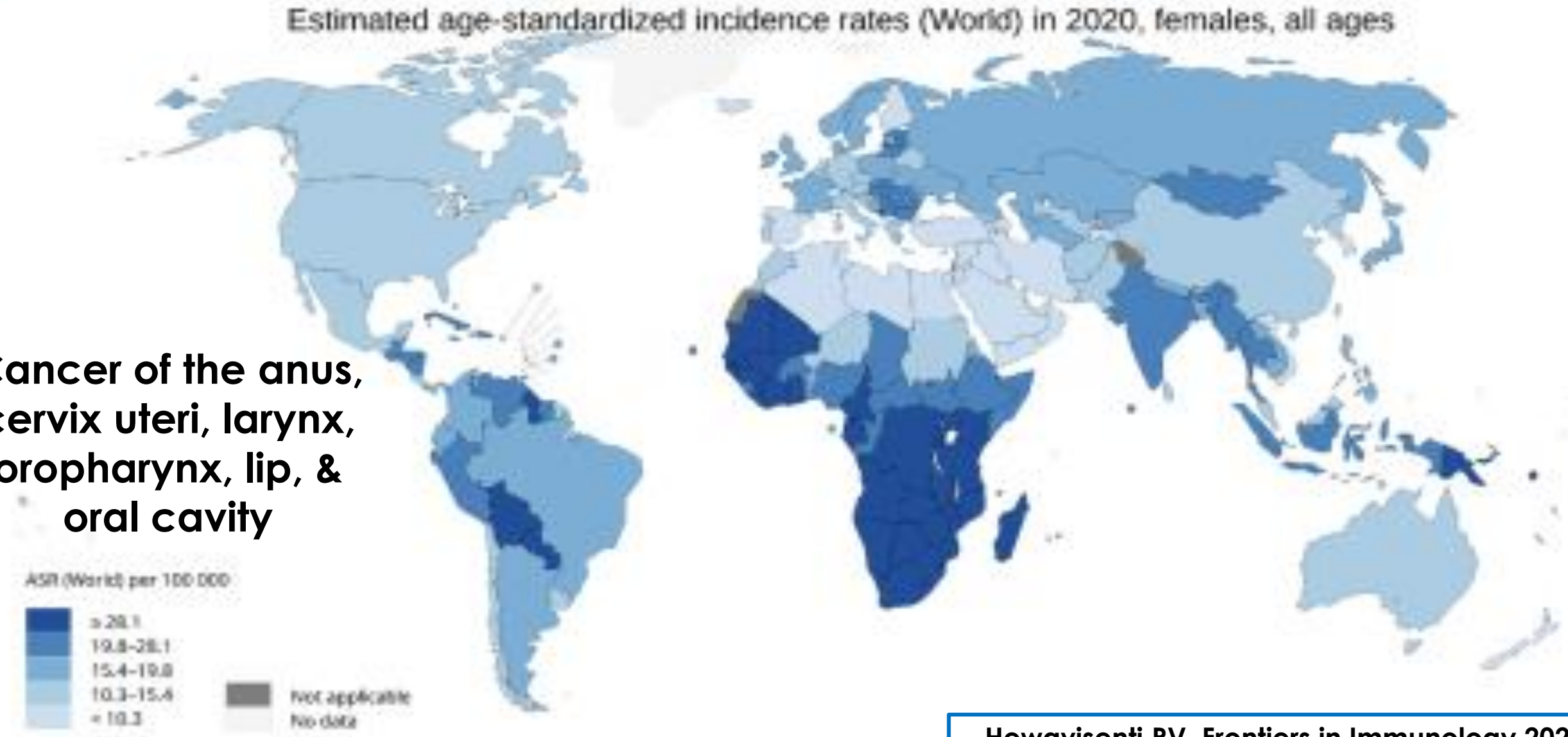
Incidence of HPV associated malignancies in 2020

B



Cancer of the anus, cervix uteri, larynx, oropharynx, lip, & oral cavity

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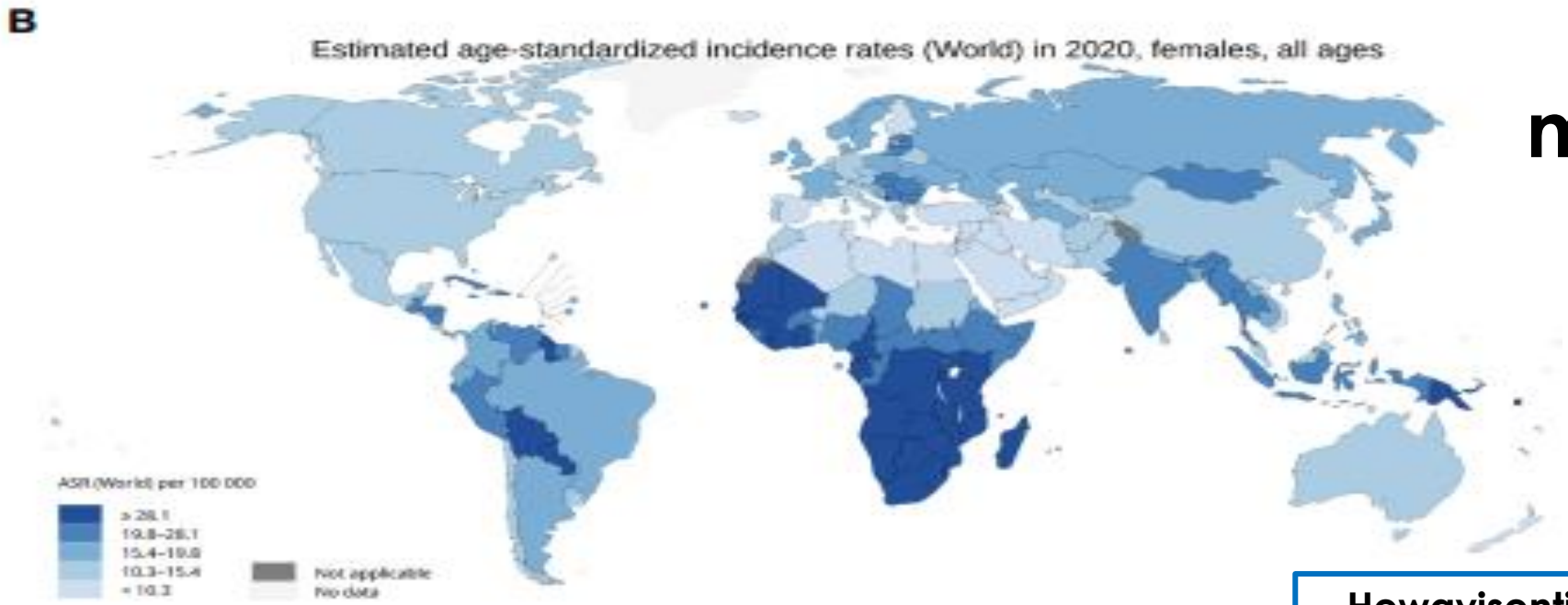
Incidence of HPV associated malignancies in 2020



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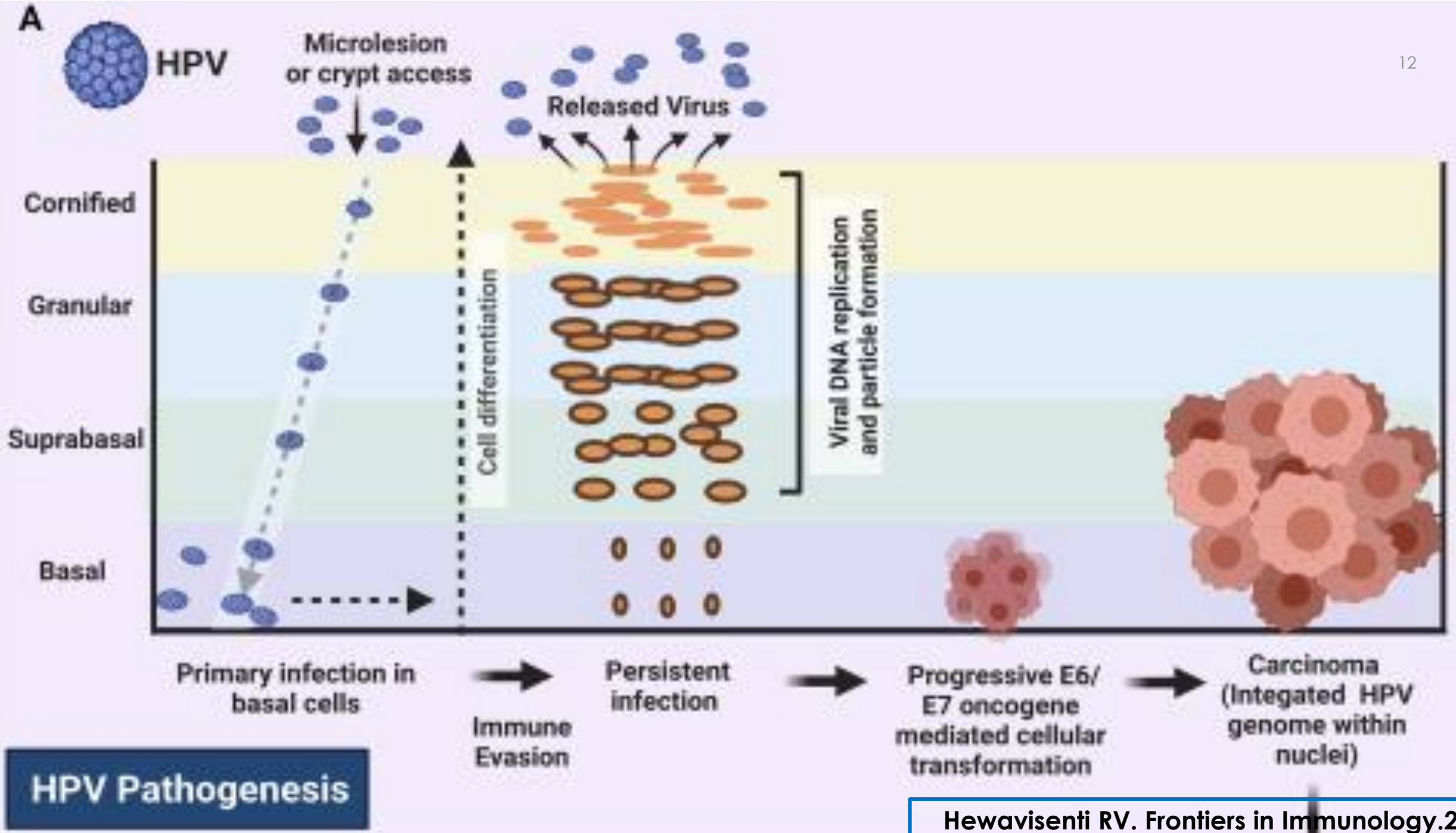
TRANSMISSION

- All you need to do is intimate skin-to-skin contact with the infected body part of a person.
- The typical body parts & areas where an HPV infection can be transmitted include the genitals, throat, & mouth.
- The risk of HPV via kissing exists but falls on the low end when compared to other forms of intimate contact.



HPV Pathogenesis

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RISK FACTORS ASSOCIATED WITH HPV PROGRESSION TO CANCEROUS LESIONS

1. HPV type
2. Tobacco smoking
3. High parity
4. Oral hormonal contraception ??
5. Diet ??
6. Immunodeficiency

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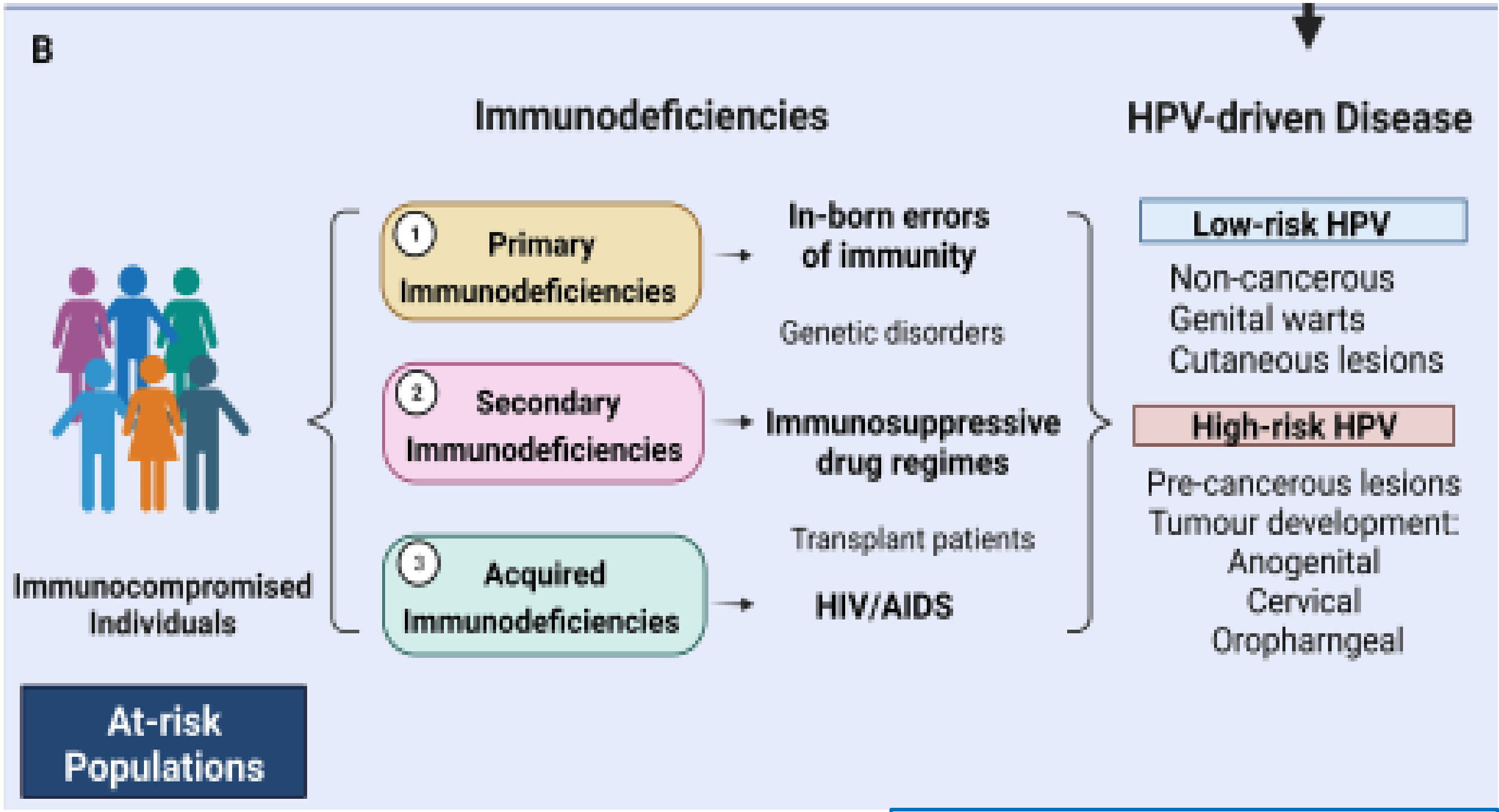

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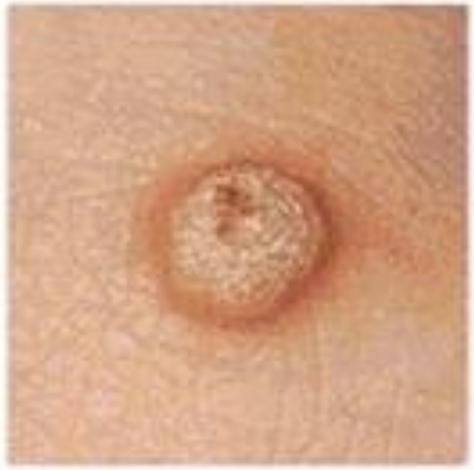
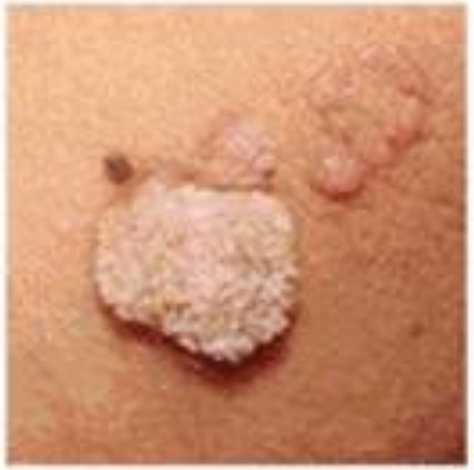
THE DIFFERENT KINDS OF WARTS

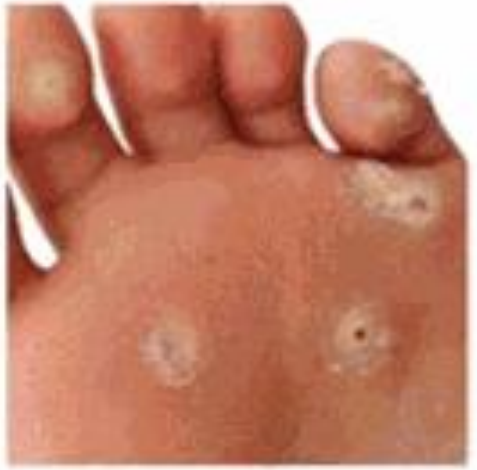


common wart



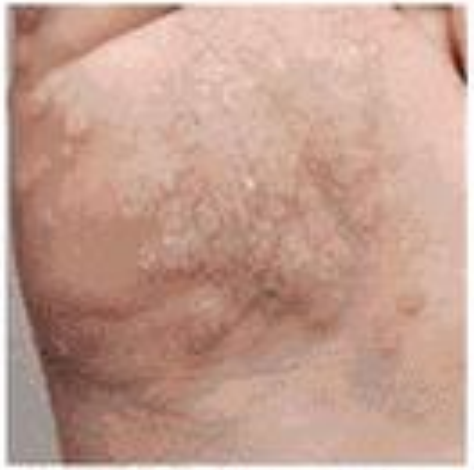
filiform wart

flat wart

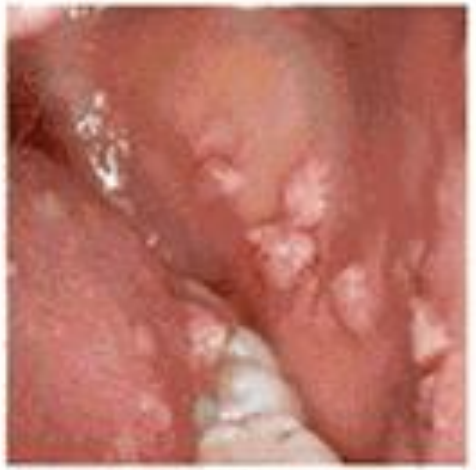


plantar wart

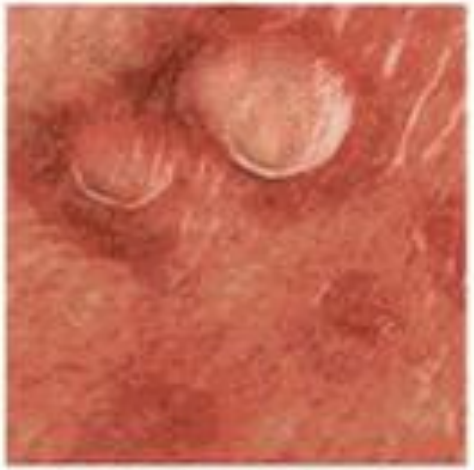
periungual wart



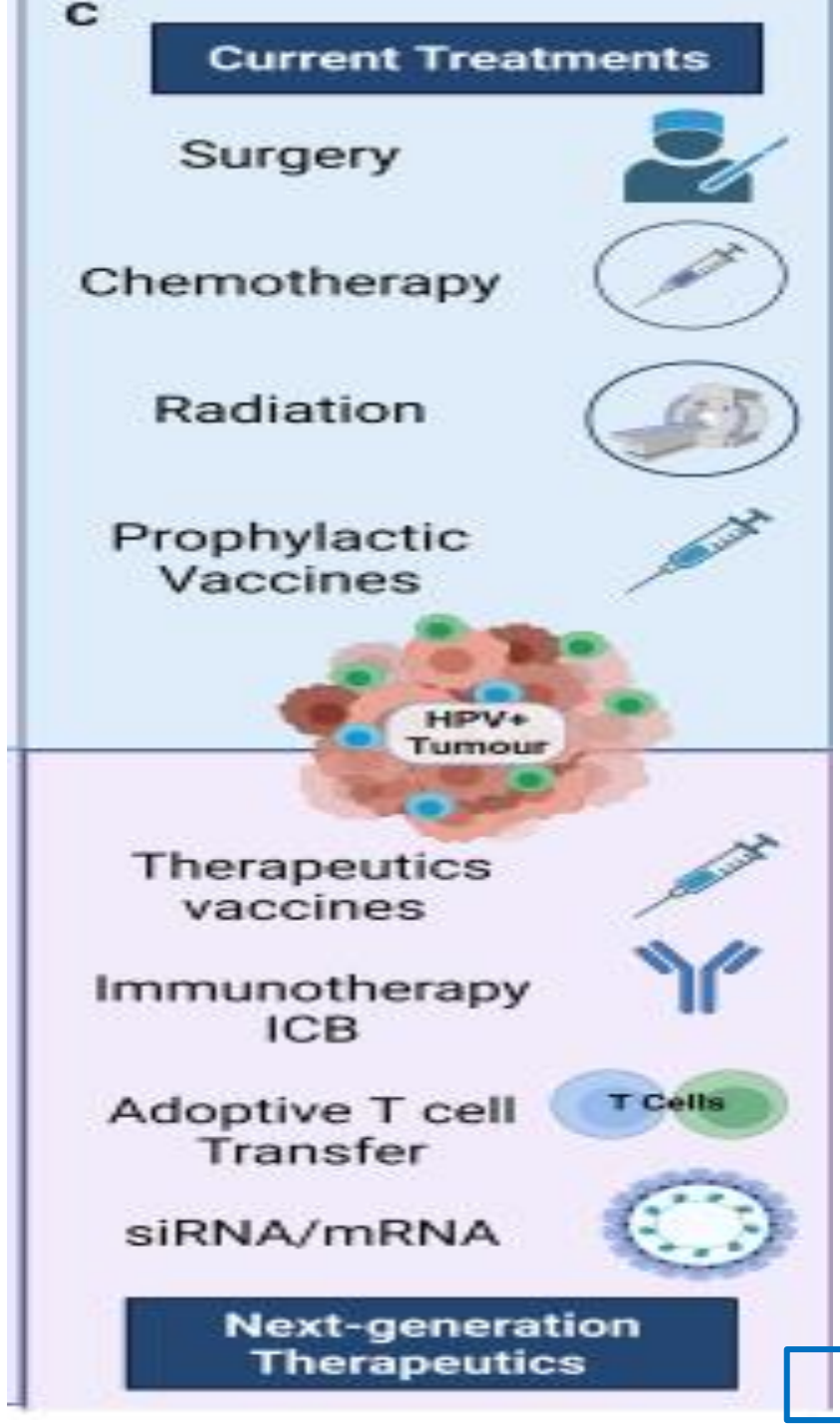
mosaic wart



oral wart



genital wart



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Human Papillomavirus in Kidney Transplant Recipients

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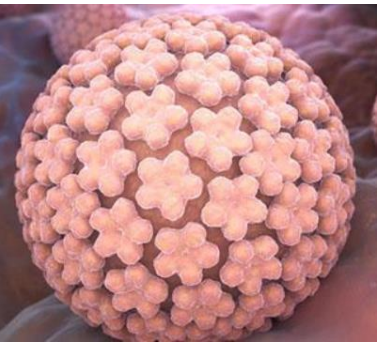
I. Virology

Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide. It is an important cause of cervical, vaginal, vulvar, penile, anal and head and neck cancers in kidney transplant recipients (1). These are small DNA viruses, each comprising 7900 base pairs. There are over 100 distinct HPV subtypes. Of these, there are high-risk and low-risk types, distinguished by their association with invasive cancer – high in "high-risk" and low in "low-risk". Types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 are designated as high-risk types. Although low-risk types such as 6 and 11 do not cause invasive cancer, they are associated with anogenital warts. Types 16 and 18 (included in all three commercially available HPV prophylactic vaccines) are the most common HPV types found in cervical cancer, accounting for 70% of these malignancies (2,



HPV IN KTRS

- The prevalence of warts is linked directly to the duration of immunosuppression.
- In patients who have been transplanted 4-5 years ago, the proportion of patients with warts reaches as high as 50-92%.
- Ultraviolet light is thought to be a risk factor in KTRs.

Chin-Hong P. Semin Neph. sep 2016

HPV VACCINATION

- The CDC: HPV vaccinations for all people through age 26
- The U.S. FDA approved the use of Gardasil 9 for males & females ages 9 to 45.
- If you're ages 27 to 45, discuss your risks with your health care team to decide if you should get the HPV vaccine.

HPV VACCINES FOR KTR

Vaccine	Who to give	When to give	How to give	Adverse effects
Nonavalent (HPV types 6, 11, 16, 18, 31, 33, 45, 52, 58; Gardasil 9, Merck, Whitehouse Station, New Jersey)	Routinely offer to boys and girls 11-12 years old Can vaccinate ages 9-26	Pre-transplant preferred. Also safe post transplant (non-infectious)	Three doses at months 0, 2 and 6	Minimal Mild to moderate localized pain, erythema, swelling

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Quadrivalent (HPV types 6, 11, 16, 18; Gardasil, Merck, Whitehouse Station, New Jersey)	Routinely offer to boys and girls 11-12 years old Can vaccinate ages 9-26	Pre-transplant preferred. Also safe post transplant (non-infectious)	Three doses at months 0, 2 and 6	Minimal Mild to moderate localized pain, erythema, swelling

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Quadrivalent (HPV types 6, 11, 16, 18; Gardasil, Merck, Whitehouse Station, New Jersey)	Routinely offer to boys and girls 11-12 years old Can vaccinate ages 9-26	Pre-transplant preferred. Also safe post transplant (non-infectious)	Three doses at months 0, 2 and 6	Minimal Mild to moderate localized pain, erythema, swelling
Bivalent (HPV types 16, 18; Cervarix, GlaxoSmithKline, Rixensart, Belgium)	Routinely offer girls 11-12 years old Can vaccinate ages 9-26	Pre-transplant preferred. Also safe post transplant (non-infectious)	Three doses at months 0, 1 and 6	Minimal Mild to moderate localized pain, erythema, swelling

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Papilloguard (Type 16 , 18)

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NIHMSID: NIHMS724124
PMID: 23837399

Immunogenicity of Quadrivalent Human Papillomavirus Vaccine in Organ Transplant Recipients

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Abstract

Go to:

Solid organ transplant recipients are at risk of morbidity from human papillomavirus (HPV)-related

DEMOGRAPHIC CHARACTERISTICS OF THE PATIENTS

Characteristic	N = 47
Age, median (range), years	25.9 (18–35)
IQR (years)	22–30
Gender (men/women)	16/31 (34%/66%)
Time from transplant, years (median; range)	2.7 (0.28–13.6)
Type of transplant	
Kidney	30 (63.8%)
Lung	11 (23.4%)
Heart	3 (6.4%)
Liver	1 (2.1%)
Other (heart/lung; multivisceral)	2 (4.3%)
Number of vaccine doses	
1	47 (100%)
2	45 (95.7%)
3	43 (91.5%)
Immunosuppression	
Prednisone	36 (76.6%)
Dose (mg, median, IQR)	5.0 (2.5–8.75)
Calcineurin-inhibitor	43 (91.5%)
Cyclosporin trough level (µg/L; median)	179
Tacrolimus trough level (µg/L; median)	6.7
Mycophenolate mofetil	42 (87.5%)
Dose (mg, median, IQR)	2000 (1470–2000)
Sirolimus	3 (6.4%)

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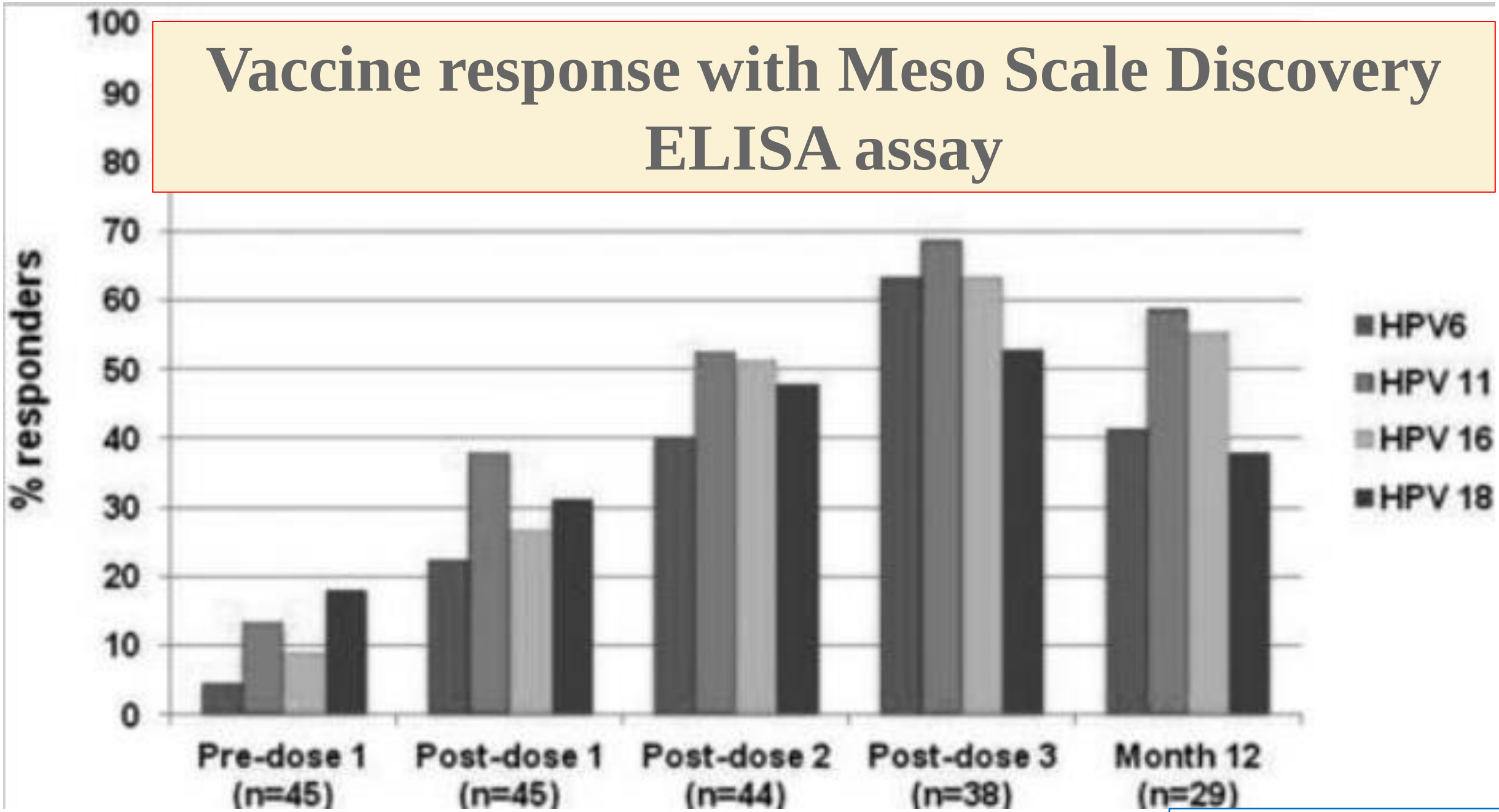
Vaccine response with Meso Scale Discovery ELISA assay



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Univariate analysis of factors affecting response to at least one HPV vaccine type

Variable	Odds ratio (95% CI)	p value
Age (18–26 vs. ≥27 years)	0.71 (0.15–3.41)	0.67
Male gender	0.76 (0.17–3.47)	0.73
Time from transplant (≤1 year vs. >1 year)	0.21 (0.04–1.03)	0.05
Type of transplant (lung vs. other)	0.21 (0.04–1.02)	0.05
Immunosuppression		
Prednisone use	0.60 (0.06–5.9)	0.66
MMF use	0.92 (0.08–10.2)	0.95
Tacrolimus level	0.64 (0.43–0.95)	0.03

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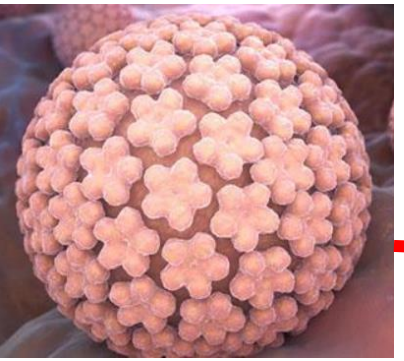

CONCLUSION

- We found suboptimal responses in posttransplant recipients.
- As with other vaccines, pretransplant vaccination may be more beneficial.
- Vaccination at a younger age may provide greater titers.
- Further studies are needed to determine ways to enhance immunogenicity.

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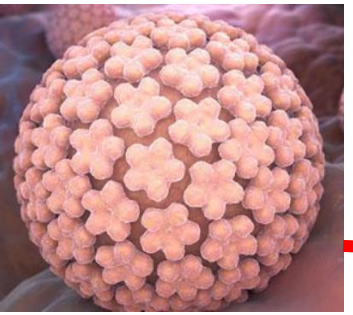

HPV SCREENING

- Guidelines recommend screening in women from ages 21 until 65.
- For the first year following transplantation, a cervical Pap test should be performed every 6 months.
- If these are both normal, the screening interval can be increased to once yearly.

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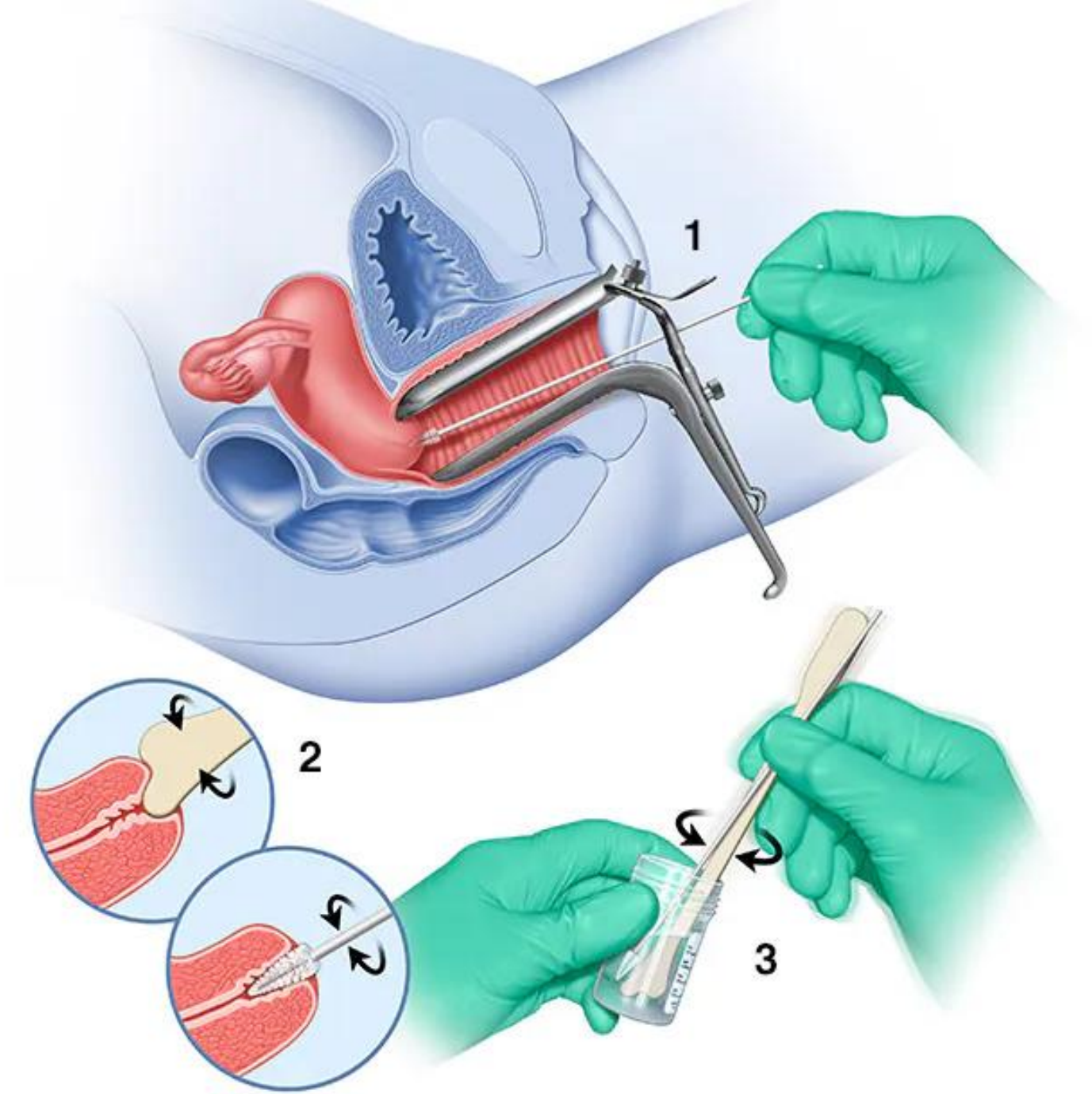
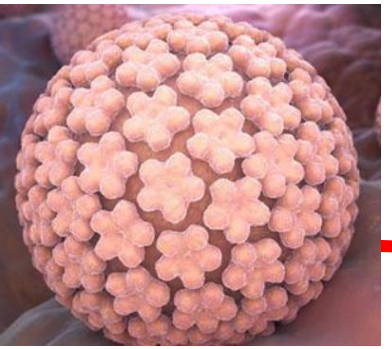


Pap test



HPV SCREENING

- It may be reasonable to reset the screening intervals back to twice yearly for one year if the patient has been treated for rejection, particularly if AT agents are used.
- Use of high-risk HPV testing is recommended for women aged ≥ 30 ys in conjunction with a Pap test in the general population.
- If both tests are negative, then every 3 - 5 ys.
- Among immunocompromised women such as KTRs, most are screened every 6-12 ms.

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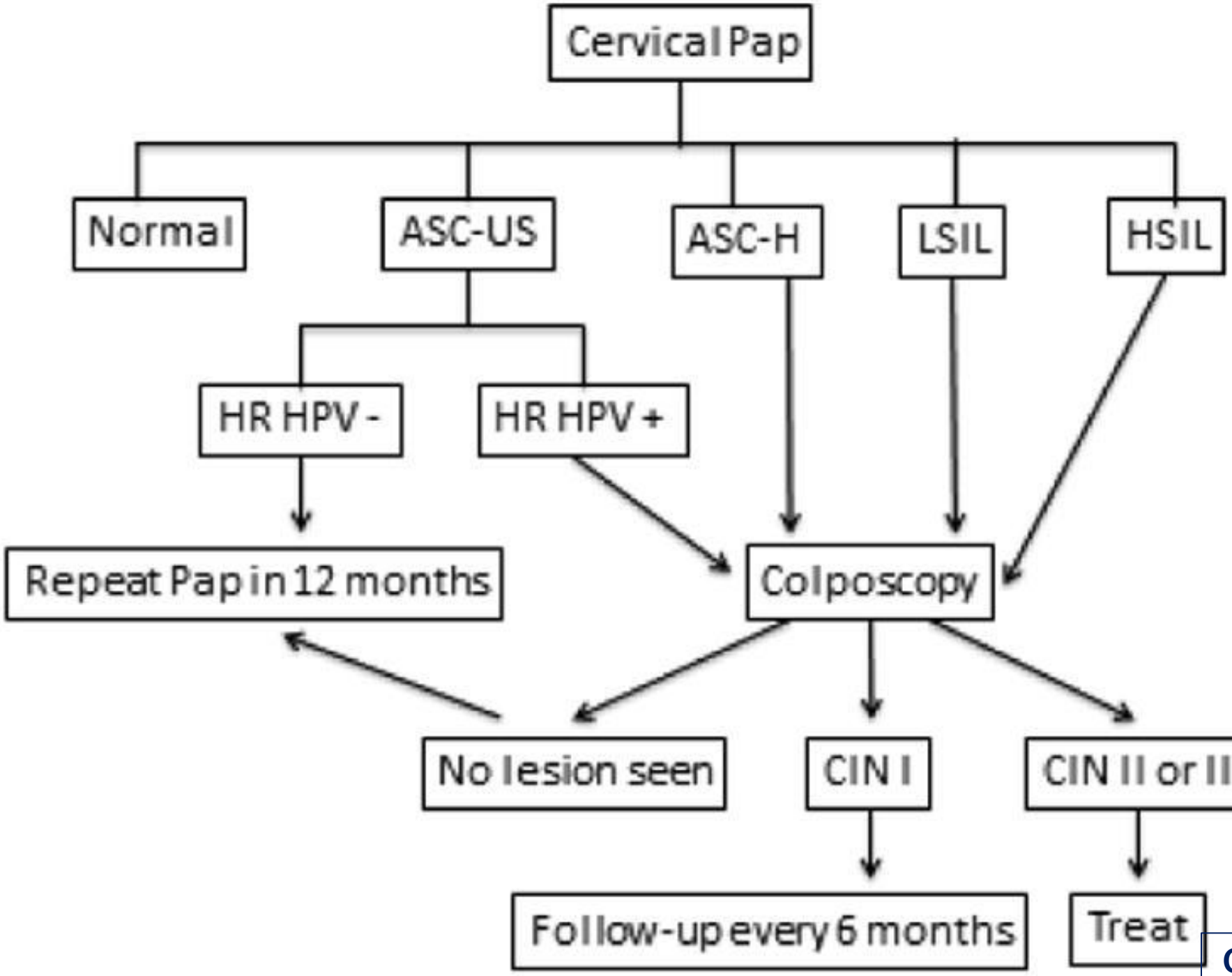

Screening for CIN & cervical cancer in the KTRs

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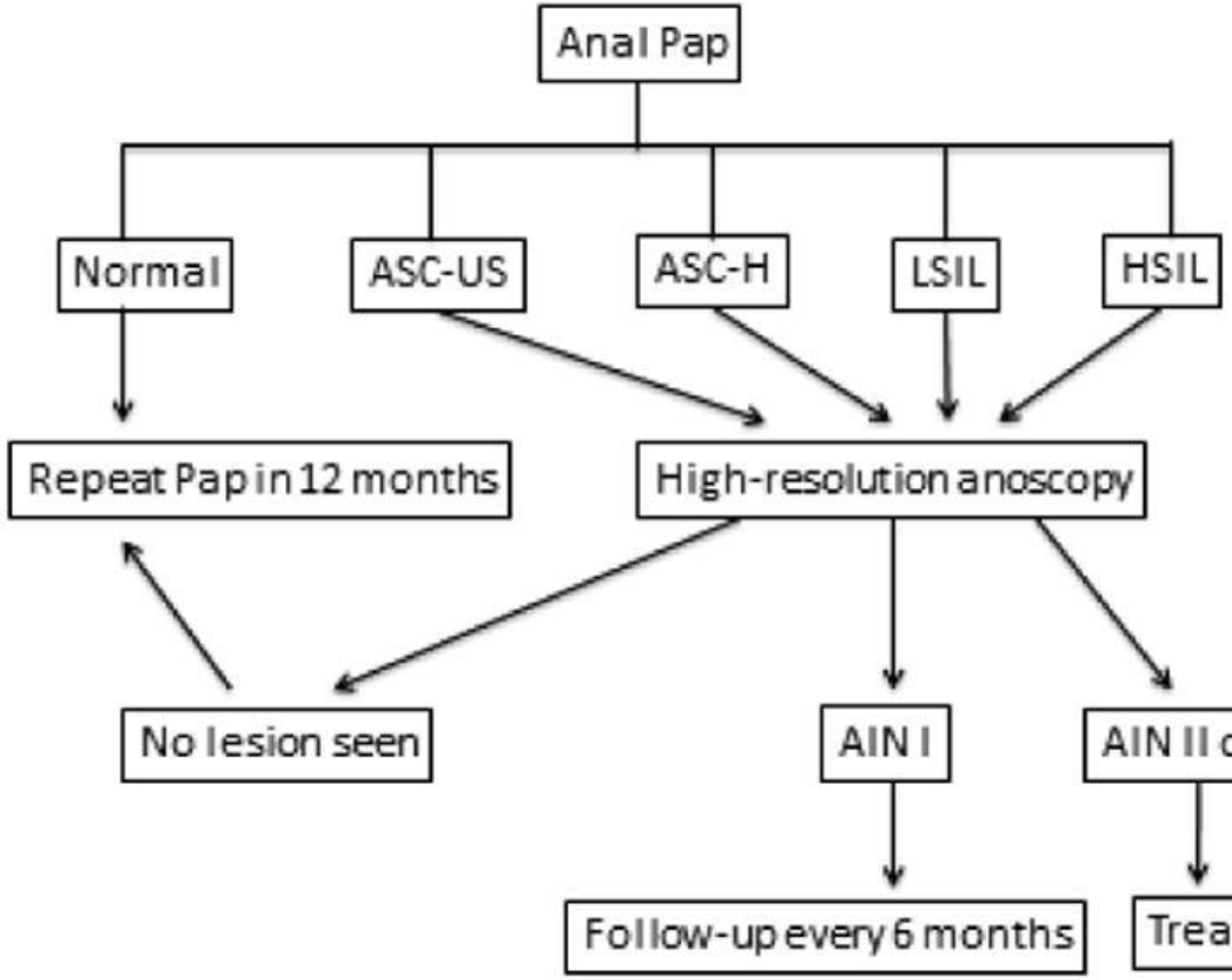

Screening for AIN & anal cancer in the KTRs

Chin-Hong P. Semin Neph. 2016

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Original Article | Free Access

Reactivation of Latent HPV Infections After Renal Transplantation

F. Hinten, L. B. Hilbrands, K. A. P. Meeuwis, J. IntHout, W. G. V. Quint, A. J. Hoitsma, L. F. A. G. Massuger, W. J. G. Melchers, J. A. de Hullu

First published: 23 December 2016 | https://doi.org/10.1111/ajt.14181 | Cited by: 6

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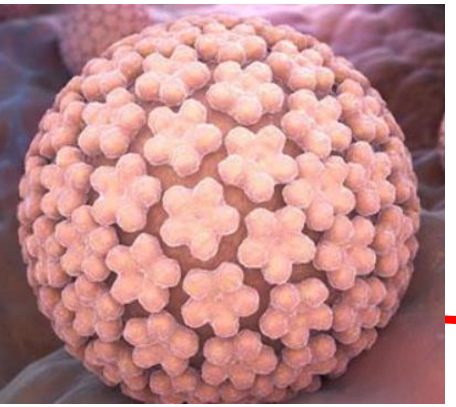
Abstract

Female renal transplant recipients (RTRs) have an increased risk for developing human papillomavirus (HPV)–related (pre)malignant lesions of the genital tract. This study aims



Reactivation of Latent HPV Infections After Renal Tx

- In 65 patients who underwent KT, the hrHPV prevalence as assessed with the highly sensitive SPF_{10} -$LiPA_{25}$ test increased significantly from 19% before to 31% after KT (p = 0.045).
- Conclusion:
  - Activation of latent HPV infections may contribute to the increased risk of HPV-related (pre)malignant lesions in female KTRs.

Hinten F. AJT. 2017

Sirolimus-Based Immunosuppression for Treatment of Cutaneous Warts in Kidney Transplant Recipients

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[1]Isfahan Kidney Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Poursina Hakim Research Institute, Isfahan, Iran

Keywords. human papillomavirus, kidney transplantation, sirolimus, viral infections, warts

Dermatological complications, especially skin infections, are very common following organ transplantation, and result in a lot of distress in the recipient. Herpes zoster, herpes simplex, and human papillomavirus infections are common infections in kidney transplant recipients, and therapeutic management is usually disappointing in immunosuppression state. We report here 2 cases of kidney transplant recipients who developed diffuse human papillomavirus-induced cutaneous warts with no response to conventional treatments. According to similar reports in organ transplant recipients, we modified the immunosuppressive regimen by converting to sirolimus, which led to a rapid relief from cutaneous warts in both patients. This evidence along with other case reports suggest that conversion to sirolimus may be considered as an effective strategy in cases of giant or multiple viral warts in kidney and perhaps other transplant recipients.

IJKD 2011;5:351-3
www.ijkd.org

Shahidi Sh. IJKD, 2011

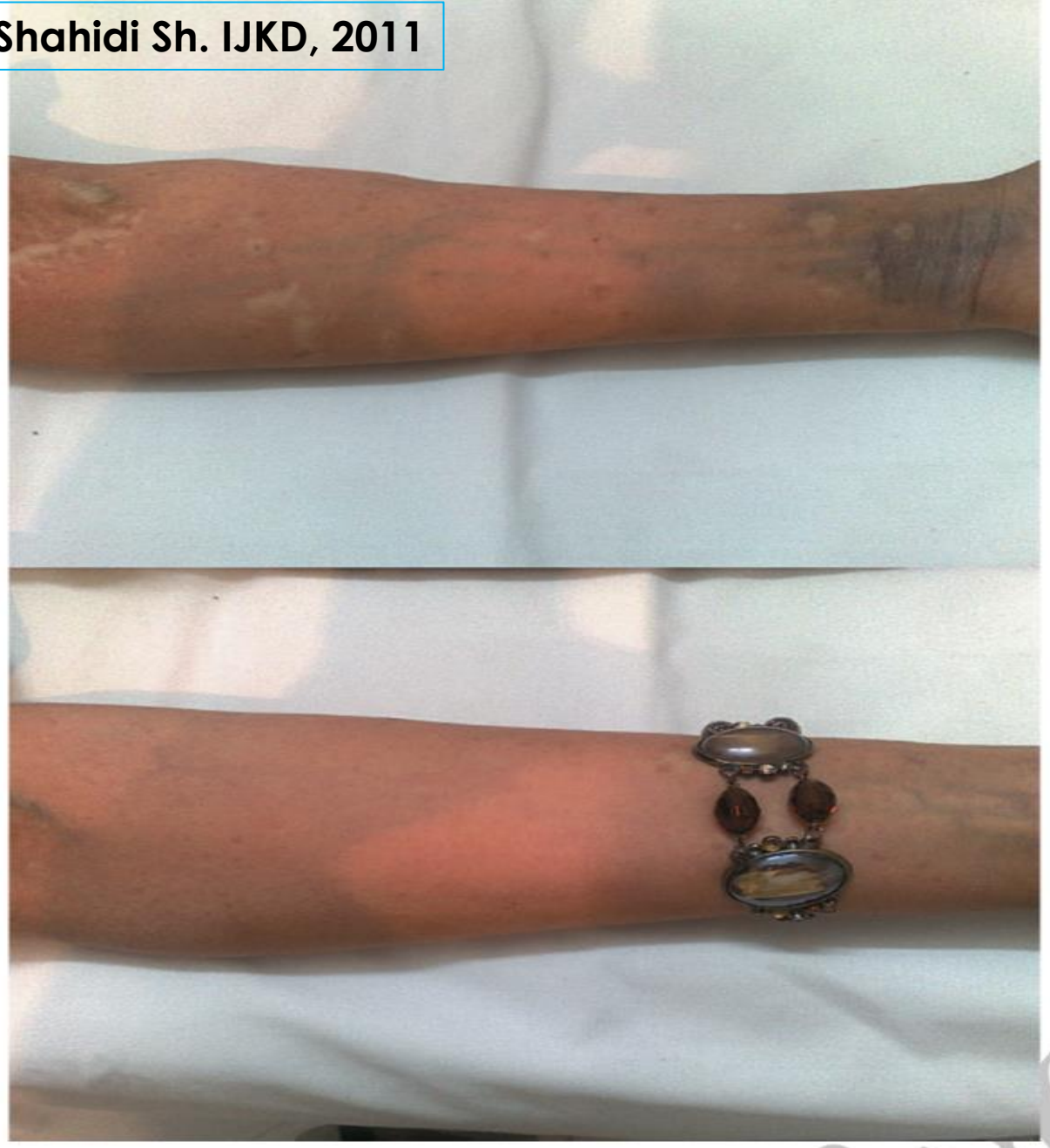


Figure 1. Top, Warts in a kidney transplant recipients. **Bottom**, improvement of the warts after conversion of cyclosporine to sirolimus.

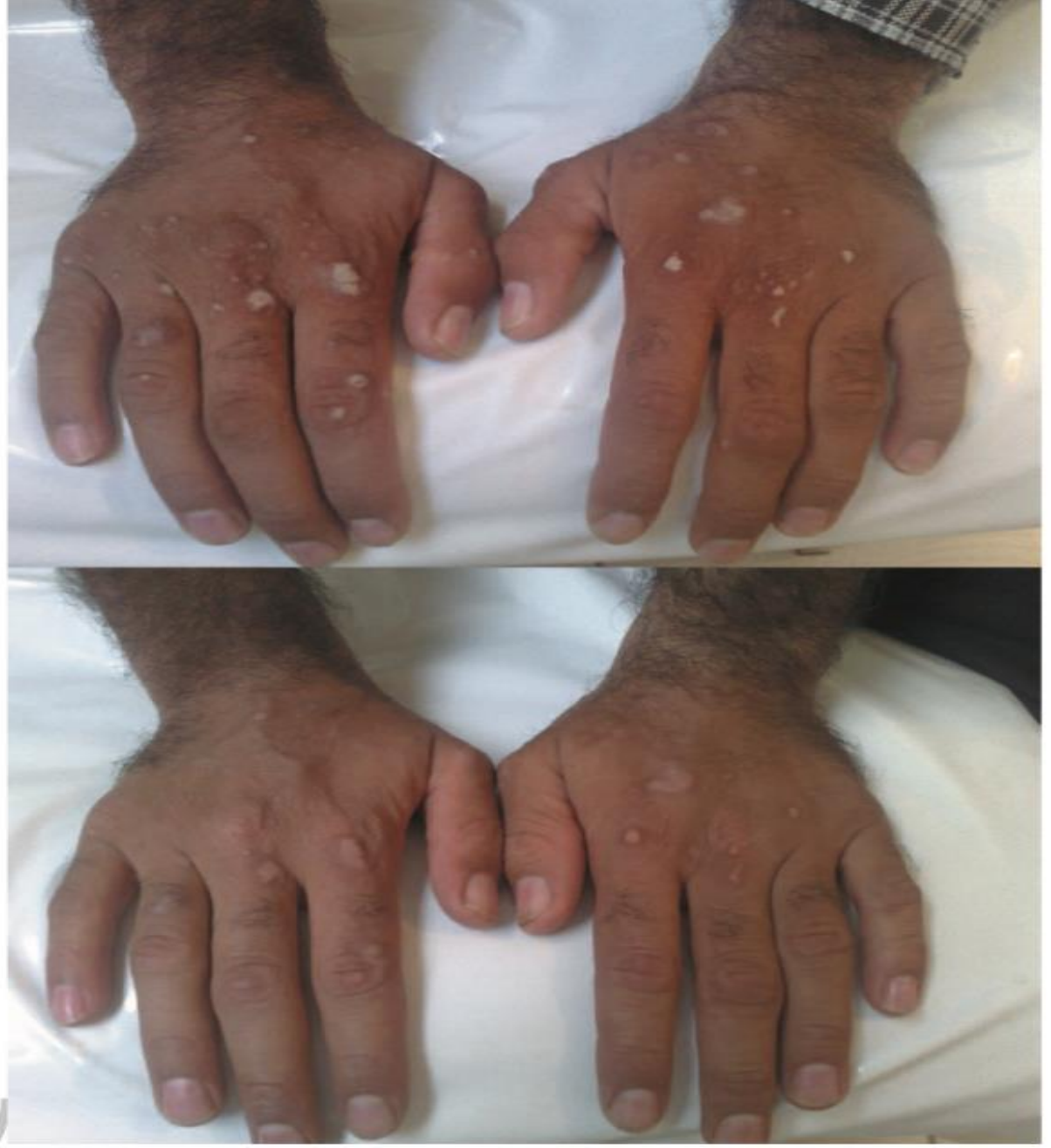
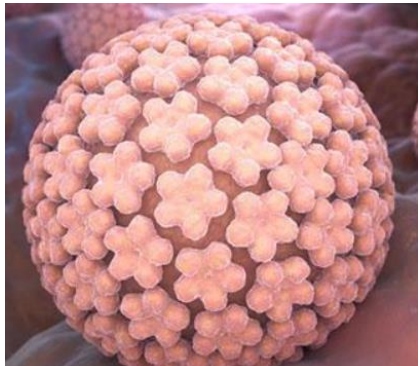


Figure 2. Top, Warts in a kidney transplant recipients. **Bottom**, improvement of the warts after conversion of cyclosporine to sirolimus.

HPV SUMMARY

- Using a foundation of Pap testing & careful & methodical routine PE, many precancer lesions can be identified & treated before progression to cancer.
- It is unfortunate that screening guideline uptake for HPV cancers in the KTRs is low.
- This is a silent epidemic that deserves our close attention & advocacy.



THANKS FOR YOUR ATTENTION