CASE 5

Short case number: 3_18_5
Category: Endocrine & Reproductive Symptoms
Discipline: Obstetrics & Gynaecology
Setting: General Practice
Topic: Premalignant disease of the cervix.

Case

Natalie Casarotto is 30years old, she presents at your request for follow-up of her cervical screening test result.
Natalie's cervical screening test taken 2 weeks ago has been reported: HPV 16 positive, cytology shows a possible high grade squamous intraepithelial lesion. Colposcopic examination and biopsy are recommended.
Natalie has been asymptomatic and this is her first abnormal cervical screening test. She has not been vaccinated for HPV.

Questions

1. What will you explain to Natalie about her result?
2. Outline the current recommendations for cervical screening in Australia.
3. Outline the current classification system used in Australia for reporting cervical cytology
4. What would be the next step in Natalie's management?
5. Outline in a flow chart the process of investigation and management of an abnormal cervical screening test. What are the current recommendations for follow-up after treatment?
6. Describe the human papilloma virus and outline its pathogenesis.
7. What are the current recommendations for HPV vaccination in Australia? Describe the two vaccines currently available in Australia.

Suggested reading:

1. Abbott, J., Bowyer, L., & Finn, M. (2014). *Obstetrics and Gynaecology: an evidence-based guide (2nd ed).* Australia, Elsevier.
2. Australian Institute of Health and Welfare 2018: Cervical Screening in Australia 2018. Cat no CAN111. Canberra AIHW ISBN 978-1-76054-325-9 (PDF) https://www.aihw.gov.au/getmedia/8a26b34d-a912-4f01-b646-dc5d0ca54f03/aihw-can-111.pdf.aspx?inline=true
3. May, J. HPV vaccination A paradigm shift in public health. Australian Family Physician Vol. 36, No. 3, March 2007 http://search.informit.com.au.ipacez.nd.edu.au/fullText;dn=359790709828739;res=IELHEA

[Accessed November 2018]

4. Australian Medicines Handbook 2018

ANSWERS

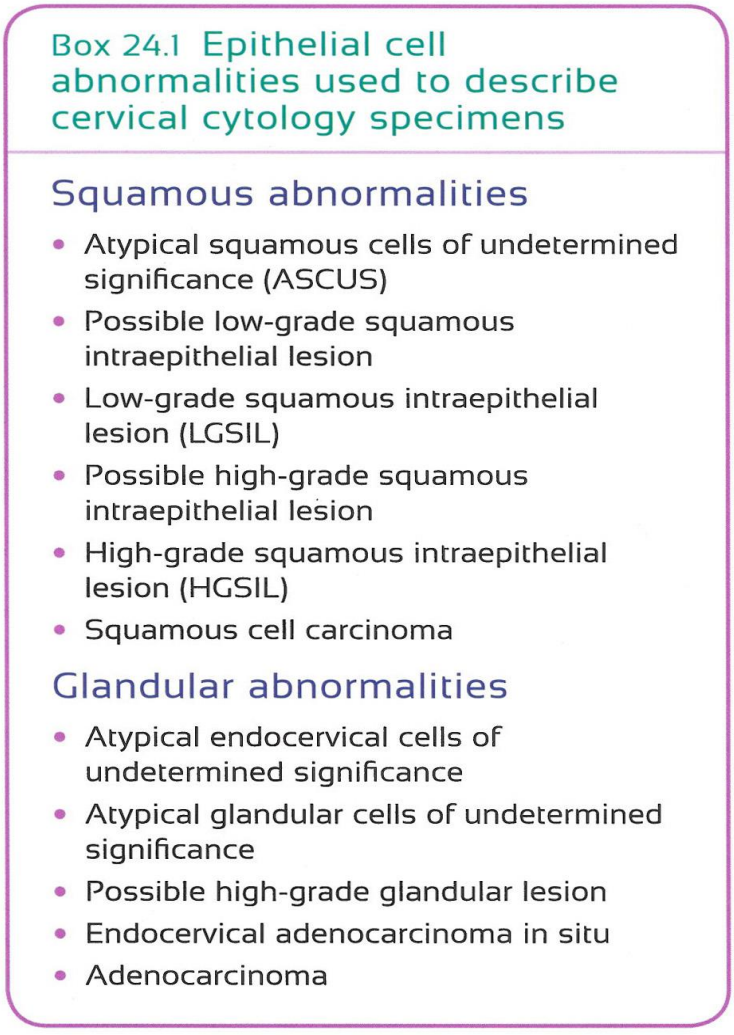
What will you explain to Natalie about her result?

HPV16 positive, cytology – possible high grade squamous intraepithelial lesion.

The cervical screening test is a screening test, not a diagnostic test. Natalie has screened positive for HPV 16. This virus may clear over the next 2 years. Cervical cancer is a rare outcome of HPV infection. HPV is a common and mainly sexually transmitted infection. It can be found in almost all cases of cervical cancer. However, most HPV infections will not progress to cancer. The invasive disease usually does not develop unless there is persistence of HPV DNA.
As HPV 16 positive (and high grade squamous intraepithelial cells noted) Natalie needs further investigation with colposcopy and possible biopsy of the cervix to confirm the presence of abnormal changes.

2. **Outline the current recommendations for cervical screening in Australia and the current classification system used in Australia for reporting cervical cytology**.

   Five yearly cervical screening using a primary HPV test with partial HPV genotyping and reflex liquid based cytology (LBC) triage, for HPV vaccinated and unvaccinated women 25-69 years of age, with exit testing of women up to 74 years of age.



Box 24.1 Epithelial cell abnormalities used to describe cervical cytology specimens

Squamous abnormalities

- Atypical squamous cells of undetermined significance (ASCUS)
- Possible low-grade squamous intraepithelial lesion
- Low-grade squamous intraepithelial lesion (LGSIL)
- Possible high-grade squamous intraepithelial lesion
- High-grade squamous intraepithelial lesion (HGSIL)
- Squamous cell carcinoma

Glandular abnormalities

- Atypical endocervical cells of undetermined significance
- Atypical glandular cells of undetermined significance
- Possible high-grade glandular lesion
- Endocervical adenocarcinoma in situ
- Adenocarcinoma

Figure 24.1 from *Obstetrics and Gynaecology: an evidence-based guide (2nd ed).* p. 312, 2014 Australia, Elsevier

3. What would be the next step in Natalie's management? Outline in a flow chart the process of investigation and management of an abnormal cervical screening test.

Colposcopy is recommended if HPV16, 18 positive irrespective of cytology result.

Colposcopy = Using magnifier/microscope to visualise cervix in closer detail - can take biopsy if any malignancy is seen.

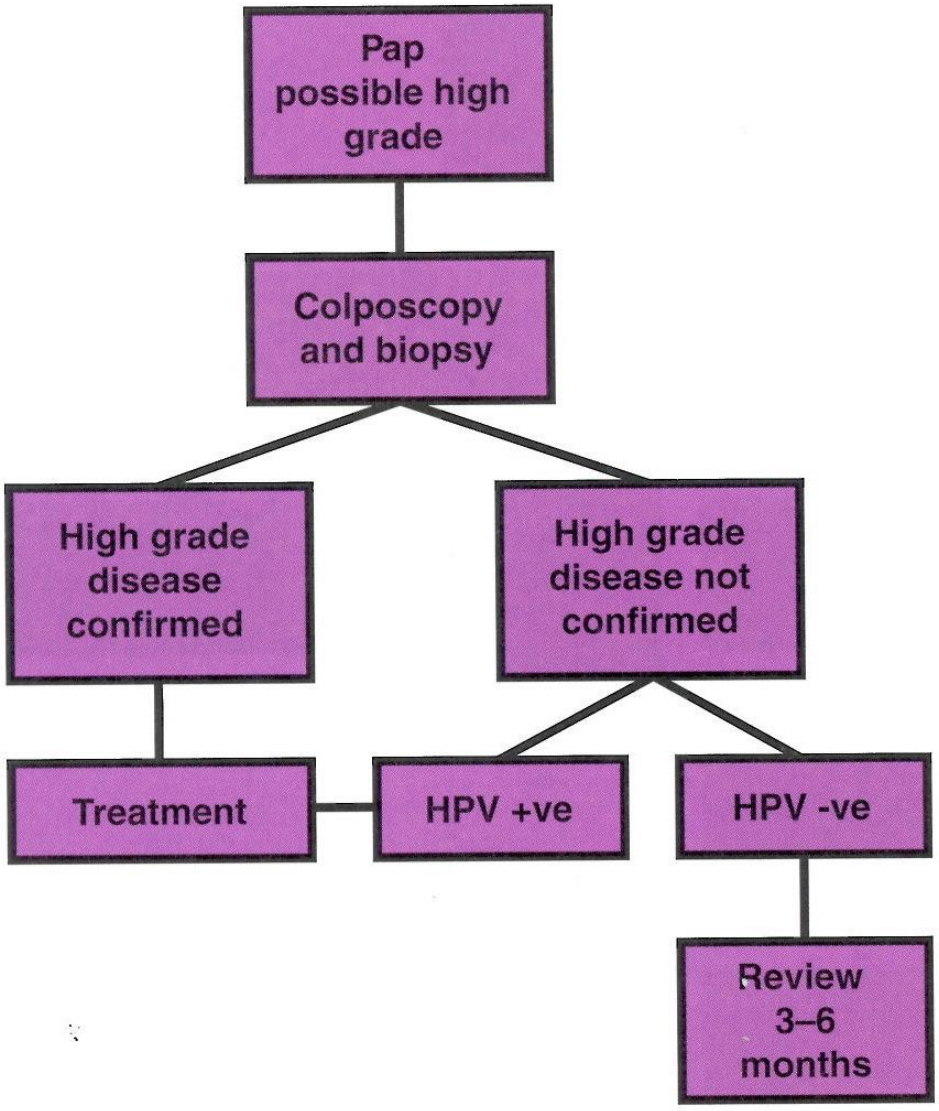


Figure 24.6 from *Obstetrics and Gynaecology: an evidence-based guide (2nd Ed).* 2014. Australia, Elsevier.

4. What are the current recommendations for follow-up after treatment?

It is recommended that a woman previously treated for HSIL undergo a colposcopy and cervical cytology at 4–6 months after treatment. Cervical cytology and HPV typing should then be carried out at 12 months after treatment and annually thereafter until the woman has tested negative by both tests on two consecutive occasions. At this point, the woman should continue to be screened according to the recommendation for the average population.

5. Describe the human papilloma virus and outline its pathogenesis.

HPV is a nonenveloped double stranded circular DNA virus. The virus is highly infective with transmission rates of over 50% following exposure to a person with productive anogenital

infection. The highest prevalence of HPV infection has been identified in sexually active women 25y of age and younger.
Infection occurs largely through any type of genital contact. Condoms can reduce transmission, but do not prevent it.

Infection is often subclinical but may present as condylomas (warts), cervical or anogenital abnormalitites and cancers.

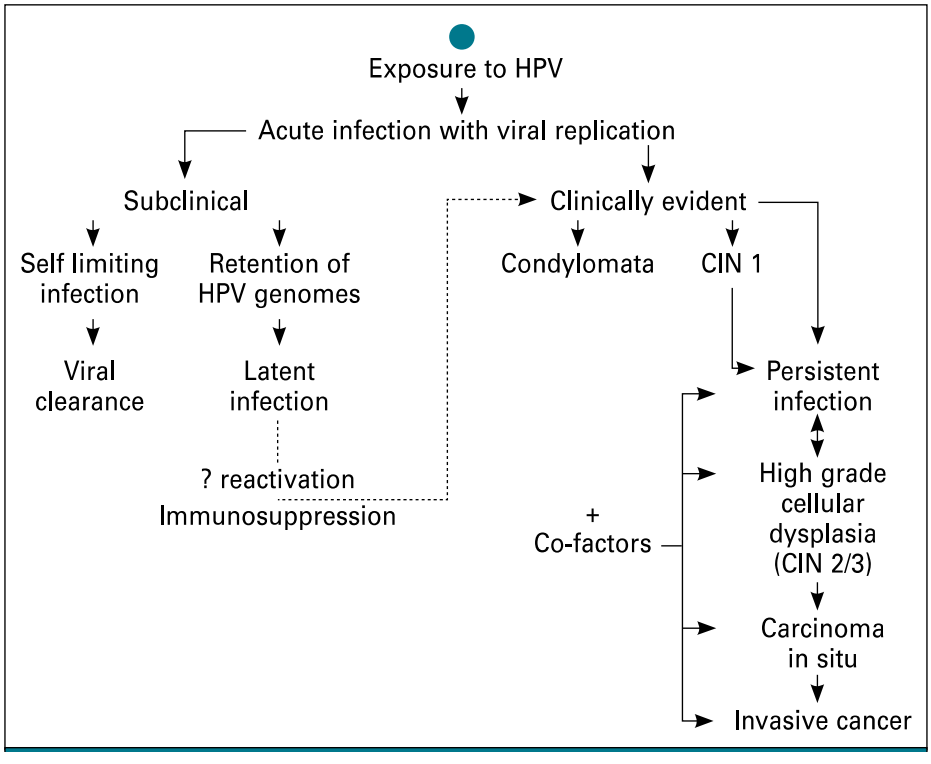
Most women who contract HPV clear it spontaneously within a median of 8-14 months with persistence of a high risk HPV type occurring in 3-10% of women.

HPV is now universally recognised as a necessary agent for the development of cervical cancer with HPV being present in 99.7% of cervical cancers. The virus is also associated with over 90% of genital wart cases, approx 70% of anal cancers, approx 50% of penile cancer lesions, and approx 20% of oropharyngeal cancers.

EFFECTS OF HPV

HPV type	Women	Men
16/18	• 70% of cervical cancer[5] • 50% of CIN 2/3[6] (HSIL) • 25% of CIN 1[7] (LSIL) • Most anal cancers[4]	• Most anal cancers[4] • Potentially prevention of infection (reduced transmission to women)
6/11	• 10% of CIN 1[7] • >90% of genital warts[3]	• Potentially prevention of infection (reduced transmission to women) • >90% of genital warts[3]

NATURAL HISTORY OF HPV INFECTION



6. **What are the current recommendations for HPV vaccination in Australia? Describe the two vaccines currently available in Australia.**

Both human papillomavirus (HPV) vaccines contain 2 recombinant virus-like particles containing capsid (L1) protein from HPV genotypes 16 and 18 (oncogenic). Gardasil 9 vaccine also contains 16,18,31,33,45,52,58 and similar proteins from HPV 6 and 11 which cause most genital warts and recurrent respiratory papillomatosis (low oncogenic risk).

Indications

Immunisation against HPV infection is part of the standard vaccination schedule for females aged 12-13 years

Cervarix®: Prevention of cervical cancer

Gardasil®: Prevention of genital warts and cervical, vulvar and vaginal cancer in females and Prevention of HPV infection in males

Adverse effects

Common: headache, myalgia, fatigue

Common or infrequent: transient injection site reactions, transient fever, fainting

Rare: allergic reactions including anaphylaxis

Dosage – Human papillomavirus vaccine

- Cervarix®: *14–45 years*, IM 0.5 mL at 0, 1 and 6 months, 10-14 years 2 doses 0 and 5-13 months. .

- Gardasil 9 IM 3x 0.5 mL at 0, 2 and 6 months. 9-14 years 2 doses at o and 5-13 months.

Counselling

This vaccine will not completely prevent cervical cancer, so screening will still be necessary.

Practice points

- in young females both vaccines protect against infection due to HPV types 16 and 18 (responsible for 70–80% of cervical cancers); Gardasil® also protects against HPV types 6 and 11 (cause >90% of genital warts)
- likely to be most effective if given to females before they become sexually active
- only prevent disease due to vaccine virus types
- do not affect existing infection or disease due to a vaccine virus type
- antibody concentrations from Gardasil® vaccination of 10–15 year old girls and boys are greater than those in 16–23 year old women
- clinical efficacy of the vaccines in males has not been shown
- duration of immunity following vaccination exceeds 4 years and appears to be sustained; requirement for booster vaccination is unknown