Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

- Abnormal cytology following routine cervical screening
  - Suspected invasive cancer or glandular neoplasia
    - Refer urgently to appropriate specialist (within 2 weeks)
  - Moderate or severe dyskaryosis (CIN 2/3)
    - Consider referral for colposcopy
  - Borderline nuclear change/mild dyskaryosis (CIN 1)
    - Return to routine recall
  - Benign endometrial cells
    - Refer urgently to an appropriate specialist (must be seen within 2 weeks) if indicated
  - Management of glandular abnormalities
  - Go to cervical cancer - management
  - Refer for colposcopy
    - Perform colposcopy
      - Considerations for pregnant women
        - Planned excisional treatment for invasive disease
          - Go to cervical cancer - management
        - Considerations for punch biopsy
          - Is colposcopic biopsy appropriate?
            - Yes - colposcopic biopsy is appropriate
              - Abnormal (high grade) results
                - Go to cervical dysplasia - management
            - No - follow up with cytology and possibly colposcopy
              - Negative or low grade results
                - Go to cervical dysplasia - management
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

1 Background information

Quick info:
Scope:
• assessment and management of cervical dysplasia (cervical intra-epithelial neoplasia; CIN) and squamous and adenomatous cell cervical cancers in primary and secondary care in:
  • women of reproductive age
  • adolescents (age 13-20 years)
  • pregnant women
  • postmenopausal women
• consider Menstrual cycle irregularities and post-menopausal bleeding (PMB) pathway
Out of scope:
• management of CIN and cervical cancer in immunocompromised patients
Incidence:
• cervical cancer is the second most common cancer in women worldwide [1]
• in the UK, there are approximately 2,800 cases of cervical cancer per year and 1,000 women die from cervical cancer each year [2]
• cervical cancer is rare in women younger than age 20 years, rapidly increases in incidence between ages 25 and 36 years, and has a peak incidence in the 35-39 age group [3]
• population screening reduces the incidence of cervical cancer and reduces the proportion of women with advanced disease
• it is estimated that the screening programme in the UK saves approximately 5,000 lives per year [2]
• 80% of cervical cancers are squamous cell carcinomas and 20% rare adenocarcinomas, adenosquamous carcinomas, and other rare types [1]
Aetiology:
• human papillomavirus (HPV) is the cause of pre-cancerous abnormalities of the cervix
• HPV has over 100 subtypes and is present in over 95% of pre-invasive and invasive squamous carcinomas of the cervix [4]
• CIN is the most common pre-malignant lesion characterised by atypical squamous changes in the transformation zone of the cervix; with mild, moderate or severe changes described by their depth (CIN 1, 2, or 3)
• if CIN progresses it becomes squamous cancer
• glandular pre-cancerous abnormalities (cervical glandular intra-epithelial neoplasia; cGIN) develop into cervical adenocarcinoma but are much rarer
Risk factors:
• the aetiological association is restricted to a limited number of viral types of the human papillomavirus (HPV)
• HPV DNA can be identified in all specimens of invasive cervical cancer
• infection with HPV is common but cervical cancer is not, therefore HPV infection alone is not sufficient to cause cervical cancer
• cofactors that increase the risk of developing cervical cancer among HPV DNA positive females include:
  • the use of oral contraceptives for 5 years or more
  • smoking
  • multiplicity of sexual partners
  • early participation in sexual activity
  • previous exposure to other sexually transmitted infections (STIs), such as:
    • Chlamydia trachomatis (C. trachomatis)
    • herpes virus type 2
• infection with HIV increases the risk of:
  • HPV infection
  • HPV DNA persistency; and
• progression of HPV lesions to cervical cancer
Prognosis:
• survival ranges from almost 100% 5-year disease-free survival for treated stage IA disease to 5-15% in stage IV disease [1]
• survival in women with more locally advanced tumours is influenced by:
  • tumour bulk
  • the person's age
  • coexistent medical conditions
  • untreated mortality in locally advanced disease is high
NB: This information appears on each page of this pathway.
References:
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening


2 Information resources for patients and carers

Quick info:
Patients and carers in England can access this pathway through NHS Choices at http://healthguides.mapofmedicine.com/choices/map/cervical_dysplasia_and_cancer1.html
The following resources have been produced by organisations certified by The Information Standard:
- 'Cervical cancer' (URL) from Bupa at http://www.bupa.co.uk
- 'Cervical cancer' (URL) from Cancer Help UK at http://www.cancerhelp.org.uk
- 'Cervical cancer' (URL) from Datapharm at http://www.medguides.medicines.org.uk
- 'Cervical cancer' (URL) from Macmillan Cancer Support at http://www.macmillan.org.uk
- 'Cervical Cancer (Cancer of the Cervix)' (PDF) from Patient UK at http://www.patient.co.uk
Information for carers and people with disabilities is available at:
- 'Caring for someone' (URL) from Directgov at http://www.direct.gov.uk
- 'Disabled people' (URL) from Directgov at http://www.direct.gov.uk
Patient stories describing their care journeys are available at 'Healthtalkonline' (URL) from DIPEx at http://www.healthtalkonline.org
Explanations of clinical laboratory tests used in diagnosis and treatment are available at 'Understanding Your Tests' (URL) from Lab Tests Online-UK at http://www.labtestsonline.org.uk
The Map of Medicine is committed to providing high quality health and social care information for patients and carers. For details on how these resources are identified, please see Map of Medicine Patient and Carer Information.
NB: This information appears on each page of this pathway.

3 Updates to this pathway

Quick info:
Date of publication: 29-Jul-2011
Interim update:
This pathway has been updated according to feedback from the National Cancer Action Team (NCAT).
Date of publication: 29-Apr-2011
Interim update:
This pathway has been updated according to feedback from the National Cancer Action Team (NCAT) and information added in line with the following reference:
Date of publication: 31-Jan-2011
Three floating nodes now appear at the top of each pathway page. These provide:
- easy access to scope and background information on each page of the pathway whilst reducing repetition between nodes
- easy access to patient resources/leaflets
- information on pathway updates
This pathway was updated in line with the following guidelines:
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening


Further information was provided by the following references: [4,8,11,12,15-22,26-28]

For further information, please see the pathway's Provenance.

The pathway has been completely restructured and redrafted in line with the Map of Medicine editorial methodology and to bring it in line with current clinical practice.

NB: This information appears on each page of this pathway.

4 Abnormal cytology following routine cervical screening

Quick info:

Abnormal cytology results after a routine cervical screening include [6]:
- borderline nuclear abnormality
- mild, moderate or severe dyskaryosis
- severe dyskaryosis or suspected invasive carcinoma
- glandular neoplasia or suspected glandular neoplasia

Results following a screening can also be [6]:
- negative (no nuclear abnormalities identified)
- inadequate
- negative but with incidental observations

Manage negative results [6]:
- inform the patient of the result
- use the term 'normal' when informing the patient about a negative result
- recall if appropriate

Inadequate results refers to samples with any of the following [8]:
- consisting mainly of blood and pus or inflammatory exudate
- excessive cytolysis rendering samples unsuitable
- insufficient or unsuitable material present
- unlabelled, damaged, or incorrectly labelled sample containers [11]

Manage inadequate results:
- if the sample was technically inadequate, inform the patient and repeat no sooner than 3 months after initial sample was taken [6]
- if there is infection or atrophy present, provide treatment and then repeat test after 3 months [7]
- if inadequate results persist, ie three inadequate samples, refer for assessment by colposcopy [7]

Incidental observations with no nuclear abnormalities include vaginal infections without evidence of dyskaryosis or borderline nuclear change [6].

Investigate and manage incidental observations with no nuclear abnormalities [6]:
- inform the patient of the result
- be aware that:
  - there are consequences of a diagnosis of a sexually transmitted infection (STI)
  - the patient may not know that this result can be reported as a result of a cervical screen
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

- the patient may be asymptomatic and not expecting the report
- investigate and manage the infection as appropriate

NB: This page of the cervical cancer pathway is based on the NHS Cervical Screening Programme (NHSCSP) guidelines (2010) which dictate the management of abnormal cytology.

References:

5 Suspected invasive cancer or glandular neoplasia

Quick info:
Suspected invasive cancer or glandular neoplasia may represent [6]:
- endocervical adenocarcinoma in situ; or
- endocervical adenocarcinoma of the cervix; or
- adenocarcinoma of the endometrium; or
- extra-uterine adenocarcinoma
- cervical intra-epithelial neoplasia grade 3 (CIN 3) can co-exist with adenocarcinoma in situ – it is not always possible to distinguish them cytologically [6]
- less than 0.1% of samples suggest invasive carcinoma [6]
- women with a cytology result of invasive cancer or glandular neoplasia should be urgently referred for suspected cancer and seen within 2 weeks [7]

References:

6 Moderate or severe dyskaryosis (CIN 2/3)

Quick info:
Moderate or severe dyskaryosis refers to:
- nuclear and cellular abnormalities indicating probable cervical intra-epithelial neoplasia grade 2 or 3 with additional features suggesting the possibility of invasive cancer [6]
- women with a cytology result of moderate or severe dyskaryosis should be urgently referred for suspected cancer within 2 weeks [7]:
  - in England, women referred with a high grade cytological abnormality must start treatment within 62 days
  - once cancer has been excluded these women must enter the 18-week pathway

NB: CIN 3 refers to high grade CIN found on biopsy and is also classified as carcinoma in situ [6].

References:

7 Borderline nuclear change/mild dyskaryosis (CIN 1)

Quick info:
Borderline nuclear change or mild dyskaryosis (cervical intraepithelial neoplasia; CIN 1):
- is often reported in the presence of human papillomavirus (HPV) type changes [6]
- borderline nuclear abnormality refers to [6]:
  - nuclear changes that cannot be described as normal
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

- a sample where there is doubt as to whether the nuclear changes reflect dyskaryosis
- treat any associated treatable condition (if one is present) [6]
- repeat tests [7]:
  - recommended for the first occurrence of borderline changes
  - a second repeat may be requested for borderline changes, but after three such samples, consider colposcopy
  - the recommended interval for repeat tests is usually 6 months – this takes into account the time needed for resolution of borderline changes
- HPV testing – there are currently pilot studies underway assessing the potential benefits of introducing HPV testing to triage women with borderline and mildly abnormal results [7]
- women with a mild dyskaryotic result should be seen and assessed but not necessarily treated – to prevent possible over-treatment, they should not be managed on a ‘see and treat’ basis [7]
- refer women for colposcopy if they have had three tests reported as abnormal at any grade in a 10 year period, even if returned to routine recall on one or more occasions in that period – women should be seen within 8 weeks of referral [7]
- refer any woman for colposcopy if previously treated for CIN and who have not been returned to routine recall, and subsequent testing indicates mild dyskaryosis or worse [7]

References:

8 Benign endometrial cells

Quick info:
Benign endometrial cells:
- benign-appearing endometrial cells are observed in up to 12% of cervical cancer screenings, and are more common in premenopausal than in postmenopausal women [7]
- in women under age 40 years, their presence is not significant and requires no action [7]
- in women age 40 years and over, their significance varies with the menstrual cycle phase:
  - after day 14, the presence of normal endometrial cells may indicate endometrial pathology [7,13]
  - normal endometrial cells should always be reported if the menstrual, drug and contraceptive history is unknown or if the woman is postmenopausal [7]
  - if an opinion is necessary urgently refer the patient to be seen within 2 weeks [7]
  - consider sampling of the endometrium with endometrial biopsy or dilation and curettage to rule out endometrial cancer [13]

References:

12 Consider referral for colposcopy

Quick info:
Consider referral for colposcopy for [7]:
- mild dyskaryosis:
  - women with two test results reported as mild dyskaryosis should be referred, without a return to routine recall
- borderline nuclear change:
  - if borderline changes are seen in endocervical cells, or there is a suspicion of high grade disease, refer the woman immediately to colposcopy rather than waiting for repeat tests
  - if cytological surveillance is recommended, the woman should be referred for colposcopy if, in a 10 year period, there are three borderline or more severe results
  - if cervical changes are difficult to interpret
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

NB: If colposcopic appearances are non-specific, a more accurate assessment may be obtained with cytological review, colposcopic appearances, and histological biopsy of any abnormality seen – review and management should be decided by a cytopathologist, a gynaecologist and a histopathologist [7].

Reference:

13 Return to routine recall

Quick info:
Return to routine recall [7]:

• following mild dyskaryosis or borderline nuclear change, a woman should be returned to routine recall only after a minimum of three negative tests each at least 6 months apart or colposcopic assessment indicating no abnormality
• before recall is ceased for reasons of age, at least three negative follow-up tests should be reported after borderline nuclear change

Reference:

14 Management of glandular abnormalities

Quick info:
Management of glandular abnormalities [7]:

• patients with glandular neoplasia or borderline glandular neoplasia cytology need to be investigated urgently by [6]:
  • colposcopy; and
  • appropriate cervical or endometrial biopsy
• endometrial biopsy is recommended for women with atypical endometrial cells on a sample, with or without irregular vaginal bleeding and regardless of menopausal status – these women:
  • should be seen urgently, within 2 weeks of referral by a gynaecologist
  • should not be referred to colposcopy and repeat cervical cytology is not recommended
• if cervical histology is negative, consider other gynaecological or non-gynaecological conditions
• if careful follow-up is carried out, expectant management after cone biopsy appears safe provided that the lesion appears to have been completely excised
• follow-up with expectant management involves cytology and colposcopy
• recent data indicates a recurrence rate of 15% at 4 years, though a slightly higher proportion will require further investigation for abnormalities detected during follow-up

References:

15 Provide patient information

Quick info:
Inform patient that referral for colposcopy is needed for further investigation [7]:

• effective information and communication are crucial to reducing anxiety [7,17] – high anxiety levels before colposcopy can have psychological consequences, including [17]:
  • pain
  • discomfort
  • failure to return for follow-up

Offer each woman [6,7]:
• verbal and written information before colposcopy, including national and individualised information leaflets
• counselling
• a contact name and number

Published: 21-Jul-2011    Valid until: 31-Aug-2012 © Map of Medicine Ltd   All rights reserved
This care map was published by International. A printed version of this document is not controlled so may not be up-to-date with the latest clinical information.
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

- results and management plans before their attendance

Advise the woman:
- that it is very rare for the abnormalities found in the cytology to be cancer [6]
- that some of the abnormalities will return to normal on their own, but most will be cured after simple out-patient treatment [6]
- to avoid using tampons for 4 weeks following treatment [7]
- to abstain from vaginal intercourse for 4 weeks following treatment [7]
- to avoid swimming for 2 weeks following treatment [7]
- that they may drive following loop excision or local treatment, unless advised otherwise by the examining colposcopist [7]
- that other normal activities, including light exercise, may continue [7]
- that there may be a temporary change in the menstrual pattern following loop excision [7]
- that single conisation, cervical diathermy and loop excision are each associated with a small but significant increase in the incidence of preterm labour and preterm prelabour rupture of membranes [7]

References:

17 Perform colposcopy

Quick info:

Colposcopy examination:
- in England, women who have been referred from the screening programme to colposcopy services will be included within the 62-day treatment pathway introduced by the Cancer Reform Strategy [7]
- colposcopy is the visualisation of the cervix using a binocular microscope [17]:
  - acetic acid solution is applied to the cervix to help visualise abnormal areas [6]
  - abnormal areas have atypical vessel formation, raised or ulcerated surface, and turn white on acetic acid staining [6]
- ensure the following is recorded at the colposcopic examination [7]:
  - reason for referral
  - grade of cytological abnormality
  - whether the examination is satisfactory (this is defined as the entire squamocolumnar junction having been seen and the upper limit of any cervical lesion also being seen)
  - the presence or absence of vaginal and/or endocervical extension
  - the colposcopic features
  - the colposcopic impression of lesion grade
  - reasons for not performing a biopsy, ie in pregnant women must be recorded [7]

Review previous cytology results [6]:
- before the colposcopic examination commences, the cytology results (from the previous cytology tests) should be available to the colposcopist
- knowledge of the cytological result improves the identification of colposcopic images of high grade cervical intra-epithelial neoplasia (CIN)

A satisfactory colposcopy is defined as one which visualises [8]:
- the entire squamocolumnar junction; and
- the entire margin of any suspicious lesions

References:
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

Quick info:

Colposcopy in pregnant women [7]:
- a woman who meets the criteria for colposcopy should be examined in the colposcopy clinic even if she is pregnant
- the aim of colposcopy for pregnant women is to exclude invasive disease and to defer biopsy or treatment until the woman has delivered
- women seen in early pregnancy may need further assessment in the late second trimester at the clinician’s discretion
- if colposcopy has been performed during pregnancy, postpartum assessment of women with an abnormal cytology or biopsy-proven CIN is essential
- colposcopic evaluation of the pregnant woman requires a high degree of skill:
  - if CIN 1 or less is suspected, repeat the examination 3 months following delivery
  - if CIN 2 or 3 is suspected, repeat colposcopy at the end of the second trimester or, if the pregnancy has already advanced beyond that point, 3 months following delivery
- if invasive disease is suspected clinically or colposcopically, a biopsy is essential:
  - cone, wedge and diathermy loop biopsies are all associated with a risk of haemorrhage and such biopsies should be taken where appropriate facilities to deal with haemorrhage are available
  - punch biopsy suggesting only CIN cannot reliably exclude invasion

Reference:

19 Planned excisional treatment for invasive disease

Quick info:
An excisional form of biopsy is recommended when [7]:
- most of the ectocervix is replaced with high grade abnormality
- low grade colposcopic change is associated with severe dyskaryosis or worse
  - a lesion extends into the canal – sufficient canal must be removed with endocervical extension of abnormality
In these situations, a punch biopsy is not reliably informative [7].

NB: Pregnancy is a reason for not performing a punch biopsy [7]. However, excision is indicated if invasion is suspected [11].

References:

20 Considerations for punch biopsy

Quick info:
Unless an excisional treatment is planned, colposcopy directed punch biopsy should be carried out when the cytology indicates [7]:
- moderate dyskaryosis or worse
- a recognisably atypical transformation zone is present

A biopsy and treatment are not always necessary for:
- mild dyskaryosis or less; and
- if colposcopy findings are satisfactory and normal

NB: Pregnancy is a reason for not performing a punch biopsy [7]. However, excision is indicated if invasion is suspected [11].

References:

21 Is colposcopic biopsy appropriate?

Quick info:
A biopsy and treatment are not always necessary for [7]:
- mild dyskaryosis or less; and
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

- if colposcopy findings are satisfactory and normal

Reference:

22 Yes - colposcopic biopsy is appropriate

Quick info:
Confirmation of the clinical colposcopic impression of a low grade lesion by biopsy is normally undertaken to confirm the diagnosis [7].
NB: Pregnancy is a reason for not performing a punch biopsy [7]. However, excision is indicated if invasion is suspected [11].
References:

23 No - follow up with cytology and possibly colposcopy

Quick info:
For patients with mild dyskaryosis or less and a normal and satisfactory colposcopic examination, treatment is not usually recommended [7]:
- management is best determined by repeat cytological assessment at 6 months
- if 6 month cytology is:
  - normal – return to recall
  - borderline – repeat test in 12 months
  - mild dyskaryosis – routine return to colposcopy
  - any other result than the above – further colposcopy as soon as is convenient with or without biopsies
- if abnormality persists (for 2 years at the most) refer to colposcopy clinic. At this stage:
  - at least a biopsy is necessary
  - many patients are offered treatment because persistent surveillance can lead to patients not attending appointments
  - females referred to colposcopy with borderline nuclear changes or mild dyskaryosis whose colposcopy findings are normal and whose repeat smear in the clinic is non-dyskaryotic may be discharged for routine screening as the risk of high-grade disease in the next 5 years is small

Reference:

24 Abnormal (high grade) results

Quick info:
Abnormal (high grade) results includes cervical intra-epithelial neoplasia grade 2 (CIN 2) and over [7].

Reference:

25 Negative or low grade results

Quick info:
Negative or low grade results includes cervical intra-epithelial neoplasia grade 1 (CIN 1) or less [7].

Reference:
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

Key Dates

Published: 21-Jul-2011, by International
Valid until: 31-Aug-2012

Accreditations

The care map is accredited by:

National Cancer Action Team (NCAT):
Disclaimer

The care map is accredited by:
The Chief Knowledge Officer of the NHS:
Disclaimer

Evidence summary for Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

This pathway has been developed according to the Map of Medicine editorial methodology (http://mapofmedicine.com/whatisthemap/editorialmethodology). The content of this pathway is based on high-quality guidelines [1-3,5-7,9,10,13,14,23-25], critically appraised meta-analyses and systematic reviews [4,12,15-22,26,28]. Practice-based knowledge has been added by contributors with front-line clinical experience [8,11], including any literature endorsed by the contributor group [27,29].

Search date: Sep-2010

References

This is a list of all the references that have passed critical appraisal for use in the care map Cervical dysplasia and cancer

<table>
<thead>
<tr>
<th>ID</th>
<th>Reference</th>
</tr>
</thead>
</table>
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

ID Reference
11 Contributors representing National Cancer Action Team. 2011.
13 Institute for Clinical Systems Improvement (ICSI). Initial management of abnormal cervical cytology (pap test) and HPV test in adult and adolescent females. Bloomington, MN: ICSI; 2010.
   http://www.icsi.org/new_category_10659/cervical_cytology__pap_smear_and_hpv_testing_initial_m
   anagement_of_abnormal_pdf.html

Disclaimers

Published: 21-Jul-2011    Valid until: 31-Aug-2012 © Map of Medicine Ltd    All rights reserved
This care map was published by International. A printed version of this document is not controlled so may not be up-to-date with the latest clinical information.
Cervical dysplasia and cancer - abnormal cytology following routine cervical screening

National Cancer Action Team (NCAT)

It is not the function of the National Cancer Action Team to substitute for the role of the clinician, but to support the clinician in enabling access to know-how and knowledge. Users of the Map of Medicine are therefore urged to use their own professional judgement to ensure that the patient receives the best possible care. Whilst reasonable efforts have been made to ensure the accuracy of the information on this online clinical knowledge resource, we cannot guarantee its correctness or completeness. The information on the Map of Medicine is subject to change and we cannot guarantee that it is up-to-date.

The Chief Knowledge Officer of the NHS

It is not the function of the Chief Knowledge Officer of the NHS to substitute for the role of the clinician, but to support the clinician in enabling access to know-how and knowledge. Users of the Map of Medicine are therefore urged to use their own professional judgement to ensure that the patient receives the best possible care. Whilst reasonable efforts have been made to ensure the accuracy of the information on this online clinical knowledge resource, we cannot guarantee its correctness or completeness. The information on the Map of Medicine is subject to change and we cannot guarantee that it is up-to-date.