The Dutch College of General Practitioners (NHG) Practice Guideline
This NHG Practice Guideline is a translation of the Dutch guideline. It is specifically written for Dutch general practitioners in the Dutch environment. The advice which is given may therefore not be in accordance with the views of general practitioners in other countries.

NHG Practice Guideline 'Vaginal bleeding' (first revision)
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The practice guideline has been revised with respect to the previous version (Huisarts Wet 1992;35:475-81). The most important changes are:
- The levonorgestrel-releasing IUD has been added as an option in the treatment of excessive bleeding without an underlying cause and excessive bleeding associated with a copper IUD.
- The use of transvaginal ultrasonography has been included in the section on the management of postmenopausal bleeding.
- Incidental heavy or prolonged bleeding is not dealt with as a separate topic but is included in the section on excessive bleeding without underlying cause.

INTRODUCTION
The NHG Practice Guideline 'Vaginal bleeding' provides guidance for the diagnosis and treatment of vaginal bleeding which is defined as bleeding that is different from what the woman previously experienced or considers normal. Amenorrhoea, oligomenorrhoea, and bleeding during a known pregnancy are not discussed in this practice guideline but will be found in the NHG Practice Guidelines 'Amenorrhoea' and 'Miscarriage'.
Complaints associated with dysmenorrhoea are also beyond the scope of this practice guideline.
In this practice guideline, distinctions are made among excessive, irregular, breakthrough, and postmenopausal bleeding, since the differential diagnosis and management of these may differ. In addition, on the basis of the history and findings during the examination, a distinction is made between bleeding from the endometrium and bleeding originating outside the endometrium. The therapeutic guidelines in this practice guideline are limited to bleeding originating from the endometrium.
In general practice, the incidence of excessive or irregular bleeding is approximately 15 per 1,000 women per year, that of breakthrough bleeding is about 5 per 1,000 women per year, and that of postmenopausal bleeding is about 3 per 1,000 women per year.
During the reproductive phase of life, including the perimenopausal years, referral for diagnostic curettage is rarely necessary, because endometrial carcinoma is rare during this time. On the other hand, bleeding after the menopause requires a different approach, because malignancies are then found in approximately 10% of women. The risk of a malignancy being the underlying cause of bleeding increases markedly with age.
In premenopausal vaginal bleeding, it is important that the general practitioner distinguishes between conditions for which watchful waiting is justified and those for which it is not. Examples of the latter are pelvic inflammatory disease (PID), ectopic pregnancies, and cervical carcinoma. The way in which a general practitioner can distinguish between these conditions is described in this practice guideline.

Terminology
Excessive bleeding: cyclical bleeding that is excessive in volume or duration, compared with what the woman usually experiences. The synonyms hypermenorrhoea and menorrhagia are also used.
Irregular bleeding: non-cyclical bleeding, as a result of which menstrual bleeding can no
longer be separately recognized. The synonym for this is metrorrhagia. Breakthrough bleeding: bleeding in the interval between recognizable episodes of menstrual bleeding. The synonym for this is intermenstrual bleeding. Breakthrough bleeding can occur either at a fixed point during the cycle or at different points. Postmenopausal bleeding: bleeding that occurs at least one year after the last menstruation (the menopause). Abnormal vaginal bleeding in the postmenopause is the term used for any bleeding that is not withdrawal bleeding associated with the use of oestrogens and progestagens.

Background
The menstrual cycle is regulated by a combination of the hypothalamus, hypophysis, ovaries, and uterus. The interval between the start of follicle maturation and ovulation is known as the follicular phase. The interval between ovulation and menstruation is the luteal phase. The duration of the follicular phase varies, while the duration of the luteal phase is relatively constant at about 13 days. A normal cycle can range from 20 to 40 days. There can be large intra-individual variation in cycle length, particularly during the first years after menarche and the last years before the menopause. In half of all cases, no underlying cause can be found for excessive bleeding. In these cases, excessive bleeding is assumed to be caused by hormonal fluctuations. Shortly after menarche, there may be heavy or prolonged bleeding for 2-3 weeks, also known as "metrorragie des jeunes vierges". Heavy menstruation can also occur during the final years before the menopause. Other causes of heavy bleeding include myomas, an IUD, an endometrial polyp, endometriosis, and drugs such as corticosteroids or anticoagulants. Myomas are most common from 30 years of age to the menopause, after which they undergo involution. When an IUD is inserted, menstruation usually begins more slowly and lasts longer than the woman has been accustomed to. Heavy bleeding occurs mainly during the first months after the IUD is inserted. In rare cases a coagulation disorder may be the cause of heavy bleeding. Heavy bleeding can eventually lead to iron deficiency anaemia.

Often no cause can be found for irregular bleeding, as well. It is especially common during the first years after menarche and in the last years before the menopause. The cycles are often anovulatory during these periods. Other causes include complications of pregnancy such as threatened abortion and ectopic pregnancy, drugs such as corticosteroids, oestrogens, and progestagens, and endometrial carcinoma. Breakthrough bleeding at a fixed point during the cycle is usually not caused by an underlying defect but is instead indicative of hormonal fluctuations. The use of oral contraceptives can also cause this type of bleeding. Breakthrough bleeding at varying points during the cycle is usually due to the use of hormonal contraceptives. Sometimes the cause is an endometrial polyp. In PID (pelvic inflammatory disease), the woman may at first complain of breakthrough bleeding. Other causes include cervical or vaginal disorders. The presence of contact bleeding is indicative of these types of problems. Postmenopausal bleeding is caused by endometrial carcinoma in about 10% of cases. In at least half the cases, no cause can be found by additional diagnostic investigation. In some cases, postmenopausal bleeding may be desirable: in order to prevent endometrial carcinoma associated with the use of oestrogens, withdrawal bleeding can be stimulated regularly with progestagens.

DIAGNOSTIC GUIDELINES
In many cultures menstruation is seen as a symbol of fertility and femininity, but also as a
source of shame which makes it very important to hide menstruation. When a woman menstruates, subconscious or unspoken personal and cultural norms about the desired duration of the cycle and of menstruation often play a role. The general practitioner should therefore pay attention to how the woman perceives the complaint and how it affects her daily life. Bleeding can be accompanied by a fear of disease or infertility. Sometimes it may cause problems, as when the woman is exercising and during intercourse, and if the bleeding is heavy, in daily life.

**History**
The general practitioner should determine whether the woman is in the reproductive or postmenopausal phase of life. The history taking of *women in the reproductive phase of life* should include the following:
- onset, duration, and course of the symptoms
- recognizability and duration of the cycle, duration of menstruation versus what is normal for the woman
- increased bleeding\(^{15}\)
- breakthrough bleeding at a fixed or varying point of the cycle, contact bleeding
- pain in the lower abdomen, increased menstrual pain
- sexual contacts, possibility of sexually transmitted disease (STD)\(^{16}\)
- possibility of pregnancy
- contraceptives, duration of use
- use of medication (corticosteroids, anticoagulants)

If heavy bleeding is long-standing, the general practitioner should also ask whether bruises develop quickly, whether small wounds bleed for a long time, and whether there are any coagulation disorders in the family. The history taking of *women in the postmenopausal phase of life* should be limited to the following:
- onset, duration, and course of symptoms
- contact bleeding
- use of medication (corticosteroids, anticoagulants, oestrogen substitution with or without progestagens)

**Physical examination**
In young women during the 5 years following menarche and women with breakthrough bleeding who are using hormonal contraceptives, an internal examination is not necessary except if there is contact bleeding or if the possibility of an STD cannot be excluded.\(^{17}\) In all other cases the general practitioner should carry out the following examination:
- inspection of the vulva and perineum
- speculum examination: vaginal lesions, cervical polyps, ectropion, *in situ* IUD, indications of vaginal or cervical malignancy, and in *postmenopausal women*, special attention should be paid to atrophy of the vaginal mucosa. If the speculum examination cannot be evaluated satisfactorily because of bleeding, the woman should be asked to return at a later date;
- bimanual examination of the uterus: size, consistency, and tenderness of the uterus, size and tenderness of adnexa

**Supplementary investigations**
For *women in the reproductive phase of life*:
- Keeping a menstruation calendar can provide greater insight into the nature and pattern of the bleeding. The days of bleeding and use of hormonal contraceptives, if applicable, should be recorded on the calendar.
• Tests for iron deficiency anaemia should be carried out if heavy bleeding has persisted for more than 3 months.  
• Body temperature should be taken and the ESR should be measured if there are signs of PID.  
• PID is present if, in addition to bleeding, the woman has lower abdominal pain and the examination reveals a tender uterus or tender adnexa.  
• A pregnancy test should be carried out on the same day if pregnancy cannot be excluded on the basis of the history.  
• A cervical smear should be taken if:
  • contact bleeding occurs as a result of sexual intercourse or the cervix is abnormal in some way or bleeds easily upon physical examination;  
  • breakthrough bleeding occurs at varying points during the cycle and cannot be explained by the use of hormonal contraceptives, vaginal or cervical infection, or vulval or vaginal lesions.  
  • The dates and results of previous smears are irrelevant to this recommendation.  
• A sample for a *Chlamydia* test should be taken if the possibility of an STD cannot be excluded.  
• Ultrasonography can be performed if nodules or masses are felt adjacent to the uterus during bimanual examination or there are other suspicious findings.  
• Investigation for coagulation disorders is indicated if there is prolonged heavy bleeding or other signs of coagulation disorders in the history.

**For postmenopausal women:**  
• A cervical smear should be taken.  
• Transvaginal ultrasonography should be performed to measure the thickness of the endometrium unless the bleeding is related to hormone substitution therapy. This can be requested by the general practitioner, or carried out via referral to a gynaecologist.

**Evaluation**  
The differential diagnosis should distinguish between bleeding from the endometrium and bleeding originating outside the endometrium.  

**Causes of bleeding from the endometrium:**  
• Excessive bleeding in a woman in the reproductive phase of life, without an apparent underlying cause, is assumed to be caused by hormonal fluctuations.  
• Excessive bleeding caused by myomas may be signalled by an enlarged uterus in the absence of pregnancy.  
• Excessive bleeding can be caused by an IUD, but if the bleeding occurs after a problem-free period of IUD use, other causes should be considered first.  
• Irregular or breakthrough bleeding with no underlying cause is also assumed to be due to hormonal fluctuations.  
• Abnormal vaginal bleeding can occur during the postmenopause, without abnormalities revealed by physical examination.  
• Coagulation disorder.  
• Oestrogen, progestogen, or corticosteroid use. The use of the medication should be reconsidered.

**Causes of bleeding originating outside the endometrium:**  
• Conditions involving the perineum, vulva, or vagina. This is usually accompanied by breakthrough bleeding at varying points during the cycle or contact bleeding. The management of these problems is outside the scope of this practice guideline.  
• Suspected PID: lower abdominal pain, tender uterus or adnexa, fever, elevated ESR.
For the treatment of PID, refer to the NHG Practice Guideline 'Pelvic inflammatory disease'.

- *Chlamydia* infection: positive *Chlamydia* test. For treatment refer to the NHG Practice Guideline 'Vaginal discharge'.

- Abnormal cervical cytology. For management refer to the NHG Practice Guideline 'Cervical smears'.

- Threatened abortion or ectopic pregnancy: positive pregnancy test and bleeding during the first trimester. For the management refer to the NHG Practice Guideline 'Miscarriage'.

**MANAGEMENT GUIDELINES**

**Information**

If the woman is *in the reproductive phase of life*, and no underlying abnormalities can be found, the general practitioner should explain that the bleeding is probably caused by hormonal fluctuations. This is common, particularly during the first years following menarche and the years immediately preceding the menopause. The general practitioner should emphasize that variations in cycle length and amount of blood lost occur regularly through the years. Only 30% of women have a cycle of 28-30 days. A change in bleeding pattern is harmless. Anaemia will develop only after months of excessive bleeding. In most cases the problem disappears spontaneously. In discussion with the woman, the general practitioner should determine whether she wants medication and whether she wishes to have children at present.

For abnormal bleeding during the postmenopause, further investigations are always necessary. If transvaginal ultrasonography reveals that the endometrium is <4 mm thick, the general practitioner should explain that the cause of bleeding is benign. If the bleeding recurs, the woman should return.

**Drug therapy**

*Excessive bleeding without an underlying cause*

*Progestagens* are indicated if the woman wishes the excessive bleeding to stop quickly. The general practitioner should prescribe either 10 mg medroxyprogesterone once daily, 10 mg lynestrenol once daily, or 5 mg norethisterone three times daily, for 10 days. If the bleeding started more than 1 week ago, a *sub-50 pill* can be prescribed 4 times daily for 5 days. In both cases, the bleeding will usually be markedly reduced within 2 days. There will be heavy withdrawal bleeding 2-4 days after the course of treatment ends and the woman should be warned of this. After 7 medication-free days, follow-up treatment with a sub-50 pill for 3 cycles can be considered.

If the woman wishes drug therapy for less heavy bleeding, a *sub-50 pill* is preferred because of its efficacy and low number of side effects. For guidance in selecting a preparation and for information about contraindications, refer to the NHG Practice Guideline 'Hormonal contraception'.

*NSAIDs* are the second choice for treatment and can be prescribed for women who wish to have children. They reduce bleeding by 20-30%. Their advantages are that they only have to be taken during the first 3 days of menstruation and they also have an analgesic effect. The choices are: 400 mg ibuprofen 3 times daily, 50 mg diclofenac 3 times daily, or 500 mg naproxen twice daily.

*Tranexamic acid* can be used if NSAIDs are insufficiently effective. This drug reduces bleeding by approximately 45% but it does have side effects, especially nausea, dizziness, and diarrhoea. As with NSAIDs, tranexamic acid is only taken during the first 3 days of menstruation. The dose is 1,000 mg 3 times daily.

Treatment with an NSAID or tranexamic acid can be stopped after 3-6 months to see
whether the symptoms return. 

Finally, a levonorgestrel-releasing IUD is also an option. It is an effective form of treatment for excessive bleeding and is also a reliable contraceptive. The levonorgestrel-releasing IUD should be replaced every 5 years. Refer also to the NHG Practice Guideline 'Intrauterine devices'.

Excessive bleeding due to myomas
Bleeding can be reduced with a sub-50 pill (see above). The second option is treatment with a progestagen on days 15-25 of 3 cycles, in the form of 10 mg medroxyprogesterone once daily, 10 mg lynestrenol once daily, or 5 mg norethisterone 3 times daily. The general practitioner should also explain that the first course of this treatment may be followed by heavy withdrawal bleeding. If the effect of a progestagen is unsatisfactory, tranexamic acid can be prescribed, as described above. After 3-6 months, treatment can be stopped to see whether the symptoms recur.

Excessive bleeding caused by an IUD
The general practitioner and the woman can discuss three options: removal of the IUD, use of an NSAID as described above, or replacement of the IUD with a levonorgestrel-releasing IUD.

Irregular and breakthrough bleeding without an underlying cause
Only treatment with a hormonal contraceptive will make the cycle more regular. A sub-50 pill is the preferred treatment.

Follow-up
For women in the reproductive phase of life, follow-up consultations are not usually indicated. During the first 5 years after menarche, the woman should wait for the cycle to adjust to its natural pattern. If the symptoms become worse, the general practitioner should again discuss drug therapy options. The woman should be advised to return for repetition of the diagnostic procedures if vaginal bleeding has not reverted to the normal pattern within 3 months.

For abnormal vaginal bleeding during the postmenopause, when the endometrial thickness has been found to be <4 mm by transvaginal ultrasonography, the general practitioner should advise watchful waiting and should instruct the woman to return if the bleeding recurs.

Consultation and referral
Consultation with or referral to a gynaecologist is indicated for:
- persistent complaints of vaginal bleeding which do not respond adequately to the above-mentioned treatment
- abnormal vaginal bleeding in the postmenopause: referral is indicated if transvaginal ultrasonography in the general practice revealed an endometrial thickness >4 mm
- persistence or recurrence of abnormal vaginal bleeding in the postmenopause
- irregular bleeding during hormonal substitution therapy in the postmenopause
If there are indications of a coagulation disorder, the woman should be referred to an internist.

Note 1
There is much inter-individual variation in the amount of blood lost during menstruation. In
a population study in 476 women 15-50 years of age, the mean blood loss measured by
the alkaline haematin method was 43 ml. In women who considered their bleeding to be
normal and who did not have anaemia, the mean loss was 33 ml. Five percent of the
women lost >80 ml of blood per menstruation. In 67% of these women the Hb was <12
g/100 ml (= 7.45 mmol/l).¹ In most studies 80 ml has been used as the lower limit for
excessive bleeding. Regardless of the total amount of blood lost, more than 90% of the
blood is lost during the first 3 days of menstruation.²

Variation at different ages and attempts to define normality. Acta Obstet Gynecol

note 2

Bijl D, Eijkelenburg-Waterreus JJH, de Jong HM, et al. NHG-Standaard
Amenorrhoe [NHG Practice Guideline 'Amenorrhoea']. In: Thomas S, Geijer
RMM, van der Laan JR, Wiersma Tj. NHG-Standaarden voor de huisarts deel
II [NHG Practice Guidelines for the general practitioner, part II]. Utrecht:
Bunge, 1996;54-8.

note 3

Population studies in women in Western Europe found that 9-14% had excessive vaginal
bleeding without an underlying cause.¹ The data on incidence in general practice quoted
in the practice guideline are taken from the Transition Project.² Comparing data from
population studies with data from general practice reveals that less than one-tenth of
the women who have excessive bleeding visit their general practitioner for this reason. It would
appear that most women do not perceive excessive bleeding to be a problem. It is not
known to what extent this also applies to other forms of abnormal vaginal bleeding.

2. Lamberts H. In het huis van de huisarts. Verslag van het Transitieproject [In the

note 4

According to the Transition Project, 'other malignant neoplasms', mainly endometrial
carcinoma, will eventually be diagnosed in 10% of women with postmenopausal bleeding.
Nevertheless, only 45% of women are referred to a gynaecologist at the first consultation
for postmenopausal bleeding.¹ In a retrospective study, malignancies were found in 12.5%
of 764 women 45 years of age or older with vaginal bleeding after at least 1 year of
amenorrhoea. The malignancies were primarily corpus and cervical carcinomas, in a ratio
of 5:3. Malignancies were found mainly in women over 60 years of age and their frequency
increased with the lateness of onset of menopause and the lateness in occurrence of
bleeding during the postmenopause. The nature and duration of bleeding had no
predictive significance for a malignancy as the cause of bleeding.² In a prospective
Scandinavian study in 457 women with postmenopausal bleeding who were referred to a
gynaecologist, none of the women under 50 years of age were found to have endometrial
carcinoma, compared with 23.8% of women over 80 years of age. Emanuel et al. studied
the prevalence of uterine abnormalities in 1,202 women who were referred for abnormal
vaginal bleeding. Of these, 287 were postmenopausal and had been referred by the
general practitioner. Hysteroscopy revealed a normal or inactive endometrium in 52%
of the women, while 22% had an endometrial polyp, 9% had an endocervical polyp, and 7%
had endometrial carcinoma.⁴

1. Lamberts H. In het huis van de huisarts. Verslag van het Transitieproject [In the

note 5
Treloar et al. investigated the duration of the menstrual cycle. Data were collected during a 28-year period and by 1961 there were 25,825 person-years of data available. The first 5-7 years after menarche and the last 6-8 years before the menopause are characterized by the greatest variation in cycle length, both long and short cycles occurring. Cycles are most regular during the ages of 20-40 years.¹


note 6
The Transition Project found that there is no diagnosis in 60% of the cases of excessive or irregular bleeding, while myomas are found in 10%, an IUD is the cause in 6%, hormonal contraceptives in 5%, and other medications in 4%. There is no diagnosis in 34% of the cases of breakthrough bleeding, while hormonal contraceptives are the cause in 18%, other medicinal products in 16%, an IUD in 9%, and pelvic infections in 3% of the cases.


note 7
Vaginal bleeding arising from the uterus with no identifiable underlying local organic cause is described in the literature as dysfunctional bleeding. This type of bleeding results from perturbation of the neuroendocrine regulation of the menstrual cycle. Different forms of dysfunctional bleeding are listed below, together with their pathophysiological background:

- Oestrogen withdrawal bleeding occurs when the endometrial lining is shed during the proliferative phase, due to withdrawal of oestrogen stimulation.
- Oestrogen breakthrough bleeding occurs when oestrogen stimulation of the endometrium is not supported by progesterone, thus in anovulatory cycles. The proliferative phase does not proceed to the secretory phase and thus the endometrial lining is partially shed, usually before the anticipated time of menstruation.
- Progestagen withdrawal bleeding occurs when too little progesterone is produced by the corpus luteum to enable successful conversion to a strong secretory endometrial lining. The result is similar to that of oestrogen breakthrough bleeding, there being partial shedding of the endometrial lining at a time which usually differs from that of the anticipated menstruation.


note 8
Menstrual disorders can arise as side effects of corticosteroid use.¹ No data could be found on the frequency of this side-effect. Menstrual disorders and postmenopausal bleeding
were mentioned incidentally in association with intra-articular injections of corticosteroids.\(^2\) The incidence of excessive bleeding in women taking oral anticoagulants was investigated by Van Eijkeren et al. In 11 women using oral anticoagulants, menstrual blood loss was measured during one cycle. The average blood loss was 98 ml.\(^3\) Compared with the average blood loss of 43 ml in the general population, these results support the supposition that the use of oral anticoagulants results in heavier menstruation.


**Note 9**
Coagulation disorders can rapidly lead to heavy bleeding in adolescents following menarche. Claessens and Cowell found a coagulation disorder in 29% of 59 adolescents who were admitted with heavy menorrhagia, but this was a highly selected clinical population.\(^1\) In a study of the incidence of coagulation disorders in 150 women who were referred because of menorrhagia and in whom the measured loss of blood exceeded 80 ml per menstruation, a hereditary coagulation disorder was found in 17%. Of the 150 women, 13% had von Willebrand's disease, in two-thirds of whom menorrhagia had occurred since menarche. A history of other symptoms of a coagulation disorder, such as small wounds that bleed for a long time and easy bruising, was significantly more common in these women.\(^2\)

The relationship between hypothyroidism and excessive bleeding is mentioned regularly in textbooks, but very few scientific data are available on this subject. In one study subclinical hypothyroidism was found in 15 of 67 women who complained of excessive bleeding.\(^3\) This suggests a link, but more research is necessary before a conclusion relevant to clinical practice can be drawn.


**Note 10**
In the study by Hallberg et al., 67% of the women with a blood loss >80 ml per menstruation were found to be anaemic. In those women who lost <60 ml, 23% were anaemic.\(^1\)


**Note 11**
Ovulatory cycles are a prerequisite for regular menstruation. During the first 2 years after menarche, about half of the cycles are anovulatory. Approximately 5 years after menarche, 80% of the cycles are ovulatory.\(^1\) There is a similar period of irregular menstruation during
the 6-8 years preceding the menopause. It is likely that this irregularity is also caused by anovulatory cycles.


note 12
Mid-cycle bleeding indicates oestrogen deficiency or ovulation. Premenstrual bleeding is usually due to a relative deficiency of progestagens.

note 13
Lower abdominal pain is usually the main symptom, possibly in combination with fever or general malaise.

note 14
In women receiving oestrogen substitution therapy and in whom no regular withdrawal bleeding was stimulated by progestagens, the risk of developing endometrial carcinoma was found to be increased nine-fold.

note 15
In a study by Chimbira et al., blood loss was measured during 2 cycles in 92 women with complaints of excessive blood loss for which no underlying cause had been found. No correlation was found between measured blood loss and the woman's own perception of the amount of blood lost and the number of sanitary pads and tampons used. The authors concluded that a woman is only able to detect an increase in blood loss. In a similar study in 69 women, only 38% of those complaining of excessive bleeding lost >80 ml of blood per menstruation. Furthermore, although the group as a whole was reasonably capable of accurately detecting an increase or decrease in bleeding from day to day, large errors of estimation were found at an individual level. Janssen et al. studied the value of a score card on which the number of pads and tampons was recorded, as well as the volume of clots lost. There was a good correlation with the 'gold standard', the alkaline haematin method. Use of such a score card in general practice is limited by the fact that only a single brand of sanitary pads and tampons was used in this study. Although the loss of clots is regarded by various authors to be a sign of excessive blood loss, that supposition could not be confirmed in this study.

note 16
In order to estimate the risk of an STD, the general practitioner should ask:
- about unprotected sexual contact with different partners (or a partner with different contacts) or a new partner, and
- whether the partner has symptoms of urethritis or diagnosed STD.

note 17
In this group, findings based on internal examinations contribute little to the diagnostic procedures and further management of the patient. During the first 5 years following menarche, irregular bleeding is almost always caused by anovulatory cycles. Only 5 years after menarche 80% of the cycles are ovulatory. This figure is considered normal for the reproductive phase of life.¹ In rare cases in which there is an underlying cause, the cause will involve conditions which cannot be diagnosed by means of an internal examination.²,³
Neoplasms are extremely rare in this group.

note 18
This guideline is based on consensus within the work group. Research by Hallberg et al. has shown that 67% of women who lose >80 ml blood per menstruation are anaemic.¹ It is not known how long the anaemia takes to develop. Measurement of the Hb level would give an impression of the degree of blood loss and the need to treat.

note 19
Smears are not indicated in women with excessive and irregular bleeding, in the absence of an abnormal or easily bleeding cervix. For information on the implementation and further course of action, refer to the NHG Practice Guideline 'Cervical smears'.
  Appelman CLM, Bruinsma M, Collette C, Van Weel C, Geijer RM.

note 20
Chlamydia trachomatis may cause cervicitis and subsequently endometritis. Cervicitis may cause contact bleeding, and endometritis may lead to breakthrough bleeding.¹ It is unclear whether breakthrough bleeding is common as a first sign of Chlamydia infection. It is equally unclear whether Chlamydia infections occur more frequently in women with breakthrough bleeding. Nevertheless, it would seem wise to investigate the presence of Chlamydia in breakthrough bleeding for which no cause is apparent, especially in at-risk groups (i.e., women who have different contacts or have a partner who has different contacts).²
  1. Dekker JH, Boeke AJP, Damme D, et al. NHG-Standaard Fluor Vaginalis [NHG


Note 21
In a multicentre study, transvaginal ultrasonography was performed in 1,168 women due to undergo curettage because of postmenopausal bleeding. Only 5.5% of the women with an endometrial thickness of 4 mm or less were found to have an abnormal endometrium upon curettage. None of these involved a malignancy. In a review, Van Niel and Pieters described the value of transvaginal ultrasonography in postmenopausal blood loss, in terms of the diagnosis of endometrial carcinoma. In the studies examined, the selected cut-off value ranged from 4 to 6 mm. The sensitivity was 100% in nearly all the studies, and the specificity ranged from 50 to 85%. There are no known data about the sensitivity and specificity of transvaginal ultrasonography using different cut-off points. In this practice guideline, a threshold value of 4 mm has been chosen in accordance with the guidelines issued by the Dutch Society of Obstetrics and Gynaecology. The risk of missing a case of endometrial carcinoma when applying this threshold value is extremely small, yet it reduces the number of curettages by at least 50%.


Note 22


Note 23


Note 24


Note 25

Flikweert S, Meijer LJ, De Haan M, Wiersma Tj. NHG-Standaard Miskraam (eerste herziening) [NHG Miscarriage Practice Guideline (first revision)].
Huisarts Wet 1997;40:661-70.

Note 26
The American literature includes reports of intravenous administration of conjugated oestrogen in a dose of 25 mg every 4 hours until the bleeding ceases, followed by oral oestrogen plus progestagen. This involved women with such severe blood loss that immediate treatment was essential. For less severe bleeding that can be treated in general practice, the use of high doses of progestagen is a good option. This treatment results in a decrease in bleeding within 8-12 hours and bleeding can be expected to stop within 24-48 hours. The progestogen was chosen on the basis of price. There are very few published comparisons of different types of progestagens.

Various authors recommend the use of a combination of progestagen and oestrogen to treat prolonged excessive bleeding. This advice is based on the theory that in prolonged excessive bleeding, a progestagen alone is no longer sufficient to stimulate maturation of the endometrium. However, support for this theory in the form of comparative research cannot be found. Based on theoretical considerations, 1 sub-50 pill 4 times daily can be used to treat excessive bleeding that has persisted for more than 1 week.


Note 27
A meta-analysis of 31 randomized, controlled trials of the effect of drug therapy on excessive bleeding found that NSAIDs reduced bleeding by 20-30%. There were few reports of side effects. Mefenamic acid (not available in the Netherlands) was studied most extensively. Trials using ibuprofen, diclofenac, and naproxen gave comparable results. Tranexamic acid was found to reduce bleeding by approximately 45%, but was associated with more side effects. Almost all of the available studies on the use of hormonal contraception and excessive bleeding are observational in design. Only one trial could be found. In it, bleeding was reduced by 43%. When administered on days 19-26 of the cycle, the progestogen norethisterone was found not to reduce excessive bleeding. However, in a recent trial in which norethisterone was compared with a levonorgestrel-releasing IUD, norethisterone reduced excessive bleeding by 87%. The drug was taken on days 5-26 of the cycle in a dose of 5 mg 3 times daily. It was suggested that the norethisterone dose and duration of use in the previous studies were inadequate.


Note 28

Note 29
Tranexamic acid is an antifibrinolytic. It is equally effective in the treatment of excessive bleeding for which there is no underlying cause, such as that due to an IUD or a myoma. Side effects (nausea, diarrhoea, and dizziness) occur relatively frequently. There are a few
case reports of intracranial thrombosis with the use of this product.


**Note 30**

Not enough information is available on whether excessive vaginal bleeding recurs after medicinal therapy is discontinued. It is assumed that in some women a normal pattern will develop following an anovulatory period. NSAIDs and antifibrinolytics are only effective during the period when they are being taken. However, the permanent effect of progestagens ('chemical curettage') has also not been proved.

**Note 31**

In one trial, the efficacy of the levonorgestrel-releasing IUD was compared with hysteroscopic resection of the endometrium in 70 women who were referred for a hysterectomy. In the group of women who received the IUD, bleeding decreased by 79% after 1 year, compared with 89% in those who underwent endometrial resection. The IUD was well tolerated. A comparable result was found in another trial in 44 women in whom the IUD was compared with norethisterone on days 5-26 in a dose of 5 mg 3 times daily. After 3 cycles, bleeding had decreased by 94% in the IUD group and by 87% in the norethisterone group. Lähteenmäki et al. investigated the levonorgestrel-releasing IUD in a randomized trial in 56 women for whom a hysterectomy was planned due to excessive bleeding. Women with myomas were excluded from the trial. After 6 months, 64% of the women who received an IUD chose not to have the operation, compared with 14% of the control group.


**Note 32**

Hormonal contraception reduces blood loss due to myomas by 25%. The package inserts warn of the risk that myomas may increase in size. This has been reported in case reports in the literature. However, there are indications of an inverse relationship between hormonal contraception and the development of myomas. A study by Ross et al. found that the longer hormonal contraceptives were taken, the smaller the risk of myomas. The recommendation to administer progestagens in the treatment of excessive bleeding due to myomas is not supported by comparative research but is based on long-term practical experience. Two trials on the effect of NSAIDs (naproxen and ibuprofen) in the treatment of excessive bleeding found that these drugs did not reduce bleeding in women with myomas.


note 33
The effects of tranexamic acid and diclofenac were studied in a double-blind, placebo-controlled trial in 19 women with excessive vaginal bleeding caused by an IUD. Diclofenac reduced bleeding by 20% and tranexamic acid by 50%, but tranexamic acid had more side effects.


note 34
If bleeding does not respond to medicinal therapy, the patient should be referred for further diagnosis by curettage or hysteroscopy. However, curettage has been found to have no therapeutic effect, except for polyps. In a study by Nilsson and Rybo, curettage was performed in 78 women with excessive bleeding. During the 4 cycles after curettage, there was markedly less bleeding only during the first cycle.¹ Hysteroscopic treatment by means of thermal resection of the endometrium is seen as an alternative to a hysterectomy.²


note 35
Over a 2-year period, Feldman et al. followed 263 women who had been examined for postmenopausal or perimenopausal bleeding and in whom no malignancy was found by curettage. In 86 of these women bleeding persisted and when histological examination was repeated, a malignancy was found. After an initial period of postmenopausal bleeding, the spontaneous course of the condition is usually favourable. If bleeding persists or recurs, further investigations are desirable in order to detect treatable benign conditions.