# Guidelines for management of patients under antivitamin K treatment in oral surgery

**Francophone society of oral medicine and oral surgery,**

**with the collaboration of**

**the French society of cardiology**

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# GENERAL METHODOLOGY

## Aim

The variety of references in the literature relating to the hemorrhagic risk following anti-vitamin K (AVK) treatment and the techniques of haemostasis in odontology or stomatology as well as the need of understanding of the thromboembolic risk have lead the Francophone society of oral medicine and oral surgery, in collaboration with the French society of cardiology, to construct a work group with the task of defining the guidelines on the management of patients under antivitamin K treatment in oral surgery.

## Questions asked to the work group

1. What are the indications of AVKs and what are the molecules implicated ?
2. What are the risks of the interruption or the modification of an AVK treatment ?
3. How to evaluate the hemorrhagic risk in oral surgery of a patient under AVK treatment ?
4. How to prevent the hemorrhagic risk in oral surgery in a patient under AVK treatment ?
5. How to treat a hemorrhagic complication in oral surgery in a patient under AVK treatment ?

## Criteria of bibliographic research

**Languages**
1. English
2. French

**Limits**
1. Publications from 1985 through 2005
2. Human studies

**Research (data base)**
1. AFSSAPS (Agence Française de Sécurité Sanitaire des Produits de Santé)
2. ANAES (Agence Nationale d'Accréditation et d'Evaluation en Santé)
3. Bibliodent
4. Bibliothèques
5. Cochrane
6. Embase
7. EMC (Encyclopédie Médico-chirurgicale)
8. HAS (Haute Autorité de Santé)
9. Internet
10. Medline
11. Pascal
12. SFAR (Société Française d'Anesthésie et de Réanimation)
13. SFC (Société Française de Cardiologie)
14. SFMBCB (Société Francophone de Médecine Buccale et de Chirurgie Buccale)

**MeSH (key words)**
1. Anticoagulants
2. Antivitamins K

3. Dental Care
4. Hemorrhage, Bleeding
5. Oral surgery
6. Periodontal surgery
7. Thrombosis
8. Tooth extraction, Dental extraction
9. Vitamin K antagonists

**Journals (systematic study of summaries)**

1. Archives des Maladies du Cœurs et des Vaisseaux
2. British Dental Journal
3. British Journal of Haematology
4. Circulation
5. International Journal of Oral and Maxillofacial Surgery
6. Journal of American College of Cardiology
7. Journal of Cranio-Maxillo-Facial Surgery
8. Journal of Dental Research
9. Journal of Thrombosis and Haemostasis
10. Médecine Buccale Chirurgie Buccale
11. Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodonty
12. Revue de Stomatologie et de Chirurgie Maxillo-Faciale
13. Journal of Heart Valve Disease
14. Thrombosis and Haemostasis

## METHODOLOGY

The elaboration and the redaction of the argumentary and the guidelines of this work were based on the methodology proposed by the European society of cardiology[1]. Each bibliographic reference was analysed while evaluating its methodological quality in order to attribute to each one a scientific proof from A to C. The guidelines are classified according to their power in classes (I, II or III), as based on the level of scientific proof of the studies on which they rely.

| Level of scientific proof of the studies | Power of the guidelines (grade) |
|---|---|
| • **Level A :**<br>Based on the results of several randomised studies with a large number of patients.<br><br>• **Level B :**<br>Based on results from a limited number of randomised studies of a small number of patients, or quality studies, non randomised, or observation data.<br><br>• **Level C :**<br>Based on a consensus of consulting experts. | › **Class I :**<br>In situations where there are proofs and/or a general accord on the efficiency of treatment.<br><br>› **Class II :**<br>In situations where there are contradictory elements and/or divergences in opinions concerning the utility or the efficiency of treatment.<br>· **IIa :** The weight of the proof is rather in favour of the technique.<br>· **IIb :** The weight of the proof is rather insufficient to have an opinion.<br><br>› **Class III :**<br>In situations where there are proofs and/or general agreement to say that the treatment is neither useful nor efficient, eventually harmful. |

## GUIDELINES

## Introduction

Antivitamins K (AVKs) are frequently used in curative or preventive treatment from thromboembolic accidents (arterial or veinous), with the main complication being haemorrhage. Therefore, before a surgical act in oral surgery, the correct attitude to carry out is: transitory interruption with or without alternation with heparinotherapy, or maintenance of the treatment without reduction of the posology. The choice between these different strategies depends on the hemorrhagic risk and the thromboembolic risk that should be evaluated in each patient in order to obtain the best benefice/risk ratio.
Several recent studies proved the possibility to practice acts in oral surgery without interruption or diminution of the posology of the AVKs, however :

- A strict operative protocol has to be respected, and a value of INR (International Normalised Ratio) has to be stable and inferior to 4.
- A systematic use of local haemostasis has to be achieved.
- A continuous postoperative follow-up has to be respected (the patient has to imperatively be able to get hold the address of the clinician or the emergency service). The interruption of the AVKs along with the instauration of a relay with heparin [non fractioned heparins (NFH) or low-molecular weight heparins (LMWH)] during or after the oral surgery is an alternative. This could be a choice in cases where the hemorrhagic risk is high or if the patient is not compliant.

There is no case of aftereffects or of death due to postoperative haemorrhage reported in the literature in patients in which an oral surgery has been performed without modification of the AVK treatment. However, deadly sequels were noted in cases where the AVK treatment has been interrupted or diminished.
The goal of these guidelines is to define an attitude for management of patients under AVK treatment, having to go through an oral surgery.
**These guidelines concern AVKs prescribed on the long term. Patients who suffer from a non stabilised cardiovascular pathology and/or have other constitutional or haemostasis-induced anomalies, as well as patients treated by an association of AVK/antiplatelet drugs are not concerned by these guidelines. These cases require hospitalisation, a pluridisciplinary consultation and a specific haemostasis plan to each particular case.**
These guidelines are addressed to odontologists, stomatologists, general physicians, and specialists (cardiology, haematology, anesthesiology, internal medicine, vascular medicine…).

## Modalities of management of a patient treated by AVKs in oral surgery

1. A preliminary dialogue with the physician responsible of the course of the AVK treatment is imperative. **(I C)**
2. The systematic interruption of the AVK treatment before an oral, periodontal, or implant surgery is not justified. **(I A)**
3. The continuation of the AVK treatment is recommended in oral, periodontal, or implant surgery, unless a medical risk is associated. In that case, the cooperation of the patient and the proximity of hospital service is important, in order to rapidly interfere in case of complications. **(I A)**
4. The value of INR should be stable and inferior to 4. **(I A)**
5. A biological status sheet with amongst others the value of INR should be achieved in the 24 hours that precede the surgery. **(I A)**
6. Techniques of local haemostasis should be systematically performed. **(I A)**
7. The continuity of dental care should be assured. Each patient under AVK treatment and having a hemorrhagic postoperative complication should be able to easily contact a competent physician or a service of stomatology or odontology. **(I C)**
8. Management of these types of patients could be done by private clinicians or practitioners who are in possession of the necessary techniques for local haemostasis, for patients who have an INR value equal to or inferior to 3, and for surgical acts where the hemorrhagic risk is moderate or inexistent. **(I C)**
9. Management of these patients in a hospital environment is recommended if the INR is superior and/or if the hemorrhagic risk is high and/or if there is an associated medical risk **(especially for patients treated by an association of AVK/antiplatelet drugs). (I C)**
10. The instauration of a relay AVK treatment with heparins by NFH or LMWH in a hospital environment, during or after the surgical phase is possible, but should not be the rule. **(II B)**
11. Locoregional anaesthesia is not advisable. Local anaesthesia should contain a vasoconstrictor except in cases of its contraindication. **(I C)**
12. In case of dental extractions, the systematic use of a resorbable intra-alveolar haemostatic material is recommended. Every intraoral wound has to be sutured. Suturing material

could be resorbable or not. Single sutures are preferred. In case of hemorrhagic oral acts, the use of a biological sealant and/or antifibrinolytic agent is recommended. A local compression should be immediately applied postoperatively for least 10 minutes. **(I C)**

**13.** Antibiotic prophylaxis is obligatory when the prevention of infectious endocarditis is indicated. **(I A)**

## Prevention of hemorrhagic risks

**14.** Pain control is done by paracetamol in first intention. Acetylsalicylic acid is contraindicated. Opiates could be prescribed (antalgics of level 2 or 3). Non steroidal anti-inflammatory (NSAI) drugs should not be used for pain control. **(I A)**

If **an anti-inflammatory prescription** is necessary, a short-term corticoid treatment should, in the absence of contraindication, replace the NSAIs.

In the case of an **antiinfectious prescription**, sporadic cases of increases in the value of INR were documented in association with amoxicillin, clindamycine, or erythromycin. Patients should be informed and careful. **(I B)**

Prescription of antibiotics in the prevention of infectious endocarditis does not interfere with haemostasis and should follow the normal course. **(I B)**

The prescription of miconazole in patients with AVK treatment is absolutely contraindicated. **(I A)**

Every other prescription should be investigated for its eventual interaction with AVKs.

## Treatment of postoperative hemorrhagic complications

**15.** In the case of postoperative haemorrhage, surgical intervention is necessary. After local anaesthesia, the wound should be reopened and verified, and procedures of local haemostasis should be recapitulated. **(I C)**

Postoperative guidelines should also be emphasised.

**16.** The investigation of haemostasis should include measures of INR and platelet counting. **(I C)**

**17.** In cases where, despite recapitulation of haemostasis, bleeding continues, the patient should be hospitalised. **(I C)**

# ARGUMENTARY

## Introduction

Antivitamins K (AVKs) are frequently used in the curative or preventive treatment of thromboembolic arterious or veinous accidents. Their use necessitates a regular biological supervision by INR (International Normalized Ratio). A goal value of INR is between 1 and 3. The major complication of the AVK treatment is haemorrhage. Because of that, before an oral, periodontal, or implant surgery, the choice is difficult concerning the attitude to take in these patients: transitory interruption with or without alternation with heparinotherapy, maintenance of the treatment without reduction of the posology. It has to be stressed that whatever attitude is taken, the patient is exposed to an increased thromboembolic risk[2-25]. The increase in that risk is between 0.02% and 1%, varying with various studies and depending on the indication of the anticoagulant treatment[26]. Thromboembolic complications are associated to a morbidity and a mortality which should not be underestimated. Sequels are

found in 70 to 75% of the cases in patients who are victim to a thromboembolic arterial accident and in 4 to 10% of the cases for a thromboembolic veinous accident[26].

**In the literature, there is no case of aftereffects or death due to postoperative haemorrhage in patients in which an oral surgery has been effectuated without modification of the AVK treatment.** Several recent studies[26-57] have confirmed the possibility to practice surgical acts in odontology or stomatology without interruption or modification of the AVK treatment. This possibility necessitates however the installation of a strict operative protocol and a stable INR value.

Means of local haemostasis should be systematically used and the clinician able to correctly manage such situations in case of postoperative haemorrhage. Finally, the continuation of the treatment is imperative; the patient has to always and in anytime is able to contact the practitioner or hospital emergency in case of complications.

The interruption of the AVK treatment after a surgical act should represent an exceptional therapeutic choice and the decision to do so should be taken along with the accord of the treating physician. This strategy should be carefully re-evaluated in patients in whom the thromboembolic risk is weak[9,58,59].

Another alternative is the interruption of the AVK treatment along with its relay with NFH or LMWH before, during and after the surgical act[60-69]. However, it is important to mention that the alternation of the AVK with NFH or LMWH is poorly documented in the literature. No randomised studies actually exist, only case studies[62-64, 70]. Thromboembolic complications were also documented with relay of AVKs with LMWH. This strategy is however still used and could be beneficial in cases where the hemorrhagic risk is very high: high local inflammatory state, multiple extractions, and an extended flap elevation. This method is equally used in cases where the patient is not cooperative.

Management of a patient who is under AVK treatment under general aesthesia is a particular situation. In most cases, general anaesthesia is indicated in cases where the surgical acts are important and when the patient is not cooperative. Therefore, the majority of acts under general anaesthesia are done with a relay treatment of AVKs with heparinotherapy.

The medicolegal aspect of the situation also has to be considered:

- A clear consent of the patient has to be obtained.
- The medical chart of the patient has to always be updated, with details about the clinical situation, incidents and accidents and therapeutic modifications, even very simple ones. All telephonic or oral communications with the different practitioners (cardiologist, vascular physician, general physician) have to also be documented. Finally, it is necessary to note all telephonic communications with the patient.
- A postoperative radiography (retro-alveolar or panoramic according to the act taken) is indispensable.
- Every act has to result in a rapport mentioning all the products used.
- All biological exams and copies of prescriptions have to be conserved.

## Question 1: What are the indications of AVKs and what are the molecules implicated ?

AVKs, synthetic products active by the oral pathway, are currently the most efficient drugs in the prevention of formation or extension of a thrombus to the heart cavities and the vascular system. According to the results of the AFSSAPS, an estimative value of 1-1.5% of the French population receives treatment by AVKs[71-73].

The anticoagulating action of AVKs is an indirect one. It is done through the reduction of the hepatic synthesis of certain procoagulant vitamin K dependant factors: factors II, VII, IX and

X. The extent of anticoagulation obtained depends on the prescribed dose but also the individual susceptibility. This can be appreciated by the Quick time and the INR value. This parameter is independent on the reactive used, which is not the case for the rate of prothrombin. The values required for INR are usually between 2 and 3 when the thromboembolic risk is medium, and between 3 and 4, 5 if it is high[74-77]. The management of the AVKs is a complex process, with two permanent risks : that of not treating the patient in a proper way and thus exposing him/her to thromboembolic recurrences, and the other risk is the case where the dose is excessive and thus the patient is exposed to a hemorrhagic risk, the gravity of which depends on its localisation[78-83]. Annual incidence of general hemorrhagic complications is estimated between 3-5% for the most severe forms and of 0.6% for the deadly forms. In France, it has to be noted that AVKs constitute the number one iatrogenic cause in our country where more than 18 000 hospitalisations and probably 3 000 deaths per year are due to its hemorrhagic risk. The potential severity of this complication obliges to strictly respect the contraindications of that treatment: the existence of an acquired or congenital coagulation disorder, organic lesions that are susceptible to bleed, non-controlled severe high blood pressure, hepatocellular or severe renal insufficiency, the incapacity of the patient to respect the rules of the treatment and its biologic supervision. Most of the indications for AVKs[84-108] concern embolic cardiac pathologies. They are used:

- In patients who suffer from auricular fibrillation and who are older than 65 years, or in younger patients who suffer from mitral valvulopathies or thromboembolic risk factors, patients with a medical history of an ischemic cerebral attack, high blood pressure, diabetes or cardiac insufficiency. Several therapeutic trials propose a value of INR for the AVK treatment between 2-3; this diminishes the embolic risk of at least 60% in patients suffering from auricular fibrillation without a valvular lesion.
- In patients with a valvular prosthesis, when these are mechanical, while maintaining an INR value between 2 and 3 for the aortic prosthesis with a low thromboembolic risk and between 3 and 4.5 for the others; in case of biologic ones, and in the absence of auricular fibrillation, during the first 3 postoperative months with a low level of anticoagulation: an INR value between 2 and 3.
- In patients suffering from severe mitral valvulopathy, particularly with mitral stenosis, in a state of auricular fibrillation or in sinus rhythm, and in the existence of other factors in favour of an embolism as detected by the electrocardiogram or a medical history of a thromboembolic accident. It is therefore recommended to maintain anticoagulation at long term with an INR value between 3 and 4.5
- In patients having a medical history of myocardial infarctus complicated by mural thrombus or embolic dyskinesias.

**Table 1**: Duration of AVK treatment according to the pathology

| Indications | Duration of treatment |
|---|---|
| **Prevention of systemic embolism in case of :** | |
| - Auricular fibrillation<br>• Age > 65 years<br>• Age < 65 years with risk factors | Long term treatment |
| - Biologic valvular prothesis with sinus rhythm | 3 months |
| - Mechanical valvular prothesis | Long term treatment |
| - Mitral valvalopathies (mitral stenosis) with predisposing factors | Long term treatment |
| - Myocardial infarct with mural thrombus or embolic dyskinesias | Long term treatment |
| **Treatment of veinous tromboembolic disease :** | |
| Secondary prevention | 3 to 6 months |
| In case of cancer or multiple recurrences in thrombophilic diathesis | Long term treatment |

Veinous thromboemobolic affections represent the second greatest indication. As secondary prevention, AVKs are prescribed along with heparinotherapy, and should, in the majority of cases, be continued for 3 to 6 months or as a long term treatment in case of cancer or multiple recurrences in a thrombophilic patient. As for primary prevention, they could be prescribed for patients who are immobilised for a long period of time. In both cases the INR value should be comprised between 2 and 3.

The main indications are stated in Table 1 with the recommended duration of the treatment for each one.

Prescription of AVKs should be accompanied by a recapitulative information notebook and an compulsory follow up notebook of the treatment since January 2004 by the physician, biologist or pharmacist. This notebook enables the patient to better understand his/her treatment, answer frequently asked questions, indicates the prescribed treatment with the target INR value and also facilitates the therapeutic follow up of the treatment and the INR value at each examination.

Three molecules are available currently in France: one is a derivative of indanedione, fluindione (Previscan®), and the 2 others are derivatives of the coumarine, acenocoumarol (Sintrom® and Minisintrom®) and warfarine (Coumadine®) (appendix 1).

The delay and the duration of activity of these molecules depend on their rapidity of absorption, their degree of association to plasmatic albumin, their affinity to the hepatic

receptors and the rapidity of their catabolism. Their half-life is variable: short with the acenoucoumarol (8 to 10 hours) and long with the fluindione (31 hours) and the warfarine (35 to 45 hours). Its latency of action is mostly related to the half-life of the K-dependant factors of coagulation, an AVK with a short half-life is no less efficient than an AVK with a long half-life. Although there is no consensus enabling the systematic guidelines of the choice of an AVK with long half-life, there is a wide-spread consensus to consider that these permit a greater stability of coagulation.
The time needed for coagulation to normalise after the interruption of AVKs is also variable according to the molecule used: 1 to 4 days for acenocoumarol, 3 to 4 days for the fluindione and 4 days for the warfarine.

## Question 2 : What are the risks from the interruption or modification of the AVK treatment ?

Transitory interruption, diminution of the posology of AVKs or their relay with NFH or vith LMWH limit the hemorrhagic risk but expose the patient to a thromboemobolic risk with some very serious consequences. Between two thirds and three quarters of embolisms of cardiac origin are of cerebral topography. Sequels are found in 70-75% of the cases in patients with antecedents of an arterial thromboembolic accident and in 4 to 10% of the cases after a veinous thromboembolic accident[26].
The augmentation of the postoperative hemorrhagic risk should be weighed against the consequences of a thromboemobolic accident.
Three therapeutic options should be envisaged for patients under AVK treatment (appendix 2 and 3).
**1- The recommended therapeutic attitude in first intention should include the execution of dental extractions while maintaining an efficient AVK treatment**. A report of 2014 procedures executed in 774 patients with continuation of oral anticoagulants, in which 1964 are dental extractions, reported severe hemorrhagic complications in only 12 patients (1.5%), where more than half were a result of excessive anticoagulation[26]. A recent French study rapports concerting arguments: amongst the 2389 patients having had dental extractions and following an AVK treatment, only 2 patients (0.1%) has a major hemorrhagic complication[36]. A local re-entry was necessary in 34 cases (1.4%), mostly in ambulatory.
Hence, the execution of dental extractions under oral anticoagulant treatment is of low risk since no sequel nor deaths have been reported in the literature. On the contrary, deadly complications were actually described after the interruption of treatment with AVKs. **The execution of dental extractions without modification of the AVKs is currently advised**[26-57].
**2- In cases where this is not possible, the alternative consists of the relay of the AVKs with heparins (NFH or LMWH)** which have long been considered as the option of choice for management of patients having a high thromboemobolic risk, particularly those with mechanical valvular prosthesis. The establishment of a therapeutic window, without an oral anticoagulant, should enable a better control of the local bleeding, while diminishing the thromboembolic risk. This strategy however has to be weighed against the difficulty of balance of the anticoagulant treatment by NFH, which often necessitates a continuous veinous perfusion and thus a hospitalisation for the whole period of treatment. When a subcutanous pathway is used, especially in ambulatory, the difficulty of balance of a treatment by NFH often requires the use of LMWH. Despite some favourable arguments in certain non controlled studies in this domain, the use of LMWH remains controversial in the case of valvular prosthesis where they are not officially approved[32, 109]. The use of LMWH should be particularly cautious in elderly and is contraindicated in patients suffering from renal failure.

In practice, AVKs should be stopped for a period of 3-5 days before the act, NFH or LMWH should start when the INR value is inferior to the therapeutic zone, then the posology is adapted according to the biological chart in order to establish an efficient coagulation (activated partial thromboplastin time to 2 times the control or the activity anti-Xa between 0.5 and 1 U/ml). The use of 2 subcutanous injections of LMWH per day is preferred to 1 single injection. NFH is interrupted 4 to 6 hours before the surgical act and the LMWH 12 hours before, and then resumed 6 to 12 hours after the intervention. AVKs are resumed the same night of the intervention with the association of NFH and LMWH, which should be interrupted once the INR value exceeds 2 in two occasions, at an interval of 24 hours[41,49,110-116].

**3- In rare cases, the transitory interruption of the AVK treatment without alternation with heparins can be possible** in order to limit the hemorrhagic risk. This attitude is applied in north american guidelines in patients having an aortic valvular prosthesis with a very low thromboembolic risk, with an estimation of the thromboembolic risk of 0.1% for 3 days[117, 118]. This estimation can be discussed because it relies on old studies with selected patients. Recent studies confirm that the risk is more important with the interruption of the treatment[119]. In the case of dental extractions, a study of 542 procedures done after the interruption of AVK without heparins relay gave a rate of thromboembolic complications of 1%[26]. **The interruption of AVKs without heparin relay should hence only be envisaged, with the accord of the general physician, in patients with veinous thromboembolic disease or auricular fibrillation without an adjuvant cardiopathy, with a low thromboembolic risk.**

**This modality is highly discouraged and is not recommended in the case of mechanical valvular prosthesis.**

## Question 3: How to evaluate the hemorrhagic risk in oral surgery in a patient under AVK treatment?

The evaluation of the level of anticoagulation is done by calculating the Quick time and is expressed by INR. It is a semi-analytical test which reflects the activity of 3 of the 4 vitamin K-dependent factors (II, VII, X) and the non vitamin K-dependant factor V. The INR [(QT patient/ QT control, to the power ISI: (International Standard Index)] is a way of expressing the Quick time while avoiding discrepancies of results varying with the thromboplastine used and thus the variations in the laboratories[74]. The goal value of INR should be between 2 and 3 for the prevention of systemic embolism, myocardial infarctus with mural thrombus or embolic dyskinesia). A higher value of INR is only necessary for the other mechanical valvular prosthesis or for severe mitral valvulopathies with aggravating factors [32, 126] (Table 2). For these patients, in the majority of cases, dental care could be realised with an INR value between 3 and 3.5 with a closer observation of the INR. INR has to be measured in the 24 hours preceding the surgical act[127]. Dispositions aiming at the auto-measurement of the INR will enable a closer control of the value just one hour before the intervention[128, 129].

**Table 2**: Therapeutic zones of the INR according to the indication of the AVK treatment

| Pathologies requiring an AVK treatment | Therapeutic zone of the INR |
|---|---|
| Prevention of systemic embolism in the case of: | |
| • Auricular fibrillation | 2-3 |
| • Biologic valvular prosthesis | 2-3 |
| • Mechanical aortic prosthesis with a low embolic risk* | 2-3 |
| • Other mechanical valvular prosthesis | 3-4.5 |
| • Severe mitral valvulopathies with predisposing factors | 3-4.5 |
| • Myocardial infarctus with mural thrombus or embolic dyskinesia | 2-3 |
| Treatment of the veinous thromboembolic disease | 2-3 |

*Double wing prosthesis, a patient with sinus rhythm without history of embolic disease

Several studies show the possibility of achievement of simple dental extractions simply with the application of local haemostasis in the case where the INR value is inferior to 4[120, 130, 131]. **Factors inciting hemorrhagic accidents in patients under AVK treatment are numerous**[132-138] and require accentuated care without really being considered as contraindications :

- Associated pathologies: severe renal insufficiency (creatinine clearance lower than 20ml/mn), severe cardiac insufficiency, ischemic cerebral accidents, and non-controlled high blood pressure.
- Any affection that could interfere with the metabolism of AVKs and cause its excessive dosage: biliary or hepatic affection (cholestase), destruction of the intestinal flora (antibiotics, diarrhea).
- Associated medication: risk of potentialisation or inhibition of the action of AVKs.
- The association of AVKs with antiplatelet drugs is often found in valvular prosthesis and in patients in possession of active coronary endoprosthesis or with a high thromboembolic risk. **This requires an ambulatory management and a formal contact with the cardiologist.**
- Age: hemorrhagic accidents are more frequent in patients after 65 years of age and more severe in patients after 75 years of age.

## Question 4: How to prevent the hemorrhagic risk in oral surgery in patients undergoing AVK treatment?

It has long been proposed to interrupt the anticoagulating treatment in patients before dental extractions. This attitude is dangerous for the patient and comprises a very high risk of thromboembolic complications[28, 29].

It is only in situations where the surgical hemorrhagic risk is very high and predictable according to the act (Table 3), that it is feasible to alternate the AVK treatment with NFH and LMWH[139, 140] before, during and after the surgical phase in a hospital environment and when the INR value that is superior or equal to 3. The surgical act has to be postponed in cases where the INR is greater than 4 and, for these patients, one can require an INR lower than 4 for the day of the surgery and then 3 postoperative days.

**Table 3**: Evaluation of the hemorrhagic risk and the code of behaviour according to the type of act to achieve

| | |
|---|---|
| **Acts without a hemorrhagic risk**<br>• Conservative treatment<br>• Supragingival prosthetic treatment<br>• Para-apical, intraligamentary or intraseptal anaesthesia<br>• Scaling | **Code of behaviour**<br>No particular measure other than the awareness of the eventual infectious risk (prevention of endocarditis)* |
| **Acts with moderate hemorrhagic risk**<br>• Extraction in the same zone<br>• Single implant<br>• Sufacacage | **Code of behaviour**<br>• Local intra-alveolar compression with a haemostatic material.<br>• Sutures<br>• Tranexamic acid (compression and/or passive rinsing)<br>• Biologic sealant is advised if INR is superior to 3 |
| **Acts with a high hemorrhagic risk**<br>• Extraction of more than 3 teeth<br>• Extraction in different quadrants<br>• Periodontal or mucogingival surgery<br>• Disinclusion with a chirurgico-orthodontic traction<br>• Extraction of temporary teeth<br>• Extraction of teeth with deficient periodontal status<br>• Extraction of teeth in an inflammatory zone<br>• Extraction of inclused teeth<br>• Multiple implants<br>• Enucleation of cysts or periapical surgery<br>• Biopsy | **Code of behaviour**<br>**1) If INR is inferior to or equal to 3:**<br>• Local intra-alveolar compression with a haemostatic material<br>• Sutures<br>• Tranexamic acid (compression and/or passive rinsing)<br>• Biological sealant recommended<br><br>**2) If INR is superior to 3:**<br>• Alternative treatment of AVK with NFH or LMWH in a hospital setting<br>• Local intra-alveolar compression with the haemostatic material<br>• Sutures<br>• Systematic biologic sealant<br>• Tranexamic acid (compression and/or passive rinsing) |
| **Contraindicated acts**<br>• Free gingival graft<br>• Acts that are contraindicated according to the consensus conference in the prevention of infectious endocarditis if these measures are required<br>• All acts that represent a hemorrhagic risk in the case where the technical setting is insufficient<br>• Discouraged: locoregional anaesthesia of the inferior alveolar nerve | |

| | |
|---|---|
| ***Reminder of the modalities of the antibioprophylaxis in the prevention of infectious endocarditis (under local anaesthesia)[141]*** | • In the absence of allergy to penicillin<br>- 3g per os 1 hour before the act<br>• In case of allergy to penicillin<br>- 1g pristinamycin per os 1 hour before the act<br>- 600mg of clindamycin per os 1 hour before the act |

Several recent studies have demonstrated the possibility to manage patients under AVK treatment without modification of their treatment before any oral, periodontal, or implant surgery[26-57]. Patients undergoing these acts would have an INR value that is stable and inferior to 4[26, 56, 59, 127, 131, 142].

The protocol for these patients is as follows (appendix 4):

- A sedative premedication is recommended.
- In the absence of contraindication, local anaesthesia should include a vasoconstrictor agent[143]. It could be applied in para-apical, intraseptal, or intraligamentary technic. Locoregional or Spix anaesthesias are discouraged in order to prevent risks of pharyngeal haematoma[144, 145].
- Surgical phase should be as atraumatic as possible.
- Osseous septa and mucosal extremities should be regularised.
- Granulation tissues as well as granulomas or cysts should be curetted in their totality.
- A local haemostatic resorbable agent should be placed locally in every alveolus. This could be native collagen, gelatine or oxycellulose, in patients without an infectious risk. Direct contact of the bone with the oxycellulose should be avoided[130, 146-150, 177].
- Wounds have to systematically be sutured (silk, polyamide, polypropylene). Sutures have to be single and separate. Resorbable sutures have to possibility to be removed without re-entry. Continuous sutures should be avoided because the risk of bleeding is more important when sutures release.
- A local compression has to be applied for at least 10 mn[151, 152].
- It is recommended to use a compress that is impregnated with tranexamic acid 5% to perform a local postoperative compression[153-155]. Nevertheless, the use of an antifibrinolytic agent after the surgical act (tranexamic acid), **in association with the other local haemostatic measures**, did not prove to significantly diminish postoperative bleeding[130].
- A biological sealant should be used in addition to the local haemostatic agent and sutures in rare cases where INR is greater than 3 and/or if the act is judged as highly hemorrhagic[54, 152, 156-163]. **This product necessitates to be managed in a hospital environment and is delivered exclusively by the hospital pharmacy service.**
- Non-biologic sealant should be avoided[177].
- Silicon or resin compression splints represent a supplementary compression technique[36, 149, 150, 164].

Appendix 5 displays the different active oral haemostatic medications that are available in France.

It is preferred to program the surgical act in the morning, in the beginning of the week, in order to more easily control eventual postoperative hemorrhagic risks and keep the patient under continuous supervision till the complete interruption of the bleeding.

The management of AVKs treated patients that are not in a hospital environment is the same: patient has to be accompanied, living within less one hour of a health care institute, in a state that enables him/her to understand and observe postoperative prescriptions and advices. In case any of these conditions are not fulfilled, the surgical act has to be accomplished during the hospitalisation of the patient.

**For the postoperative phase**, instructions have to be communicated to the patient (appendix 6)

- Protect the clot within the first 3 hours of the surgical act by staying at rest.
- Not to rinse the mouth within the 24 subsequent hours.
- Not to disturb the clot by suction movements or with the help of iatrogenic objects (tooth pick).
- Not to smoke nor drink alcohol.
- Not to eat or drink hot food or beverages in the first days.
- In case of recurrence of bleeding, a local compression with tranexamic acid 5% for at least 10 min has to be applied. If bleeding persists despite the local compression, the practioner has to be contacted and surgical re-entry might be necessary.
- Follow up has to be insured in case of postoperative bleeding. The patient has to have the necessary contact information in hand.
- A control has to be realised on the 3$^{rd}$ day.

**An operative report has to be handed to the patient** (appendix 7). This should include the latest known value of the INR prior to surgery, the nature of the surgical act and the haemostatic protocol employed. This enables every practitioner to be aware precisely of the patient's situation.

**Postoperative medications** could also create interactions with the AVKs[165, 166]. For this category of patients, pain control is done through paracetamol in the first intention. Acetylsalicylic acid is contraindicated, as well as non-steroidal antiinflammatory (NSAI). Opiates could be prescribed in cases where pain is more important (antalgics of level 2 or 3).

If an antiinflammatory prescription is necessary, short-term corticoids should be indicated in cases where the patient does not have any contraindications to such treatment.

In case, for infectious reasons, amoxicillin is prescribed, studies have shown the increasment of the INR values[167-169]. Nevertheless, it does not seem to have an effect on the risk of postoperative bleeding. Metronidazole however does interact with AVKs and should be prohibited. Erythromycin interacts with derivatives of coumarine in a systematic basis, and certain patients manifest strong interactions[170-173]. However, in general, antibiotics do not modify the INR value. If their use comes to be necessary, they can be prescribed along with a closer control of the INR.

Some substances, such as barbiturics, diphenylhydantoine or rifampicine, are inhibitors of the action of AVKs; their interruption can produce an increase in the value of INR[134].

## Question 5: How to treat a hemorrhagic complication in a patient under AVK treatment in oral surgery?

Hemorrhagic accidents occur approximately in 1.5% of the cases when AVKs are not interrupted and when their posology is not modified[26, 36]. The management of a postoperative haemorrhage in a patient that is under AVK treatment relies above all on a local control of the bleeding. Surgical re-entry is often the solution. The operative zone is re-opened after anaesthesia, and the intra-alveolar compression material is pulled out. This act permits to better visualise the bleeding and detect its source. Then the initial protocol

is resumed. An intra-alveolar haemostatic material is applied, sutures, local compression and a local antifibrinolytic agent could be executed during the healing period[154, 174-181]. A biological sealant can be used if necessary.

A biological exploration of the haemostasis is required for a more precise identification of the INR of the patient. If a non-controlled bleeding occurs after surgical re-entry:

- The patient should be hospitalised for better supervision and management.
- AVKs are interrupted till the moment where the haemorrhage is controlled. This could be associated with the administration of vitamin K1 per os which allows a slow correction (6 to 8 hours) of the INR, depending on the half life of the AVK of the patient[182]. Vitamin K1 should never be used in patients with valvular prosthesis except for cases of extreme emergency, the thrombosis risk being very high. The administration of vitamin K1 intraveinously is not recommended because it can cause a severe anaphylactic reaction or resistance to AVKs. In addition, the veinous pathway is probably faster but definitively not more efficient than the oral pathway[183]. In cases of severe haemorrhages which are difficult to control and which incite a vital risk, the administration of prothrombotic complexes (concentrates of factors II, VII, IX, and X: (PPSB) and proteins C-S) could be recommended in addition to vitamin K1.
- The administration of NFH or LMWH should be started as soon as possible after the interruption of bleeding. The AVK treatment should resume afterwards.

## Proposition of a work group

As a conclusion to this work, the members of the work group suggest the following:

1- To realize studies of evaluation of the methods of management of patients under AVK treatment in oral surgery.
2- To complete the diffusion of these guidelines by courses of continuous education.
3- To include a specific page to these guidelines in the information booklet for patients under AVK treatment.
4- To establish a list of hospital services which are able to manage urgent cases of patients under AVK treatment as well as a list of clinics of anticoagulation
5- To evaluate health economies that could be encouraged by these guidelines and hence to promote a specific identification of a quoted value for the justified use of local haemostatic means.

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**Appendix 1:** List of AVKs prescribed by oral intake currently commercialised in France

| International common denomination | Speciality name | Indications |
|---|---|---|
| ***Derivatives of indanedione*** | | • Embolic cardiopathies<br>• Myocardial infarctus<br>• Treatment of deep veinous thrombosis and pulmonary embolism<br>• Prevention of veinous thrombosis and pulmonary embolism during hip surgery<br>• Prevention of thrombosis by catheter |
| Fluindione | PREVISCAN® 20 mg | |
| ***Derivatives of coumarine*** | | |
| Acenocoumarol | SINTROM® 4 mg<br>MINISINTROM® 1 mg | |
| Warfarine | COUMADINE® 2 mg, 5 mg | |

**Appendix 2:** Location of management of patients under AVK treatment

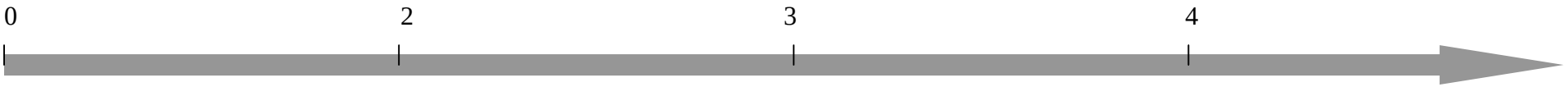
| | Acts with a moderate or no hemorrhagic risk | Acts with high hemorrhagic risk |
|---|---|---|
| **INR inferior or equal to 3** | Private practice | Hospital care |
| **INR between 3 and 4** | Hospital care | Hospital care |

These guidelines are limited to AVKs that prescribed on the long term, patients suffering from non stabilised cardiovascular disease and/or having other constitutional or induced anomalies as well as patients treated by the association AVK/ antiplatelet drugs and those that are dealt with in the emergency service are not concerned by these guidelines. These particular cases require hospitalisation, a pluridisciplinary consultation and a specific haemostasis for each case.
When these patients are dealt with in private practice, care should be limited to acts without or with a moderate hemorrhagic risk.

**Appendix 3:** Decisive tree

These guidelines are limited to AVKs that prescribed on the long term, patients suffering from non stabilised cardiovascular disease and/or having other constitutional or induced anomalies as well as patients treated by the association AVK/antiplatelet drugs and those that are dealt with in the emergency service are not concerned by these guidelines. These particular cases require hospitalisation, a pluridisciplinary consultation and a specific haemostasis for each case.

Value of INR




**Re-equilibrate AVKs, no immediate act**

Refer to physician responsible for the AVK treatment

The operative act is feasible without necessary modification of the AVK

**If the act comprises a moderate hemorrhagic risk:**

- Local haemostasis
- Sutures
- Tranexamic acid (compression and/or passive rinsing)

Private practice

**If the act comprises a high hemorrhagie risk:**

- Local haemostasis
- Sutures
- Biologic sealant is advised
- Tranexamic acid (compression and/or passive rinsing)

Hospital care

**If the act comprises a moderate hemorrhagic risk:**

- Local haemostasis
- Sutures
- Biologic sealant is advised
- Tranexamic acid (compression and/or passive rinsing)

Hospital care

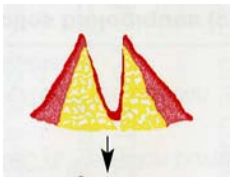
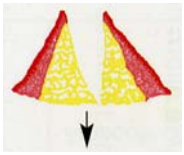
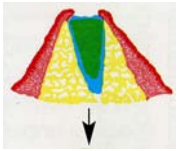
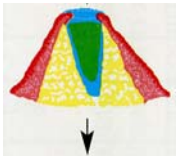
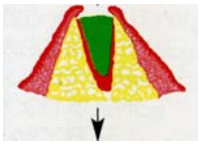
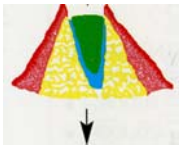
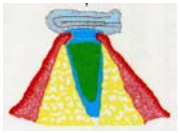
**If the act is classified as one with a high hemorrhagic risk and /or if the patient is not cooperative:**

- Hospitalisation
- Alternate AVK with NFH or LMWH
- Local haemostasis
- Sutures
- Biological sealant systematically
- Tranexamic acid (compression and/or passive rinsing)

Hospital care

**Abstention from an immediate act** and re-stabilise INR to < 4 till the day of the surgery till the 3rd day post-operative

**Appendix 4 :** Protocols of local haemostasis

| **Acts without or with moderate hemorrhagic risk and an INR inferior to or equal to 3**<br>Private practice | | **Acts with a high hemorrhagic risk or an INR between 3 and 4**<br>Hospital care | | | |
|---|---|---|---|---|---|
|  | 1) Open wound following the surgical act |  | 1) Open wound following the surgical act |  | 5) Mucosal sutures |
|  | 2) Placement of a local resorbable haemostatic agent in each alveolus |  | 2) Placement of a local biological sealant at the contact of the bone |  | 6) Placement of a local biological sealant at the surface while countersinking the sutures |
|  | 3) Mucosal sutures |  | 3) Placement of a local resorbable haemostatic agent in each alveolus |  | 7) Compression and tranexamic acid in compression or passive rinsing |
|  | 4) Compression and tranexamic acid in compression or passive rinsing |  | 4) Placement of a local biological adhesive at the surface | | |

Schemas : Frachons *et al.* (177)

**Appendix 5:** List of active haemostatic medications by local application available in France

| Designation | Composition | Forms and presentations | Mechanism of action | Use |
|---|---|---|---|---|
| **Local resorbable haemostatics** | | | | |
| GELFOAM®,<br>GELITA®,<br>CURASPON® | Gelatine from a porcine origin | • Sponge | These molecules stimulate the platelet adhesion and the coagulation system (activation of factor XII, kininogen of low molecular weight) | Place with a compression force in the alveolus and maintain with sutures |
| PANGEN®,<br>COLLAGENE Z®,<br>CURACOLL®,<br>BIOCOLLAGENE®,<br>ETIK COLLAGENE®,<br>HEMOCOLLAGENE®,<br>BLEED-X®, ANTEMA® | Collagen from a bovine origin | • Compresses<br>• Sponge<br>• Powder<br>• Reserved for hospital use (PANGEN®) | | |
| SURGICEL®, CURACEL-I® | Regenerated oxidised cellulose | | Local compression | |
| **Antifibrinolytics** | | | | |
| EXACYL® drinkable solution<br>SPOTOF® Gé drinkable solution | Tranexamic acid | • Syringe of 10m | Tranexamic acid inhibits fibrinolysis (inactivation of plasmine after an irreversible fixation to plasminogen, impregnate the compress then squeeze or use a passive buccal rinsing) | |
| **Biologic sealants (fibrin sealants)** | | | | |
| BERIPLAST®<br>BIOCOLL®<br>TISSUCOL® | • Solution A:<br>· fibrinogen<br>· fibronectine<br>· aprotinine of bovine origin<br>· factor XIII<br>· human plasminogen<br>• Solution B<br>· human thrombin | • Kit of 1ml, 2ml, 5ml<br>• When mixing the 2 solutions, a viscous solution forms which rapidly transforms into an elastic gel, of white colour, strongly adhering to tissues<br>• Reserved exclusively for hospital use (traceability) | Fibrin sealants produce the final phase of coagulation (transformation of fibrinogen to fibrin through the action of thrombin, stabilisation of the clot by the XIII factor) inhibiting the fibrinolysis (aprotinine) | Place in the alveolus and maintain with sutures |

**Appendix 6:** An example of information and postoperative guidelines that could be handed to the patients

*This document is destined to inform you on the maintenance of your anticoagulant treatment, its advantages and risks. We recommend you to read it carefully.*

**What are the advantages of the preservation of your anticoagulation treatment?**
Daily intake of your anticoagulant treatment limits the risk of recidivism of a thromboembolic accident. Its interruption, even for few days, for a dental extraction, implies a certain risk. Hence, its maintenance is justified and preferable.

**What are the inconveniences and risks related to its continuation?**
The preservation of your anticoagulant treatment increases the risk of postoperative bleeding. This however is easily limited during a dental extraction by local means. On the contrary, the stabilisation of the clot with time necessitates form your side the application of certain precautions:

**What are the post-operative measures that should be respected?**

WHAT YOU SHOULD DO:
- Apply a glass pouch against the operated region, as soon as possible after the surgical act.
- Privilege soft food cold or tepid during the first week following the act.
- Brush normally your teeth while avoiding the operated zone.

WHAT YOU SHOULD NOT DO:
- Smoke or drink alcohol since it postpones healing.
- Drink or eat hot food or beverages in the first days.
- Do antiseptic mouth rinses the day of the surgical act.
- Do antiseptic mouth rinses in order to stop the bleeding.
- Touch the wound with the tongue, aspirate or spit.

DO NOT WORRY IF:
- You see in the first days a blood stain on your pillow.
- You spit bloody saliva in the first days.
- You have a ‘blue’, an ecchymosis.
- You bleed: bite on a sterile compress during 20min. To renew if necessary.

IN CASE OF NON COTROLABLE BLEEDING:
- You should contact us on the following number ……..…….
- In case of absence, don’t hesitate to contact the emergency service of the hospital or consult your general physician.

**Appendix 7:** Example of an operative report that could be handy to the patient

*The goal of this document is to inform every practioner on the surgical act that you have gone through. We recommend you to closely keep it and present it if necessary.*

**Date of the surgical act:**

**Place and practitioner having performed the surgical act (name, address, telephone):**

**Type and posology of the anticoagulant treatment:**

**Other treatments the patients is taking:**

**Allergies presented by the patient:**

**Date and value of the latest INR:**

**Type of the surgical act:**

**Classification of the hemorrhagic risk:**

**Protocol of the local haemostasis used:**

**Postoperative prescription:**