

Antibiotic Prescription Practice in Endodontics; A Cross Sectional Study

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Abstract

To investigate the pattern of antibiotic prescribing practice among endodontists in Jordan and to evaluate their adherence to internationally accepted guidelines regarding therapeutic and prophylactic use of antibiotics.

An online survey instrument was designed, piloted, and pretested to collect information about types, indications, doses, and duration of antibiotic use by specialist endodontists. Data were analyzed using descriptive statistics and chi square test at $p < 0.05$.

The response rate was 83.1%. The first-choice antibiotic was amoxicillin with clavulanic acid (49.2%), while clindamycin was the preferred antibiotic for penicillin-allergic patients (83.6%). Respondents routinely prescribed antibiotic for acute apical abscesses with systemic involvement (100%), replantation of avulsed teeth (73.8%), and those at risk of developing infective endocarditis (86.9%). Most endodontists (70.5%) followed the American Association of Endodontists' guidelines on antibiotic prescription. 6.6% followed the regulations of the European Society of Endodontology, while 9.8% did not follow any guidelines.

Inappropriate prescription of antibiotics is common among endodontists. Emphasis should be placed on improving the knowledge of endodontists about available guidelines and indications of antibiotic use in the prophylaxis and management of endodontic diseases.

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Introduction

Endodontic pathology is caused by a polymicrobial infection of gram-positive, gram-negative, facultative aerobes and strict anaerobic bacteria¹. In initial disease stages, the pulp undergoes an inflammatory reaction to halt the progression of infection within the root canal system². If the condition is not treated, the pulp succumbs to necrosis and the root canal space becomes infected³. Consequently, different forms of inflammatory reactions can take place in the peri-radicular tissues, depending on the balance between virulence of infection and host defense reaction⁴.

Management of endodontic infections aims to eradicate pathogens and create an intra-

radicular environment that allows for peri-radicular healing using local measures of root canal debridement and the provision of fluid-tight apical and coronal seals⁵⁻⁷. In some cases, when the peri-radicular inflammatory reaction is severe, spreading and/or with systemic involvement (fever, malaise, lymphadenopathy, trismus), antibiotics prescription may be needed as an adjunct treatment measure^{8,9}.

When appropriately prescribed, antibiotics can limit the spread of infection, control signs and symptoms of acute infection and reduce serious complications of endodontic diseases such as infective endocarditis and prosthetic joint implant infection¹⁰. However, the use of antibiotics is associated with serious side effects, allergic reactions, microbial resistance, and increased cost. Dentists were responsible for 10% of the total antibiotic prescription in the United States and Europe^{11,12}, and half of dental prescriptions of antibiotics have been estimated to be inappropriate^{13,14}.

In endodontics, guidelines on antibiotics prescription vary across the world¹⁵⁻¹⁷.

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The European Society of Endodontology (ESE) recently published a position statement regarding antibiotic prescription in endodontics¹⁶. It included guidelines on systemic and topical use of ABs as well as antibiotic prophylaxis in endodontics. The American Association of Endodontists (AAE) recently updated their position statement on antibiotic prophylaxis based on recommendations from the American Heart Association (AHA) and American College of Cardiology (ACC), which reinforced their previous recommendations that antibiotic prophylaxis should be prescribed to patients at higher risk of developing infective endocarditis (IE)^{10, 15}. In the UK, the National Institute for Health and Care Excellence (NICE) guidelines are more restrictive on antibiotic prophylaxis for patients at risk of developing IE. They stated that "antibiotic prophylaxis against infective endocarditis is not recommended routinely for people undergoing dental procedures"¹⁷.

The general world-wide consensus is to limit the use of antibiotics to immunocompromised patients and those with rapidly progressing infection and/ or systemic signs and symptoms of infection^{9,15}.

Cross-section observational studies have highlighted inappropriate prescription patterns among dentists in different parts of the world^{18,19}.

This included unwarranted antibiotic prescription, and inappropriate dosage and prescription time²⁰. Zadik and Levin demonstrated that 5.9% and 10.6% of Israeli general dentists routinely prescribed antibiotics following root canal treatment and retreatment respectively²¹. Sweeney et al showed that only 8.2% of dentists prescribed penicillin V for acute dental infections²². While 5.6% of dental prescriptions in England were for combinations of antibiotics, the most frequent combination being amoxicillin and metronidazole²³. In the UK, dentists prescribed 10% of all the antibiotics issued in the National Health Service general practice in 2016. Many of these prescriptions were deemed inappropriate²⁴. Guidelines and policies to control antibiotics use in developing countries are generally lacking, leading to high prevalence of inappropriate antibiotic prescription and microbial resistance. In the present study we aimed at investigating the pattern of antibiotics prescription among endodontists in Jordan and their adherence to internationally accepted guidelines and at exploring influencing factors, if

any. Findings of the present study should help to develop policies regarding antibiotics prescription in endodontics in Jordan.

Materials and methods

This study was performed in accordance with the World Medical Declaration of Helsinki. An ethical approval was obtained from the institutional review board at the University of Jordan Hospital (IRB no. 10/2018/3638) without the need for participants' written consent.

A survey instrument was designed after reviewing the relevant literature on the use of antibiotics in endodontics. It was pilot tested and validated on a group of endodontists (n=10) to confirm clarity and reproducibility of responses and to avoid interpretation bias. This descriptive research satisfies the recommendations by Kelley et al 2003 regarding good practice in the conduct and reporting of survey research in terms of having a clear research question(s) and a cover letter explaining the purpose and details of the study, design of the research tool, piloting, data collection and reporting, and research ethics²⁵.

The final online questionnaire (Appendix 1) comprised questions that covered the following main aspects:

- Demographic & background information.
- The antibiotic of choice, course duration and guidelines followed (if any).
- Antibiotic prescription for the medically compromised patients.
- Antibiotic prescription in different endodontic conditions.

The questionnaire was distributed electronically to all Jordanian endodontists who were members of the Jordanian Endodontic Society (JES) (n=75). Retired endodontists were excluded. To increase response rate, all members were contacted by phone, and the purpose and significance of the study were explained. Two reminders were sent at two-week intervals. The responses were manually checked and compared to the list of endodontists invited to complete the survey to prevent multiple entries from the same individual as recommended by Eysenbach, G. 2004²⁶. No multiple entries from the same individual were detected. Responses were collected as excel sheet which was converted into SPSS file (SPSS Statistics 19 for

Windows, SPSS Inc., Chicago, IL, USA). Statistical analysis was performed using descriptive statistics and the chi-square test at 0.05 significance level.

Results

Response rate & demographic characteristics

Out of the 75 endodontists in the JES, 61 completed the online questionnaire resulting in a response rate of 83.1%. The study sample was composed of 35 males (57.4%) and 26 (42.6%) females. Nearly half of the participants (n= 27) completed their postgraduate training in Jordan, while the rest completed their endodontic training in different parts of the world (Table 1).

| Location | UG training number (%) | PG training number (%) |
|--------------------------------|------------------------|------------------------|
| Jordan | 48 (78.7%) | 27 (44.3%) |
| Arab country (except Jordan) | 8 (13.1%) | 7 (11.5%) |
| United States | - | 1 (1.6%) |
| United Kingdom | - | 18 (29.5%) |
| Europe (except UK) | 3 (4.9%) | 4 (6.6%) |
| Australia and New Zealand | 1 (1.6%) | 3 (4.9%) |
| Asia (except Arab countries) | 1 (1.6%) | - |
| Africa (except Arab countries) | - | 1 (1.6%) |

Table 1. Location of undergraduate and postgraduate training of the responding endodontists. (UG: undergraduate, PG: postgraduate).

| Antibiotic | Non-penicillin-allergic | Penicillin-allergic |
|----------------------------------|-------------------------|---------------------|
| Penicillin | 6 (9.8%) | - |
| Amoxicillin | 17 (27.9%) | - |
| Amoxicillin with clavulanic acid | 30 (49.2%) | - |
| Clindamycin | 3 (4.9%) | 51 (83.6%) |
| Metronidazole | 3 (4.9%) | 1 (1.6%) |
| Cephalosporin | - | 1 (1.6%) |
| Tetracycline | - | 1 (1.6%) |
| Azithromycin | - | 4 (6.6%) |
| Clarithromycin | - | 1 (1.6%) |
| Lincomycin | 1 (1.6%) | 2 (3.3%) |
| Other | 1 (1.6%) | - |

Table 2. First-choice antibiotic prescribed for penicillin-allergic and non-allergic patients.

Type of antibiotic and course duration

Most respondents chose amoxicillin either with clavulanic acid (49.2%) or plain (27.9%) as

their first-choice antibiotic (Table 2). There were no association of this choice with any of participants' demographic information ($p>0.05$). Regarding patients allergic to penicillin, 51 endodontists (83.6%) chose clindamycin as their first-choice antibiotic, while azithromycin, lincomycin, cephalosporin, tetracycline, metronidazole and clarithromycin were also chosen (Table 2). Ninety per-cent of respondents reported that they prescribe antibiotics for 5-7 days. A short prescription time of up to 4 days was reported by only 6.6% of the endodontists, while 3.3% of them reported that they prescribe antibiotics for more than one week.

Guidelines adopted for prescribing antibiotics

The majority of respondents (70.5%) followed the AAE guidelines when prescribing antibiotics. while 13.1% and 6.6% reported that they abided by the NICE and the ESE guidelines, respectively. Around one in ten endodontists reported that they did not follow any guidelines and instead relied on anecdotal experience for antibiotic prescription (Figure 1-3).

Among those who followed the AAE guidelines, the percentages of those who had completed their postgraduate training in Jordan, and Arab countries (89.9% and 87.5%, respectively) was significantly higher than those who were trained in the UK or Europe (44.5 and 50%, respectively) ($p=0.006$). However, there was no association between the adopted guidelines and other demographic categories ($p > 0.05$).

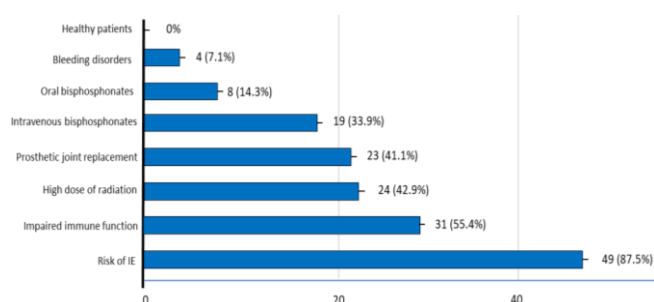


Figure 1. Percentages of endodontists who prescribe antibiotic prophylaxis in different medical conditions prior to endodontic treatment.

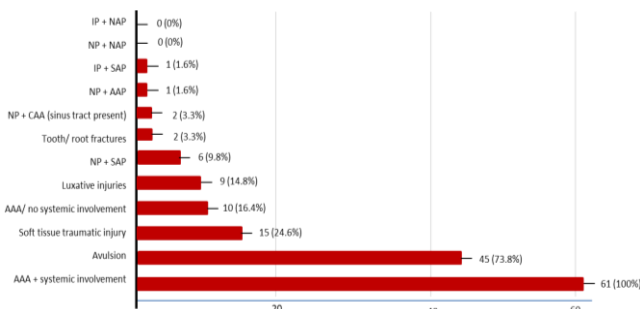


Figure 2. Different clinical diagnoses and the percentages of endodontists who prescribe antibiotics as part of their management. (*IP: irreversible pulpitis, NAP: normal apical tissues, SAP: symptomatic apical periodontitis, NP: necrotic pulp, AAP: asymptomatic apical periodontitis, AAA: acute apical abscess, CAA: chronic apical abscess*).

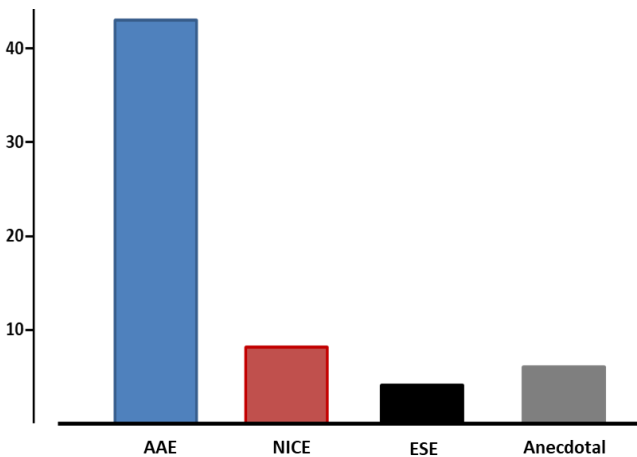


Figure 3. Bar chart showing the numbers of endodontists in Jordan following different international guidelines regarding antibiotic prescription. (*AAE: American Association of Endodontists, ESE: European Society of Endodontology, NICE: National Institute for Health and Care Excellence*).

Antibiotic prescription for the medically compromised patients

6.6% and 13.1% of respondents reported prescribing antibiotics for patients with bleeding disorders and those receiving oral bisphosphonates respectively. However, a significantly greater proportion (31.1%) reported prescribing antibiotics for patients receiving intravenous bisphosphonates ($p < 0.05$), with no significant correlation with their demographic categories ($p > 0.05$).

Most respondents (80.3%) prescribed antibiotics for patients at risk of developing IE,

while 50.8% of them prescribed antibiotics for patients with impaired immunity, without correlation with any of respondents' demographics ($p > 0.05$). While the majority who followed the AAE and ESE guidelines, (93% and 60% respectively) prescribed antibiotics in case of IE, most of those who followed the NICE guidelines (62.5%) did not do so ($p < 0.001$).

In case of patients undergoing radiation therapy or those with prosthetic joints, there were no significant difference ($p = 0.096$) between the percentages of endodontists who chose to prescribe antibiotics (39.3% and 37.7%, respectively) and those who did not (60.7% and 62.3%, respectively). In case of prosthetic joints, while none of those who follow the NICE guidelines prescribed prophylactic antibiotics, 30% and 46.5% of those who followed the ESE and the AAE guidelines, respectively, reported to prescribe antibiotics before endodontic treatment ($p = 0.038$).

Antibiotic prescription for pulpal and periapical pathology

None of the respondents reported prescribing antibiotics for irreversible pulpitis. Most respondents did not prescribe antibiotics in cases of necrotic pulp (NP) with normal apical tissues (NAT), necrotic pulp with symptomatic apical periodontitis (SAP), necrotic pulp with asymptomatic apical periodontitis (AAP) or chronic apical abscess (CAA) (93.4%, 96.7%, 98.4% and 96.7% respectively). While all respondents (100%) prescribed antibiotics for patients with acute apical abscess (AAA) with systemic manifestations such as fever, malaise, lymphadenopathy or trismus.

Regarding traumatic injuries, the percentages of endodontists prescribing antibiotics ranged from 3.3% and 13.1% with luxation and tooth fracture respectively, to 24% and 73% in cases of soft tissue injuries and avulsion, respectively ($p < 0.001$). The highest proportion (94.4%) who did not prescribe antibiotics in case of soft tissue injuries was within those who had their postgraduate training in the UK ($p = 0.045$).

Discussion

Because of the small final population size, it was feasible to contact each potential participant by phone to explain the aim of our study and to encourage their participation. Our

response rate was high (83.1%) which is representative of the population of endodontists in Jordan.

Antibiotic prescription is an important adjunctive measure in the management of AAA with systemic signs and symptoms (fever, malaise, lymphadenopathy, trismus), replantation of avulsed teeth and management of soft tissue injury, as they help prevent the spread of infection^{15,16}. On the other hand, in healthy patients, cases of necrotic pulp, apical periodontitis (symptomatic or asymptomatic), chronic apical abscess and acute apical abscess without systemic involvement should be treated with local measures without antibiotic prescription¹⁹. The infection, in such cases, is usually confined to the root canal system, and therefore local measures of chemo-mechanical disinfection, with or without drainage of purulence are usually sufficient. Antibiotics provide no additional benefit as the lack of blood supply in the root canal prevents the delivery of antibiotics within the root canal, which renders them ineffective in eliminating the infection²⁷. Furthermore, the presence of pus in the peri-radicular tissues shelters the microorganisms from the action of antibiotics²⁸. In irreversible pulpitis, the pulp remains vital and there is no infection. Therefore, antibiotics are not indicated especially as they have no role to play in pain reduction in these cases^{28,29}. Antibiotic prescription is also not warranted in the management of tooth concussion, subluxation, luxation injuries or tooth fractures.³⁰

Different guidelines regarding antibiotic prescription exist in different parts of the world. Both the AAE (based on recommendations from the American Heart Association) and the ESE (based on recommendations from the European Society of Cardiology) recommend antibiotic prophylaxis prior to invasive dental procedures that involve manipulation of the gingival or periapical tissues, or perforation of the oral mucosa (including endodontic treatments) in patients who are at high risk of developing infective endocarditis^{16,31}. This includes patients with prosthetic heart valves (or prosthetic material used for cardiac valve repair), complex congenital heart diseases, a previous history of IE, and in cardiac transplant with regurgitation due to structurally abnormal valves. In the United Kingdom, the National Institute for Health and Care Excellence (NICE) states that "antibiotic

prophylaxis against infective endocarditis is not recommended routinely for people undergoing dental procedures"^{17,32}. Their recommendation is based on the evidence that the risk of antibiotic prescription outweighs its benefits in preventing IE in this group of patients³³. The majority of endodontists in Jordan (86.9%) reported that they do prescribe prophylactic antibiotic for patients at risk of developing IE. Our results showed that the majority of those who follow the *AAE and ESE* guidelines (93% and 60% respectively), prescribed antibiotics in such cases. On the other hand, most of those who follow NICE (62.5%) did not do so ($p < 0.001$).

Due to the lack of evidence linking poor oral health to prosthetic joint infection, the AAE, ESE and NICE recommend against the routine prescription of antibiotic prophylaxis before dental treatment to prevent prosthetic joint infection. However, the ESE states that antibiotic prophylaxis should be considered during the first 3 months after joint operations¹⁶.

Patients taking bisphosphonate medication are at risk of developing osteonecrosis of the jaws following invasive dental procedures that involve the alveolar bone such as endodontic surgery³⁴. The risk is higher in patients receiving the medication intravenously and for prolonged periods¹⁹. Other risk factors include old age, poorly controlled diabetes and the use of glucocorticoids¹⁹. Antibiotic prophylaxis may be warranted in this group of patients prior to bone-invasive procedure^{19,35}.

Immunocompromised patients have a defective immune system and are more vulnerable to systemic complications following odontogenic infections¹⁹. This includes patients with acquired immune deficiency (HIV/ AIDS, leukemia), end-stage renal disease, poorly-controlled diabetes, chemotherapy, immune-suppressive drugs, and certain inherited genetic defects. The ESE and the AAE recommend antibiotic prophylaxis for this category of patients prior to invasive dental treatments including root canal treatment. Bleeding disorders do not warrant antibiotic prophylaxis prior to dental procedures unless they are part of an immunocompromising disease such as leukemia or chemotherapy.

Half of the endodontists in Jordan chose amoxicillin with clavulanic acid as their first-choice antibiotic. While amoxicillin without clavulanic acid was chosen by 27.9% of them. In

penicillin-allergic patients, clindamycin was the preferred antibiotic for the vast majority of endodontists (83.6%). These findings are similar to questionnaire results in other parts of the world^{36,37}. The AAE recommends that penicillin VK and amoxicillin should be the first-line antibiotics¹⁰. While clavulanic acid (a beta lactamase inhibitor) increases the spectrum of amoxicillin in persistent infections, its indiscriminate use is associated with potentially significant side effects including the development of bacterial resistance¹⁶.

There is no consensus on the ideal duration of antibiotic prescription. While antibiotics need time to exert their therapeutic effect, their prolonged use is associated with an increased risk of developing resistant bacterial strains³⁸. The AAE and ESE recommend that antibiotics should be discontinued as soon as there is evidence of healing of the endodontic infection^{10,16}. Martin et al. demonstrated that, provided drainage has been established, most patients with acute dentoalveolar infections showed normal temperatures and marked resolution of the swelling following a 2-3-day antibiotic course³⁸. A good practice would be to prescribe antibiotics for 3 days and then reassess the need for further antibiotic prescription¹⁰. Most endodontists in Jordan reported that they prescribe antibiotics for 5-7 days. Only 6.6% of them chose a short prescription time of up to 4 days.

The results of this study show that many endodontists in Jordan unnecessarily prescribe antibiotics in different situations, choose long prescription times, and broad-spectrum antibiotics as their first choice.

Local regulations for antibiotic prescription in Jordan are lacking. Therefore, our endodontists follow different international guidelines. While only one endodontist in Jordan received his post-graduate endodontic training in the United States, 70.5% of the endodontists reported that they follow the AAE regulations and guidelines on antibiotic prescription. The ESE was the reference for only 6.6% of endodontists in Jordan. This reflects the influence the AAE enjoys as a regulation source at an international level. Alarmingly, one in ten endodontists in Jordan do not follow any guidelines on antibiotic prescription and instead rely on their personal experience to make a decision on this matter. This reflects an urgent need for issuing and

enforcing local guidelines on antibiotic prescription not only for endodontic treatment of infection but also for the general dental and medical prescription.

Antibiotic misuse remains a serious global issue. In Jordan, the following suggestions are vital to improve the pattern of antibiotic prescription among endodontists

- 1- To create local guidelines that regulate antibiotic prescription in Jordan.
- 2- To ensure dental students receive proper education about the indications of systemic antibiotics in the treatment endodontic pathology.
- 3- To ensure endodontists stay updated on international guidelines regarding antibiotic prescription through continued professional development.
- 4- To create and enforce laws and regulations that prevent over-the-counter sale of antibiotics.

Conclusions

Many endodontists in Jordan prescribe antibiotics in situations where antibiotic prescription would not be indicated. This reflects an urgent need to regulate antibiotic prescription in Jordan through improved education, continued professional development, and the creation and enforcement of local guidelines regarding antibiotic prescription.

Declaration of Interest

All authors have made substantive contribution to this study and/or manuscript, and all have reviewed the final paper prior to its submission.

Appendix 1 – questions included in the questionnaire

- 1- Gender
 - Male
 - Female
- 2- Age group
 - 25- 29
 - 30- 50
 - >50
- 3- Years since holding a post-graduate qualification in Endodontics
 - 0-2
 - 3-9
 - 10- 20
 - >20

- 4- Country of undergraduate qualification
Jordan
Arab country
United States
United Kingdom
Europe (except UK)
Australia or New Zealand
Asia (except Arab countries)
Africa (except Arab countries)
Latin America
- 5- Country of postgraduate qualification
Jordan
Arab country
United States
United Kingdom
Europe (except UK)
Australia or New Zealand
Asia (except Arab countries)
Africa (except Arab countries)
Latin America
- 6- Practice location
Amman
North Jordan
South Jordan
Salt and Madaba
Other:
- 7- In which of the following health categories you would prescribe antibiotics prior to endodontic treatment? (check all that apply)
Healthy patients
Patients with impaired immunologic function
Patients at risk of developing infective endocarditis
Patients whose jawbones are exposed to high-dose irradiation
Patients receiving oral bisphosphonate treatment
Patients receiving intravenous bisphosphonate treatment
Patients with prosthetic joint replacement
Patients with bleeding disorders
- 8- In which of the following diagnoses you consider antibiotics are indicated in healthy individuals? (check all that apply)
Irreversible pulpitis with normal apical tissues
Irreversible pulpitis with symptomatic apical periodontitis
Necrotic pulp with normal apical tissues
Necrotic pulp with symptomatic apical periodontitis
Necrotic pulp with asymptomatic apical periodontitis
Acute apical abscess without systemic involvement (localized fluctuant swellings)
Acute apical abscess with systemic involvement (elevated body temperature >38°C, malaise, lymphadenopathy, trismus)
Necrotic pulp with chronic apical abscess (sinus tract present)(Treatment of lateral luxation, intrusion, or extrusion
Replantation of an avulsed tooth
Soft tissue traumatic injury requiring treatment
Treatment of tooth fractures
- 9- When systemic antibiotics are indicated, which of the following is your first choice in an adult patient with no medical allergies?
Penicillin
Amoxicillin
Amoxicillin + clavulanic acid
Clindamycin
Tetracycline
Cephalosporin
Clarithromycin
Azithromycin
Metronidazole
Lincomycin
Other
- 10- How long would you prescribe the antibiotic for?
1-3 day
4-7 days
>7 days
- 11- If your patient is allergic to penicillin, what would your first-choice antibiotic be?
Cephalosporin
Tetracycline
Clindamycin
Azithromycin
Clarithromycin
Metronidazole
Lincomycin
Other
- 12- Which guidelines do you follow when making you decide upon antibiotic prescription?
American Association of Endodontists
European Society of Endodontology
National Institute of Clinical Excellence (United Kingdom)
Personal experience
Other

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