Antibiotic resistance and antibiotic prescribing by dentists in England 2007–2016

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Key points

- Provides a brief history of antibiotics in dentistry.
- Describes the problems and mechanisms of antimicrobial resistance (AMR).
- Discusses the role of dental prescribing in AMR.

The early prescribers of penicillin realised that antibiotics should be used wisely and as an adjunct to traditional surgical provision. They predicted that inappropriate use would increase sensitisation to the drug. National Health Service dentists prescribed almost 10% of antibiotics issued in NHS general practice in 2016 and an audit shows that many of these may have been prescribed inappropriately. One of the causes of antimicrobial resistance is over prescription of the drugs. This paper recalls the recommendations of some early users of penicillin, reports on the current prescription patterns of dentists in England, describes the mechanism of acquisition of anti-microbial resistance and discusses dentists' role in attempting to reduce the problem.

Introduction

Twenty years ago, the now defunct Standing Medical Advisory Committee published *The path of least resistance*. In this historically important document, it was reported that dental prescriptions accounted for 7% of all antibiotics prescribed in the UK and totalled 3.5 million in 1996.[1] Over the last two decades, much work has been done to raise awareness of antimicrobial resistance (AMR), culminating in the World Health Assembly endorsing a global AMR action plan in 2015.[2] It is now known that AMR accounts for up to hundreds of thousands of deaths each year[3] and that number is projected to rise to 300 million by 2050 if the issue is left unaddressed, making it the leading cause of death worldwide.[4]

A major factor in the spread of AMR is the exposure of bacteria to antibiotics, resulting from misuse and environmental discharge which may lead to selection for resistance. While this is by no means the only trigger of resistance, which in itself may be regarded as a natural phenomenon, it is widely accepted that reducing antibiotic use will curb levels of resistance and/or the number of resistant bacteria. Thus, antibiotic stewardship has been the centre-piece of the fight to combat the imminent post-antibiotic apocalypse.

Here, we consider the role that UK dentists can play in addressing AMR, through responsible prescribing practices. First, we provide a brief overview of the history of antibiotics and their availability worldwide. We use this as context for summarising trends in dental prescribing practices in England and the links to selective resistance. Finally, we consider the impact that improved antibiotic stewardship among dental practitioners can have on reducing the global AMR burden. AMR typically refers to antibiotic resistance and we use the terms interchangeably, throughout.

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Historical perspective on antibiotics

Penicillin, discovered by accident by Alexander Fleming in 1928, was developed into a usable therapeutic agent by Florey during World War II and became readily available in 1945. As early as 1946, however, its ease of use was called 'a real clinical danger'. Hoffman wrote that penicillin can be employed: 'without regard to the correct diagnosis and proper dosage, and with a neglect of the well-established general principles of medicine, dentistry and surgery […] Penicillin can be more intelligently used by the practitioner if he has a knowledge of the history of the development of the drug, the methods of production, the fate of the administered penicillin, the blood levels necessary for therapeutic efficiency [...] the nature of the anti-bacterial action and the clinical course of the disease to be treated.'[5]

Fish asserted in 1946 that penicillin is a drug which 'opens up so many new avenues of approach to dental problems.'[6] However, many of its applications, he assumes, are topical applications, and not via a systemic route. Penicillin lozenges may be used for treatment of acute ulcerative gingivo-stomatitis, for instance. Others considered that penicillin lozenges, however, were inappropriate as they encouraged the patient to self-medicate, away from the dentist. This leads to 'incomplete cure or the development of a tolerance to penicillin, thus rendering future treatment with penicillin ineffective.'[7] The careless use of penicillin for gingival conditions, where treatment of gingivitis may be successful by other means, for instance 'deep curettage, scaling, hot salt water lavages, diet correction and toothbrush instruction' was also recognised.[8]

Table 1 The five most commonly issued dental prescriptions in England between 2007 and 2016. Numbers in brackets are the % of all dental prescriptions in the same year[11]

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Antibacterial drugs	3,706,014 (81.1)	3,669,862 (79)	3,731,080 (76)	3,850,773 (74.8)	3,935,698 (72.9)	3,924,400 (69.9)	3,805,256 (68.2)	3,696,109 (66.4)	3,437,561 (64.7)	3,198,564 (63.6)
Drugs acting on the oropharynx	475,386 (10.4)	481,149 (10.4)	509,545 (10.4)	506,564 (9.8)	519,116 (9.6)	516,000 (9.2)	492,569 (8.8)	476,706 (8.6)	431,161 (8.1)	377,839 (7.6)
Minerals	154,063 (3.4)	268,284 (5.8)	426,084 (8.7)	546,325 (10.6)	707,684 (13.1)	953,300 (17)	1,075,479 (19.3)	1,197,507 (21.5)	1,263,797 (23.8)	1,274,447 (25.5)
Drugs used in rheumatic diseases & gout	126,122 (2.8)	122,918 (2.6)	136,435 (2.8)	133,455 (2.6)	127,024 (2.4)	115,200 (2.1)	100,576 (1.8)	90,464 (1.6)	75,285 (1.4)	59,920 (1.2)
Analgesics	71,359 (1.6)	69,314 (1.5)	70,132 (1.4)	68,783 (1.3)	67,394 (1.2)	66,400 (1.2)	64,021 (1.1)	61,025 (1.1)	55,053 (1)	47,993 (1)

The use of penicillin in root canal therapy as a dressing was found to be ineffective, 'as penicillin is chiefly a bacteriostat, it cannot be effective in the root canal […] where there is no circulation of tissue fluids and antibodies are therefore absent'.[9] Hoffman also concluded that for dental applications, 'dead tissue must be removed […] and abscess cavities drained.'[5]

It is clear that caution about the inappropriate use of antibiotics in the treatment of oral infection, periodontal diseases and endodontics began within a few years of their introduction. The concept that antibiotics were, in the main, an adjunct to treatment rather than the primary resource for addressing many oral infections was recognised by many early users of the drugs.[6] As the range of antibiotics increased in the early 1950s, Jacobs stressed that the greatest importance was 'not so much the (antibacterial) agent used but the intelligence with which it is used.'[10]

Current prescribing practices

Prescribing data for NHS dental practitioners in England is collected by the Business Standards Authority (BSA) and analysed by NHS Digital (formerly called, Health and Social Care Information Centre [HSCIC]). Dentists are responsible for 0.5% of all prescriptions but prescribe 8.3% of all antibiotics in primary care in England.[11] Antibiotic prescriptions make up 63.6% of all prescriptions by dentists. Overall, 3,198,564 prescriptions for antibiotics were written by dentists in 2016 (Table 1), 66.1% of which were penicillin-based. Of the remaining 33.9%, 28.2% were metronidazole and almost 4% were macrolides (erythromycin-related antibiotics). The remainder were made up of clindamycin, cephalosporins and tetracyclines.

The number of antibiotics prescribed by NHS dentists in England from 2007–2016 is shown in Figure 1. There was an 18.5% reduction in antibiotics prescribed by dentists between 2012 and 2016. In contrast, over the same period there was a reduction of just 10.9% in overall antibiotic prescriptions. These data, however, only represent the prescriptions issued within NHS dental primary care and do not include numbers from secondary care, private practice, privately issued prescriptions or antibiotics dispensed directly to the patient from within the practice. The data represented in Figure 1 is therefore an understatement of the numbers of dental prescriptions issued for antibiotics. Since data is not available for private prescriptions it is not known whether this would be a significant underrepresentation.

Antibiotic resistance

The resistance of pathogenic or potentially pathogenic bacteria to antibiotics continues to be of growing, global concern. Combined with a slowing in the antibiotic development pipeline, the rise in resistance sparks concerns of a reversion to bygone eras without antimicrobial drugs. In 2017, the WHO issued a list of priority resistant organisms and later that year, the United Nations identified AMR as a key emerging issue.[12,13] The problem of the lack of antibiotic development is closely linked to the issue of AMR. Pharmaceutical researchers face a conundrum: the need for new antibiotics that will sit on a shelf until they are needed for a patient. Arguably, the irresponsible use of antibiotics that has driven the AMR crisis also drove the impressive rate of antibiotic development during the late twentieth century.

AMR can be intrinsic or acquired. It is important that dental practitioners are familiar with and consider both, when issuing prescriptions. Intrinsic resistance is that which is inherent to all strains or isolates of a particular species. Acquired resistance occurs when bacteria obtain the genetic material required to enable resistance, from another organism. The acquisition can occur by conjugation, transduction or transformation, with genetic material being carried on plasmids or transposons, known collectively as mobile genetic elements (MGEs). The horizontal transfer of resistance genes is most likely to occur between bacteria of close phylogenetic distance and is triggered as a stress response mechanism. One of the primary triggers of such a response can be the exposure to antibiotics.[14,15]

Clinical resistance is of particular concern and is defined as occurring when there is a high correlation with the possible failure of therapeutic intervention. Concerns of AMR-driven failure may typically be reserved for 'end-of-line' drugs such as vancomycin, where resistance would leave clinicians with no therapeutic options. However, the propensity of the human microbial community to develop resistance to drugs commonly prescribed by dentists should be considered.

Amoxicillin accounted for over 65% of antibacterial prescriptions by dentists in England in 2016.[11] Several studies[16,17] have shown that Amoxicillin-resistant isolates can be found within the oral and gut microbiome. However, what is more revealing in the work of Kirchner *et al.*[17] is that the relative abundance of amoxicillin resistant bacteria (*E. coli* specifically) increased after dosing amoxicillin, suggesting perhaps, the acquisition of resistance. This is not to say that the use of penicillin should be abandoned for fear of triggering resistance but rather that clinicians should be aware of the potential effects of prescribing even small doses of antibiotics.

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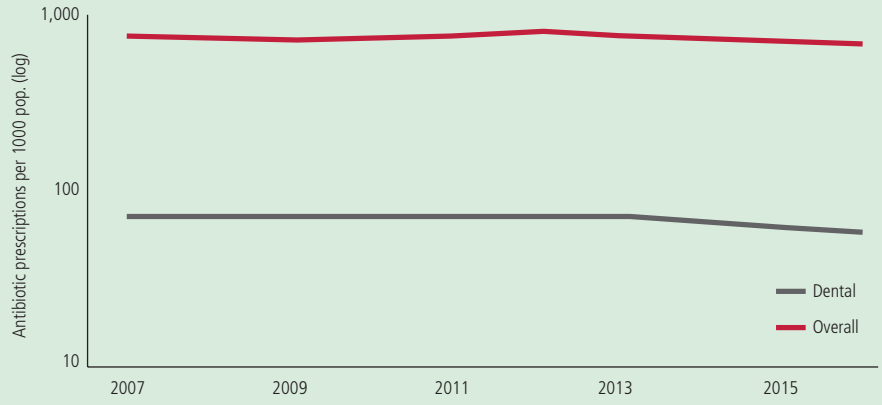
Fig. 1 Prescription data compiled from prescription cost analysis tables.[11] Population data is mid-year estimates from the Office of National Statistics[34]



Discussion

While it may not be possible to directly determine the cause and effect of the practices of a sub-group of prescribers on AMR trends, it is useful to consider the role that dentists can play in lessening the global AMR burden.

Exposure of environmental bacteria to even low levels of antibiotics can be a trigger for acquired resistance and is particularly problematic. This is because the concentration may not be high enough to be lethal to bacteria but may be high enough to cause a stress-response that triggers horizontal gene transfer.[18] The exposure of environmental bacteria to antibiotics will typically be through manufacturing discharge, agricultural run-off or, as is relevant here, disposal via the sewerage system. A common misconception is that, in developed economies such as the UK, wastewater treatment systems are sophisticated enough to remove any occurrence of antibiotic resistance genes or MGEs before discharge to the environment. While effective at removing a large proportion, by mass, of genetic material, it is possible that the highly stressful environment of biological treatment systems are selective for resistance.[19]

The pathway, then, to human exposure is more obvious: through the food chain or through direct contact with water for recreational purposes. The latter, being recently proven to increase the presence of AMR in humans by up to 300%,[20] highlights the potential scale of the problem, even in the UK. Therefore, we arrive at three main options to minimising the risk of AMR exposure: improving treatment facilities, limiting access to recreational waters or improved antibiotic stewardship. It goes without saying that the only option within the dental practitioner's power is the responsible prescribing and disposal of antimicrobials. However, the other options must not be relied upon on the grounds of cost to the consumer, in the case of wastewater treatment, or because of the numerous health benefits associated with outdoor recreation.

Antibiotic stewardship is of primary importance and dental practitioners can and must, continue to play their part.[21] The reduction in numbers of antibiotic prescriptions by dentists between 2012 and 2016 is encouraging. However, the reason for this reduction is not clear. It is possible that the removal of a financial incentive to prescribe was, in part, a cause. Before November 2012, it was possible for NHS dentists in England to claim 0.75 units of dental activity (UDAs) for a course of treatment which was solely for a prescription. When this item was removed in late 2012,[22] the financial incentive to prescribe and do nothing else was therefore removed. Equally, a rise in awareness of the problem of AMR from both the dental profession and the general public may be a contributing factor.

Despite this decline in numbers of prescriptions, there is evidence from a recent audit in Wales that one third of prescriptions were given without any further local treatment, such as drainage or extraction. The reasons given were 'Failure of previous local measures, patient unwillingness or inability to undergo treatment, patient demand for antimicrobials, time pressures, and features of a patients' medical history.'[23] The criteria for the prescription of a course of antibiotics for dental infection are well described (the presence of raised temperature, local lymph node involvement and evidence of systemic spread).[24] In medical practice, a reduction in inappropriate antibiotic prescriptions for women with the symptoms of cystitis resulted from clinicians following a simple set of three clinical rules.[25] The consistent application of three simple rules for dentists could help to reduce the numbers of inappropriate prescriptions for antibiotics in dental practice.

Education for practitioners may lead to improvements in prescribing practice. Online training for general medical practitioners, for instance, has been shown to reduce antibiotic prescription for respiratory tract infections (RTI) in children by about 10%. The training consisted of three sections, the first two of which were theory based, but the third, more importantly, stressed the importance of communication skills. Patient consultations were reinforced with an information booklet for parents.[26] To assist general dental practitioners (GDPs) in understanding their prescribing patterns, auditing tools are available from the British Dental Association (BDA) and Faculty of General Dental Practitioners (FGDP[UK]). Some regional post-graduate deaneries provide courses on good stewardship of antibiotics, which includes managing dosages and duration of treatment.

Patient education into the need or otherwise for an antibiotic prescription may be helpful in reducing requests for antibiotics. The European Union introduced the first antibiotic awareness day in 2008[27] and its effects may also be beginning to show in the reduction of prescriptions. However, a qualitative study among adolescents in 2017 found that antibiotics are perceived on the same level as pain killers and as a cure-all for any illness.[28] Most practitioners will be aware of the emergency patient who 'just wants a prescription' and despite explanations of the problem, fails to return for definitive treatment.

Education and audit alone may however not be sufficient to provide further behaviour change and consequent improvement in prescribing practices. A knowledge of the problem does not necessarily lead to a change in practice. Communities of practice – groups of individuals who share a concern about any particular topic – who meet, discuss and learn from each other may provide a better way of transferring understanding and knowledge of the problem.[29] The utilisation of intermediaries

– or Champions of Change – to visit practices both to educate and inform have been shown to be more effective in improving antibiotic prescribing practice than the provision of paper-based information alone.[30] Similarly, the concept of 'antibiotic guardians' – those who make a personal commitment to change and who may influence others, may be more effective than education alone.[31]

However, time pressures have been identified as a major barrier to effective prescribing by Newlands *et al.*[32] The BDA AMR summit called for:

'*Protected and appropriately funded emergency timeslots to be embedded in the new contract (also in out-of-hours services), as dentists are currently experiencing time constraints in treating emergency cases that lead to a pressure to prescribe rather than perform the appropriate surgical procedures.*'[33]

The management of the dental emergency patient presents GDPs with a problem. Do they reserve daily time slots which may be unused and therefore be at a financial disadvantage for doing so? Or do they squeeze emergency patients in between existing appointed patients, thus risking late running and consequently seek the quick fix of a prescription for antibiotics? The current English NHS system which pays 1.2 UDAs for emergency treatment, which could include examination, radiograph and an extraction, as opposed to three UDAs for a course of 'routine' treatment which might also include an examination, radiograph and an extraction, is anomalous and potentially not conducive to good antibiotic prescribing practice.

Conclusion

It is clear that just as the causes of AMR are multifactorial, so too are the possible methods by which dentists may be helped towards better prescribing practice. However, it is apparent that further improvement in the reduction of antibiotic prescriptions by dentists should involve financial investment. Options to help to reduce antibiotic prescribing by dentists include:

- A system of remuneration which encourages intervention rather than prescription-only treatment
- Further education for dentists, including remunerated time for regular audit of antibiotic prescribing and the appointment of Champions of Change to visit practices
- Education for patients to understand alternative modes of treatment and the wider significance of AMR.

The early users of penicillin recognised that antibiotic therapy should be an adjunct to treatment rather than a treatment in itself. They may well be surprised how little has changed in the past 70 years.

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