Antibiotic misuse and sore throat treatment

REPORT FROM THE GLOBAL RESPIRATORY INFECTION PARTNERSHIP

Meeting held 11th June, 2012, Royal College of Physicians, London
INTRODUCTION

When Alexander Fleming first discovered penicillin over 70 years ago, he predicted that microbes’ Darwinian ability to evolve and survive would result in the development of antibiotic resistance, said Chair Prof. Oxford in his opening address.

That prediction has come true, with resistance becoming a global concern. The challenge this poses for the future has been starkly outlined by the World Health Organization (WHO), which warns that antibiotic resistance may increase the cost of healthcare and jeopardise the healthcare gains made in the last 100 years by threatening a return to the pre-antibiotic era.1

While the rates of antibiotic resistance vary across the globe, there is a direct relation between the use of antibiotics and the emergence of resistance at both the individual and population levels.2 A recent WHO report called for the rational use of antibiotics in humans and animals, and improved infection prevention and control to help combat antibiotic resistance.3

In support of the WHO initiative, the inaugural meeting of the Global Respiratory Infection Partnership was held at the Royal College of Physicians, London, to discuss experiential learning from around the globe and strategies to drive the rational use of antibiotics among patients and healthcare professionals. Comprising a multi-disciplinary, international group of general practitioners, microbiologists, researchers and pharmacists, spanning primary and secondary care, the Global Respiratory Infection Partnership focused on how the management of sore throat could be utilised as a marker for rational antibiotic treatment.

A clear call to action was summarised by Prof. Essack: “We need a multi-pronged, multi-country, multiple-stakeholder co-ordinated approach to antibiotic resistance that is linked to a concrete intervention, not just a leaflet or a poster.”

THE GLOBAL RESPIRATORY INFECTION PARTNERSHIP DECLARATION:

“We, the Global Respiratory Infection Partnership, recognising the imminent onset of the post-antibiotic era and taking full cognisance of the declining numbers of new antibiotics in development hereby commit to:

• Consistent, sustainable evidence-based advocacy and intervention for rational antibiotic use and antimicrobial stewardship
• Formulating a framework for non-antibiotic treatment options for respiratory tract infections, such as sore throat, common colds, influenza and cough
• Facilitating multi-stakeholder commitment to antibiotic stewardship and rational antibiotic use.”

Global Respiratory Infection Partnership members

• Professor Attila Altiner, Head of the Institute of General Practice, University Medicine Rostock, Germany
• Mr John Bell, Principal Adviser, Pharmaceutical Society of Australia Self Care consumer health information programme, community pharmacist, Wooloahra, Australia
• Dr Martin Duerden, Honorary Senior Lecturer at Cardiff and Bangor Universities, Wales, Clinical Adviser on prescribing for the UK Royal College of General Practitioners and family physician, UK
• Professor Sabiha Essack, Dean of the School of Health Sciences, University of KwaZulu-Natal, South Africa
• Professor Roman Kozlov, Professor of the Department of Microbiology, Smolensk State Academy, Director of the Institute of Antimicrobial Chemotherapy, Head of the Scientific Centre for Monitoring Antimicrobial Resistance of Federal Agency for Healthcare & Social Development, Russia
• Professor John Oxford, Scientific Director and founder of Retroscreen Virology and Professor of Virology at St. Bartholomew’s and the Royal London Hospital, Queen Mary’s School of Medicine and Dentistry, UK, (meeting Chair)
• Professor Antonio Carlos Pignatari, Clinical Director of the Special Clinical Microbiology Laboratory of the Division of Infectious Diseases, Federal University of São Paulo, Brazil
• Dr Aurelio Sessa, family physician, Italian College of General Practitioners, Florence, Italy
• Dr Alike van der Velden, Assistant Professor, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, the Netherlands

EXECUTIVE SUMMARY

• Antibiotic resistance is an escalating global problem that poses a significant threat to future health
• A co-ordinated international, multi-pronged, multiple-stakeholder approach is essential to effectively change healthcare professional and patient behaviour to contain and combat antibiotic resistance
• Inappropriate antibiotic use in upper respiratory tract infections, such as sore throat, cough and common cold, is common in many countries and is a contributory factor to antibiotic resistance
• Healthcare professionals, particularly primary care physicians, are believed to succumb to patient pressure to prescribe antibiotics for upper respiratory tract infections
• However, the reality is that many patients simply seek symptomatic relief and reassurance
• Antibiotics are ineffective in the majority of sore throats, which are viral in origin, even those caused by bacterial infections are usually self-limiting
• General practitioners are the key healthcare professional in ensuring rational antibiotic use in sore throat and other upper respiratory infections
• While guidelines on rational antibiotic use exist at national and international level, these are often not well implemented
• Many of the guidelines available have been initiated in smaller, developed countries and there is a need for guidelines that reflect the complexities of larger, developing countries, such as Brazil and India
• There is a need for improved healthcare professional education on the diagnosis (particularly in children), antibiotic treatment and symptomatic management of sore throat as well as the development of communication skills to advise patients on appropriate use of antibiotics
• In countries where there is antibiotic accessibility through pharmacies, despite being prohibited for sale without a prescription, the enforcement of legal or fiscal measures as a deterrent would be of value
• A sustained approach is required for the public – patients – and parents seeking treatment for children – to empower them, build health literacy and promote shared decision making, with the support of healthcare professionals, on the appropriate use of antibiotics. Education on using antibiotics wisely can be part of the school curriculum
• In conclusion, a multi-faceted framework for a non-antibiotic, symptomatic sore throat management strategy for healthcare professionals and patients needs to be developed that can be adapted at country level to reflect local behaviours, cultures and healthcare provision systems

From left to right. 
Back row: Professor John Oxford, Dr Aurelio Sessa, Dr Alike van der Velden, Professor Antonio Carlos Pignatari, Professor Attila Altiner 
Front row: Professor Roman Kozlov, Dr Martin Duerden, Professor Sabiha Essack, Mr John Bell
The meeting began with an overview of antibiotic prescribing, resistance rates and awareness campaigns from around the globe. Some consistent issues emerged:

- general practitioners in primary care are the primary healthcare professional for rational antibiotic prescribing
- there are few new antibiotics in development and those that are currently available should be used sparingly
- even in countries where antibiotic use is low, rational prescribing can still be improved
- although guidelines exist in many countries, uptake of rational prescribing can still be improved
- healthcare professionals believe patients/parents presenting for consultation of respiratory tract infections wanting an antibiotic may be seeking simple reassurance, complaint prognosis, symptomatic relief and/or a ‘sick note’ to justify time absent from work
- healthcare professionals’ communication skills can be enhanced to effectively deliver the ‘antibiotic is not required’ message to patients
- patients believe that antibiotics are an effective treatment for common respiratory tract infections, even those of a viral nature.

“My theory is that GPs feel under pressure to prescribe,” said Mr Bell.

Patients have a limited understanding of antibiotics, as shown from data from Australia and the UK. Mr Bell summarised a recent survey by the Australian National Prescribing Service that found one in five patients expect antibiotics for a cough/cold, rising to four in five for ear, nose, throat, chest infection. Only 50% of patients know about antibiotic resistance, with 40% aware that antibiotics are not effective against viruses.

In the UK, research for the 2011 Antibiotic Awareness Day revealed 53% of 1,767 patients surveyed expected antibiotics and 25% believed they worked for most coughs and colds, said Dr Duerten.

“Antibiotic resistance is a very important problem, particularly in respiratory tract and urinary tract infections”

Antibiotics in children

Parental concern for their child’s upper respiratory tract infection can be a driver for antibiotic consultations. Prof. Kazlov agreed that parental demand was a concern in Russia: “While most adults do not request antibiotics from doctors, they are more likely to ask for their children.”

The realities of modern living may also play a role, suggested Prof. van der Velden, with working mothers needing to have their children make a quick recovery so they can return to work.

Prof. Pignatari raised another potential explanation why antibiotics are often prescribed for paediatric sore throat: “In adults, sore throat is easy to diagnose, but not in children. Doctors are often not confident in diagnosing children.”

Giving parents information on managing sore throats and upper respiratory tract infections is an approach that has been utilised successfully in a number of countries, such as Russia, the UK and Thailand.

Patients’ sore throat beliefs

Market research conducted among 12,859 people across 12 countries shows that the reported incidence of sore throat in some countries is lower than in others, said Reckitt Benckiser’s Adrian Shephard. Around 10% of people in Australia, UK, France, Germany and the US had experienced sore throat symptoms in the previous 12 months, compared to 40–50% in Russia, India, China, South Korea, South Africa, Brazil and Mexico. “In some countries, such as Russia, Mexico and India, sore throat is also perceived to be more painful,” he added.

A new approach to this problem has been in place since 2010. Pharmacies are required to retain antibiotic prescription for one month after dispensing. It is enforced by law with the potential for pharmacies to be closed. “This works,” concluded Prof. Pignatari. “We spent 20 years with guidelines and recommendations that did not work. Now, in one year, we have a 17% reduction in the number of antibiotics used.”

“The global picture

In many countries there appears to be a disconnect between what healthcare professionals perceive patients want from a consultation and what patients actually want.

“My theory is that GPs feel under pressure to prescribe; that patients urge them to prescribe or they will either come back or go to another doctor,” said Prof. Altiner. Yet, he cited data that show only a small number of patients expect a prescription. Patients are more concerned about prognosis and symptomatic pain, he added.

Prof. van der Velden added that the reasons for consulting a physician can be cultural. In France, 50% of patients with common cold present for a consultation, whereas in the Netherlands 1.2% consult their physician. Obtaining a sick note to legitimise being off work is one of the reasons explaining this difference.

Socioeconomics also plays a role. In Italy, antibiotic use is higher in the poorer Southern regions than in the North; an observation also seen in Brazil and the UK. Dr Duerten commented: “Depriavation is a strong driver for antibiotic use and we don’t know why.” Prof. Pignatari suggested that doctors perhaps spend more time with richer patients, affording greater opportunity for discussion and explanation on rational antibiotic use, while poorer people get more antibiotics.

Whatever the drivers, providing a prescription creates a message to the patient that antibiotics are the right treatment. Research in sore throat has shown that when doctors don’t prescribe an antibiotic, patients are less likely to return for treatment in the future, said Dr Duerten.

“But, in the UK, patients who see the doctor for self-limiting infections tend to get an antibiotic prescription.”

Perceptions and misperceptions

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Antibiotics

In children

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While around half of sufferers claiming to know the cause of their sore throat, this also differed by country. In 60% of markets, the weather or temperature was attributed as the leading casual factor in the sore throat, with infection the primary reason in only the UK and Australia. Although participants from Germany, Russia, and South Korea also believed infection was a prominent factor. Stress, tiredness, environmental pollution and allergy played an important role in some markets. Despite these variations, the trigger for treatment is consistent across most markets: the majority want symptom relief and to ensure symptoms would not worsen.

The market research also revealed some important communication cues for healthcare professionals. Sufferers identify with a number of different descriptions of sensations, such as scratchy, tickly, itchy throat, and dry throat (see Figure 1).

Data presented at the 2012 American Pain Society meeting found that the most important symptoms patients experience vary when they have a sore throat, such as sore throat pain, intensity, difficulty swallowing and swollen throat, and patients class any one of these as their chief complaint. “From a patient perspective, it’s not just sore throat; there are different articulations of sore throat and, as a result, their management expectations may be different,” said Mr Shephard.

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“Antibiotic resistance is a very important problem, particularly in respiratory tract and urinary tract infections,” said Prof. Pignatari. Despite the existence of national and international guidelines on antibiotic resistance, Prof. Pignatari felt these are ineffective. The main barriers to the implementation of rational antibiotic use on community-acquired infections are empiric treatment, patient pressure and a lack of availability of quick laboratory diagnostic tests.

In addition, accessibility of antibiotics through pharmacy sales is prevalent, despite regulations which prevent their dispensing in the absence of a prescription. An analysis of E. coli resistance in São Paulo revealed ‘hot spots’ of ciprofloxacin resistance. “We know exactly the pharmacies that are selling these drugs,” he added.
In terms of treatment, while around 70% of patients used over-the-counter remedies, prescription medicines and antibiotics rated 39% and 19%, respectively. This was often dependent on symptoms: antibiotics were more likely to be used for severe symptoms. In markets such as India, South Korea, South Africa and Brazil, antibiotics were a more popular choice. Efficacy is by far the most important attribute of treatment.

ANTIBIOTICS AND SORE THROAT
From a clinician’s perspective, the group considered the benefits of antibiotic use in sore throat and when this treatment should be considered.

Prof. van der Velden outlined data from the Cochrane review of antibiotics in sore throat that concluded the Number Needed to Treat (NNT) to prevent sore throat at day seven is 21 (against the ideal NNT of 1). In short, antibiotics are of little benefit in sore throat.

Although it has been proposed that antibiotics could be used to prevent secondary complications (e.g. quinsy, glomerulonephritis, acute rheumatic fever), this appears to vary between countries. Prof. Kazlov commented that he had seen no evidence of any decrease in complication rates with antibiotic use in Russia, while Prof. van der Velden and Dr. Duerden noted these complications were very rarely seen in the Netherlands and UK. However, Prof. Altiner pointed out that in Turkey the complication rates were higher, though it is not known why this is the case.

HEALTHCARE COMMUNICATION
“On the shoulder of the GP lies the responsibility of antibiotic resistance,” advised Dr. Sessa. To effectively manage patient demands for antibiotics for sore throats and other upper respiratory tract infections, there is a need for improved communication skills during the physician-patient interaction.

“Even in a low prescribing country there is still potential to reduce further by addressing doctor-patient communications”
This can help bridge the gap between what the GP believes the patient wants from a consultation and what the patient is really expecting. Prof. van der Velden pointed out, “Patient satisfaction is not primarily related to getting an antibiotic but to getting a good consultation, a physical examination and reassurance.” To do this effectively and have the patient achieve a satisfactory consultation can take different approaches.

RESISTANCE SNAPSHOT – ITALY
Italy has the most inappropriate use of antibiotic therapy for upper respiratory tract infections in Europe, revealed Dr. Sessa.

These infections are the driver for antibiotic use, with 30% of infections resulting in a prescription and numbers peaking in line with influenza rates. Of these, “sore throat is probably the lead infection for inappropriate antibiotic use”.

During the period 1999–2007, antibiotic use in Italy increased by 13%, with overuse of parenteral antibiotics, oral cephalosporins and quinolones. “There are wide regional differences,” Dr. Sessa added. “The south of Italy, compared to the north of Italy, has about three times the amount of antibiotic use.”

Even in a low prescribing country there is still potential to reduce further by addressing doctor-patient communications

“On the shoulder of the GP lies the responsibility of antibiotic resistance”

Prof. Pignatari advocated holding general conversations with patients about their life, health and that of their family, before informing them that an antibiotic will not be prescribed. Dr. Duerden said he asked patients what they thought they could do for them and what benefit they thought an antibiotic could have, before counteracting this belief.

The pharmacist can also play an important role in complementing and reinforcing the message the doctor gives, said Mr. Bell. In addition, they can offer prevention advice, stressing the importance of immunisation and promoting personal hygiene, and evidence-based recommendations for symptomatic relief: “We sell more treatments for cough and cold than any other therapeutic category, but it is the sector where there is the least satisfaction,” he added.

With pharmacies in some countries, such as Russia, Brazil and Italy, making prescription antibiotics more readily accessible by selling illegality to patients, Mr. Bell advocated the enforcement of legislation to stop this practice, citing recent successful measures in Brazil (see box on P. 5).

Another issue is that it is possible to obtain antibiotics from some pharmacies, even though they are not available without prescription and this practice is not officially permitted.

Measures to tackle inappropriate antibiotic use include guidelines and an annual patient campaign that runs on TV, radio and print. This advises patients to defend their remedies, not to use antibiotics for the common cold and flu, only use antibiotics given by the doctor and take antibiotics according to directions.

Dr. Sessa pointed out: “If antibiotic prescribing was as low as the average of six low-consumption regions, it could save €136m.”

For all healthcare professionals, Prof. Altiner summed up the key communication skills required: “It is important not to be paternalistic and not to have a one-way dialogue.”

RESISTANCE SNAPSHOT – GERMANY
Germany is not a high antibiotic prescribing country, which runs counter to the fact that, in general, it is a high-prescribing nation with a poly-pharmacy problem, said Prof. Altiner. Acute respiratory and urinary infections are common presenting conditions in primary care. While German physicians are aware of antibiotic resistance, non-rational prescribing is common, with many different antibiotics prescribed.

In an analysis of patient consultations, German GPs were found to be good communicators with sufficient time for discussion; however, this communication did not cover antibiotics. This learning is important: “Even in a low prescribing country there is still potential to reduce further by addressing doctor-patient communications.”

Interventions to reduce prescribing include DART (Deutsche Antibiotika-Resistenzstrategie), which encompasses surveillance on resistance and resistance development, education, co-ordination and research; guidelines on acute cough, earache, rhinosinusitis, dysuria and oral antibiotics are available. But Prof. Altiner commented: “Having a guideline is one thing, implementing it is another.”

RESISTANCE SNAPSHOT – THE NETHERLANDS
The Netherlands has a relatively low rate of antibiotic consumption. Yet, four out of five antibiotic prescriptions are from primary care, of which 60% are for respiratory tract disorders, said Prof. van der Velden.

The Dutch sore throat guideline advises that antibiotic treatment is not based on a specific diagnosis. “Antibiotics are only used for patients with severe illness or with serious risk of complications. With just Center criteria it is difficult to predict who will benefit from antibiotics,” Prof. van der Velden added.

How the guideline works in daily practice has been analysed using 452 detailed described consultations for sore throat. Antibiotics were given to 30% of patients; over 50% of prescriptions were not in line with the guideline.

In a GP-targeted Dutch intervention trial to optimize antibiotic prescription for respiratory tract infections, education on guidelines, and information on patient expectations and communication reduced antibiotic prescribing by 12%. “In the Netherlands we are still intervening to further reduce antibiotic use,” said Prof. van der Velden.
Advising patients why an antibiotic is not required is hard to explain, said Prof. Altiner. “There are maybe things we can learn from marketing as there is a difference between cognitive awareness and behaviour.” Getting the antibiotic resistance message across to younger generations is also important, although there was some pessimism. “These types of programmes don’t stop children smoking, drinking or taking drugs when they get older,” Dr Duerden pointed out.

“Around two-thirds of children will get antibiotics, around 89% for sore throat”

Overall it was clear that an easy, understandable message and framework for patients on antibiotic use needs to be created, and this may vary by country. Consistent, sustained messaging across healthcare professionals, spanning both primary and secondary care, is also vital. “We have to communicate but we have to communicate effectively and we have to do it over and over again,” said Mr Bell, citing the example of the Australian sunscreen campaign that has run for over 30 years.

Other issues include inadequate antibiotic choice and underuse in adults. But it is used effectively in Smolensk, western Russia, as a means of not prescribing antibiotics, said Prof. Kozlov, while Dr Sessa believed testing in Italy had significantly reduced the antibiotic prescribing rate.

Prof. Pignatari said Brazilian GPs had been educated that if a test is negative then antibiotics should not be prescribed, but, as outlined earlier, they are less confident in diagnosing children, so often offer a test and provide a prescription as well. “If they test positive they get antibiotics, if they test negative they get antibiotics.”

Colleagues in Scandinavia experienced increased doctor consultations and pressure, said Prof. van der Velden, adding: “This is an unwanted side effect of point-of-care tests.”

Around two-thirds of children will get antibiotics, around 89% for sore throat

**RESISTANCE SNAPSHOT – RUSSIA**

Russia has a low rate of antibiotic prescribing. However, Prof. Kozlov warned this does not reflect over-the-counter antibiotic use. “They are not on display but 52% of pharmacies do sell antibiotics,” explained Prof. Kozlov. An issue of key concern is the high frequency of inappropriate antibiotic prescribing for viral infections. “For acute pharyngitis, the prescribing rate is around 99%. Around two-thirds of children will get antibiotics, around 89% for sore throat and 98% for acute bronchitis,” explained Prof. Kozlov.

Other issues include inadequate antibiotic choice for empirical therapy, inappropriate combinations of antibiotics and the predominance of parental antibiotic use in the outpatient sector. As a result, current data show resistance is rising for penicillin and quinolones, while cephalosporin remains stable.

Behavioural interventions can make a difference. A recent multi-faceted intervention study to improve the management of sore throat in Smolensk outpatient settings provided educational materials for physicians, free GABHS testing and patient information leaflets. As a result, the frequency of inappropriate antibiotic use dropped by over 20%.

**RESISTANCE SNAPSHOT – SOUTH AFRICA**

Communicable diseases, such as infections and HIV, pose the greatest health burden in South Africa, said Prof. Essack. While HIV poses a greater health threat, antibiotic stewardship is vital to the survival of HIV patients.

“In the private sector, the antibiotic resistance rate is lower but there is a broader range of drugs against which resistance exists because antibiotic choice is unrestricted.”

There is greater use of older antibiotics in the public sector and newer agents in the private sector. “In the private sector, the antibiotic resistance rate is lower but there is a broader range of drugs against which resistance exists because antibiotic choice is unrestricted,” summarised Prof. Essack.

Rational antibiotic prescribing is achieved in the public sector by way of treatment guidelines and the essential drugs list and a national antibiotic stewardship programme enjoying endorsement from the public and private healthcare sectors is in its inception phase.
In countries where guidelines do exist, such as Germany, the Netherlands and the UK, there remains irrational prescribing. ‘GP’s will say guidelines are for average patients, but my patients are not average,’ explained Prof. van der Velden.

Prof. Essack called for the group to create a framework for non-antibiotic use, rather than a guideline, that was adaptable across countries and cultures. This framework should encompass advice to patients and consider other strategies to manage sore throat, cough and other respiratory tract infections.

Symptom Management
Sore throat is one of the leading indications for antibiotic use in many countries, despite up to 95% of sore throat infections being of viral origin. Multiple strategies can be considered to help physicians determine appropriate use and improve patient management.

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For patients, managing persistent or worsening symptoms is the key reason to seek physician treatment. The group suggested the following good practice approaches that can also be adapted to other upper respiratory tract infections:

- always examine the patient before reaching a conclusion
- advise on the duration of symptoms, giving a realistic time frame for improvement. Around 80% of patients are sore throat free within seven days
- recommend symptomatic relief – pain and fever are the leading symptoms. Treat the symptoms from the beginning to prevent sore throat inflammation continuing
- advocate bed rest, if necessary
- ask patients what they expect from antibiotic treatment, if requested inappropriately. Explain that it does not offer symptomatic relief as most sore throats are viral and, therefore, do not benefit from antibiotic treatment
- provide information on what alarm symptoms patients should be concerned about
- allow the patient to talk about their concerns – communication must be two-way
- offer a follow-up consultation if symptoms do not improve or in case patients remain concerned

Summary
The group agreed that the challenge of antibiotic resistance requires a global, multi-stakeholder approach and should seek to create a framework for international behavioural change initiatives. This has to be a sustainable campaign that targets all healthcare professionals, the public and patients simultaneously.

Harnessing mass media, social media and peer-to-peer influencers via a multi-pronged approach is required, said Prof. Essack. This should go beyond a patient leaflet or poster and translate into a concrete intervention.

“If I dissuade them from having an antibiotic in primary care, they then should not be able to go to another GP or their accident and emergency department and get one”
REFERENCES


Meeting funded by Reckitt Benckiser