Containing Antibiotic Resistance: a World Wide Challenge

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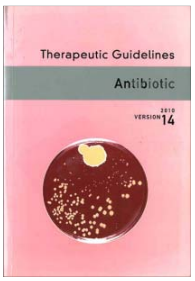
http://www.medreach.com.au

Antibiotic Resistance Conference Uppsala, Sweden, 2010

Antimicrobial Resistance Summit Sydney, Australia, 2011

Increasing antibiotic resistance coupled with the failure of industry to develop new antibiotics is a global public health problem and, like global warming, it requires local, national, regional and international action

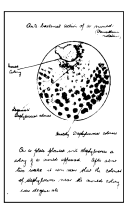
Talk outline



- The history, microbiological and social determinants of antibiotic resistance.
- The consequences of antibiotic resistance.
- Three strategies to postpone the end of the antibiotic era.
- Practical suggestions for medical and pharmacy students.

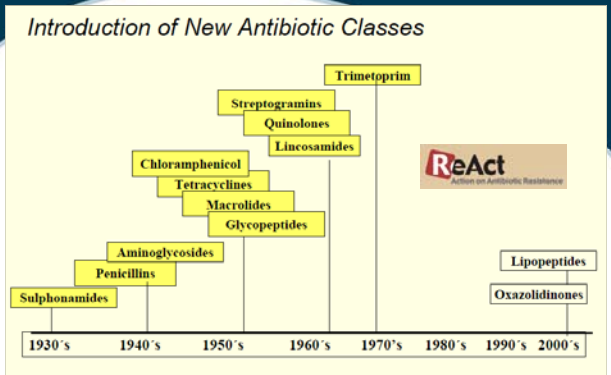
The start of antibiotic resistance: Penicillin

Fleming 1928



Florey & Chain 1940

History of resistance



Bacterial evolution vs mankind's ingenuity

- Adult humans contains 10^{14} cells; only 10% are human, the rest are bacteria.
- Antibiotic use promotes Darwinian selection of resistant bacterial species.
- Bacteria have efficient mechanisms of genetic transfer to spread resistance.
- Bacteria double every 20 minutes, humans every 30 years.
- Development of new antibiotics has slowed – resistant microorganisms are increasing.

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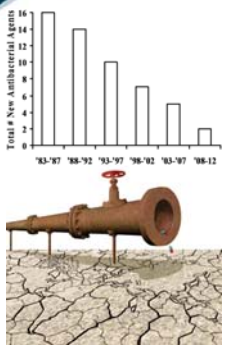
Antibiotic pipeline is drying up



- Why?
  - Only used for short term treatment;
  - New drugs restricted to treat resistant micro-organisms.
- Hence:
  - Limited profit before patent expires;
  - Not a good return on investment for industry.

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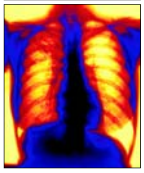
Resistance: Australia 2012

- Hospitals (ESKAPE pathogens)
  - Vancomycin-resistant Enterococci (VRE)
    - Patients with serious infection caused by VRE, such as bacteraemia) have a high mortality.
  - Methicillin (multi-resistant) Staph. aureus (MRSA)
    - In 1996, the first case of reduced susceptibility of *Staph. aureus* to vancomycin was reported in Japan. these are now common in Australian ICU and burns units.
    - In July 2002, the CDC reported the first case of vancomycin-resistant *Staph. aureus* in the US (vancomycin MIC >32 µg / mL). These strains have not yet been found in Australia.
  - Gram-negative bacteria
    - Bacteria such as Kebsiella, Acinetobacter, Pseudomonas and Enterobacter species resistant to "last-line" antibiotics, such as carbapenems (eg, meropenem), fluoroquinolones (eg, ciprofloxacin) and third-generation cephalosporins (eg, cefotaxime), are now common in Australian hospitals.

Resistance: Australia 2012

- Community
  - *Staph. aureus* 23% of isolates are MRSA
  - *Strep. pneumoniae* (Penicillins 18% ^{I}, 8% ^{R}; macrolides & tetracyclines 20% ^{R})
  - *Haemophilis influenzae* (Penicillins 20% ^{R} ; macrolides & tetracyclines 10% ^{R})
  - *E. coli (amoxycillin 48% R ; amoxy-clav 6% R ; trimeth 20%R)*
  - *Human H1N1 influenza* (many strains now resistant to oseltamivir but not H1N1 09 (human swine influenza) as yet)

Resistance: The World 2012



- In Africa and parts of Russia and China a high proportion of tuberculosis patients have XDR-TB; multi-drug resistant tuberculosis that is also resistant to at least three of the six classes of second line agents.
- Thailand has completely lost the use three of the most common anti-malaria drugs because of resistance.
- A growing number of patients now have primary resistance to AZT and other established first-line drugs for HIV-infected persons.

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Consequences of resistance

- Increased morbidity & mortality
  - "best-guess" therapy may fail with the patient's condition deteriorating before susceptibility results are available no antibiotics left to treat certain infections
- Greater health care costs
  - more investigations
  - more expensive, toxic antimicrobials required
  - expensive barrier nursing, isolation, procedures, etc.
- Therapy priced out of the reach of the poor

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Therapy priced out of the reach of the poor

- A decade ago in New Delhi, India, typhoid could be cured by three inexpensive drugs. Now, these drugs are largely ineffective.
- The cost of treating one person with multi-drug-resistant TB is a hundred times greater than the cost of treating non-resistant cases.
- New York City needed to spend nearly US$1 billion to control an outbreak of multi-drug resistant TB; a cost beyond the reach of most of the world's cities.

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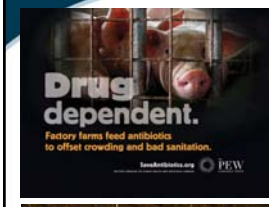
Social and cultural factors fuelling resistance

- Poverty encourages the development of resistance through under use of drugs
  - Patients unable to afford a full course of medicine
  - Sub-standard & counterfeit drugs lack potency
- In wealthy countries, resistance is emerging for the opposite reason – the overuse of drugs.
  - Unnecessary demands for drugs by patients are often eagerly met by health services and stimulated by pharmaceutical promotion
  - Culture is also important
    - Dutch antibiotic use is the lowest in Europe; French use is four times greater (the highest in Europe); Belgian and Italian use were three times greater; and German use was 1·5 times greater.
    - Protestant countries tend to consume fewer antibiotics than predominantly Catholic countries, perhaps due to the Protestant predilection for austerity and simplicity whereas Catholicism is more about rituals.

Overuse of antimicrobials in food production



- Currently, 50%-80% of all antibiotic production is used in animal husbandry and aquiculture.
- Antibiotics are used to promote growth and prevent the spread of disease in cramped conditions.
- This year, for the first time, U.S. farmers and ranchers will now need a prescription from a veterinarian before using antibiotics in farm animals.
- Just using the drugs for growth will be disallowed.

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Increased travel ensure resistant strains spread quickly

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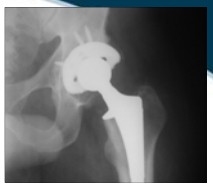
Modern medicine relies upon antibiotics



A world without antibiotics

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Postponing the end of the antibiotic era

- Antibiotic stewardship (prudent use)
- Contain the spread of resistant micro-organisms and relevant genes (infection control)
- Develop new antibiotics that have novel modes of action or circumvent bacterial mechanisms of resistance (research)

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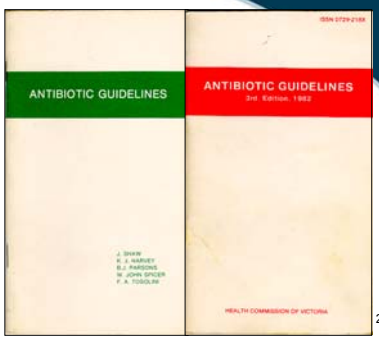
My own interest started at the RMH

Hospital acquired infection with antibiotic-resistant microorganisms

The Royal Melbourne Hospital



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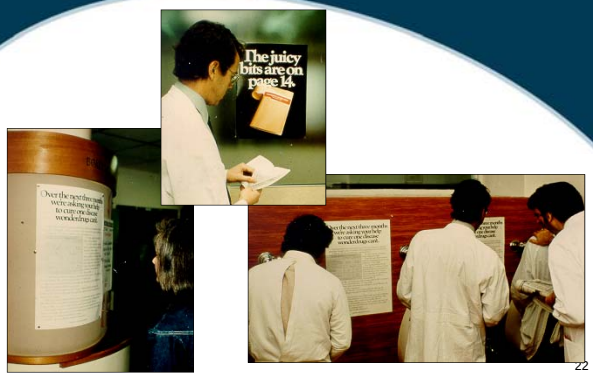
Educational campaigns



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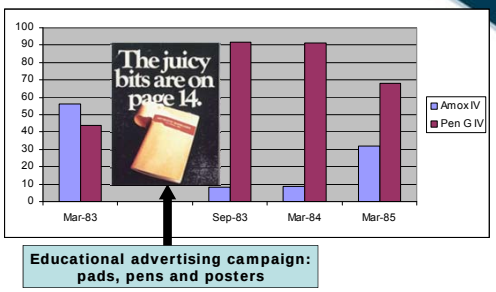
Educational campaigns

Antibiotic use for pneumonia at RMH



Educational advertising campaign: pads, pens and posters

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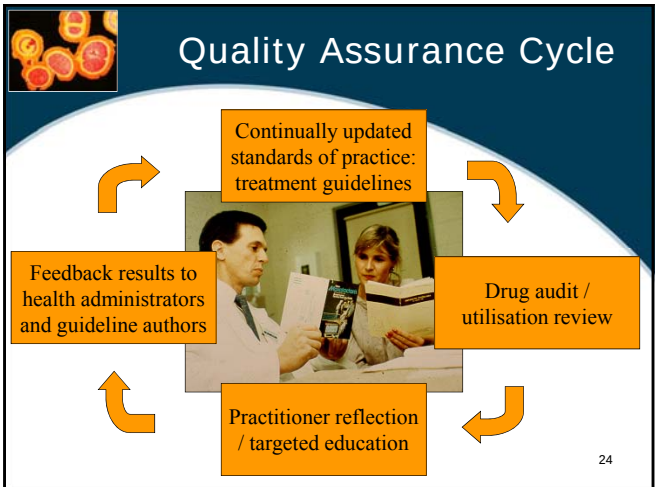
Quality Assurance Cycle



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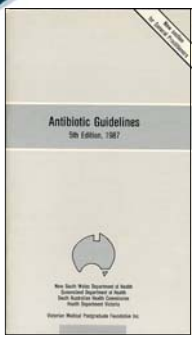
Antibiotic Guidelines



- Best practice recommendations concerning the treatment of choice for common clinical problems.
- Written by teams of national experts.
- Evidence based where possible.
- Regularly updated.
- Endorsed by Medical Associations, Colleges, etc.
- Used for medical education, problem look-up, drug audit and targeted educational campaigns.

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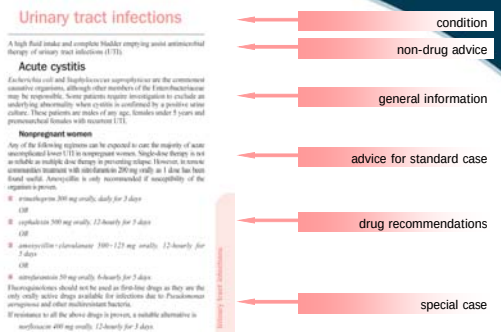
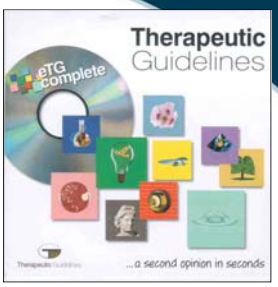
What's inside



Guidelines evolution…



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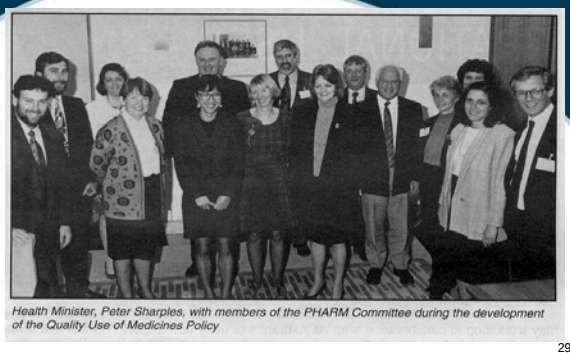
eGuidelines

Scaling up nationally



Health Minister, Peter Sharples, with members of the PHARM Committee during the development of the Quality Use of Medicines Policy

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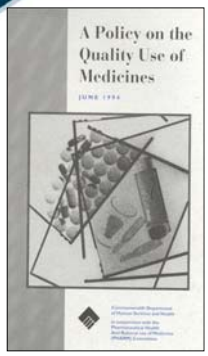
Quality Use of Medicines Policy



Strategies

- Policy development and implementation
- National facilitation and co-ordination (PHARM)
- Independent information
- Ethical behaviour
- Education and training (NPS)
- Interventions (NPS)
- Evaluation

Independent information

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Current challenge

To make best-practice Guidelines, medication review and other proven QUM techniques more accessible via physician's computers

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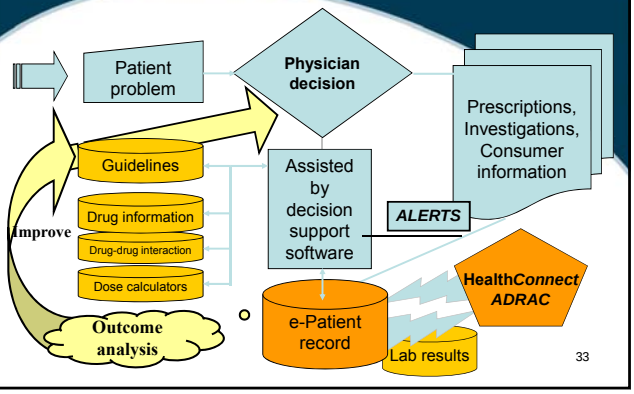
QUM^{IT}: The vision



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E-prescribing

- The uptake of computers by GPs was stimulated by the Australian government in 1999.
- A one-off grant of around $10,000 was offered to those practices that purchased a computer, promised to use prescribing software to write the majority of their prescriptions and acquired internet connectivity (an E-mail address).
- This helped to increase the numbers of GPs writing prescriptions with the aid of a computer from around 50% in 1999 to more than 95% in 2009.
- Legible, printed prescriptions have been one of several positive outcomes.

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However:

- One software vendor (Medical Director™) rapidly became the market leader, in part because its business model relied on selling pharmaceutical advertising within the software.
- The end result was that prescribers using this software (and often their patients who observed the screen) were exposed to numerous pharmaceutical advertisements.

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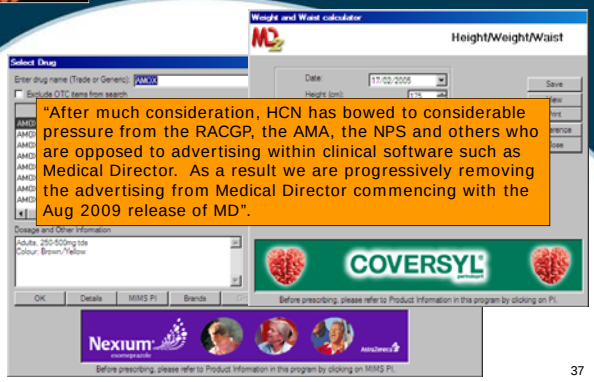
In addition:

- A study in Newcastle, NSW [1], found a higher rate of repeat prescribing with computer generated original prescriptions compared with hand-written prescriptions for many antibiotics.
- Computer-generated prescriptions were over three times more likely to result in a repeat being issued.
- This was thought to be due to default settings of the MD™ software.

1. Newby DA, et al. Med J Aust 2003;178:210–13.

Ads now removed



"After much consideration, HCN has bowed to considerable pressure from the RACGP, the AMA, the NPS and others who are opposed to advertising within clinical software such as Medical Director. As a result we are progressively removing the advertising from Medical Director commencing with the Aug 2009 release of MD".

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Why the concern?

- Pharmaceutical promotion selectively promotes the benefits of the latest and most expensive drugs.
- It provides minimal information about drug side-effects, contra-indications and opportunity costs.
- Cost-effective generic drugs and non-drug solutions are rarely promoted.

BMJ 2003;326 (31 May)

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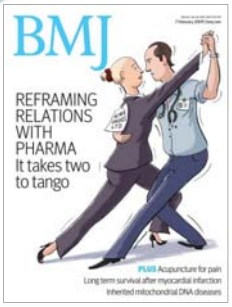
"It takes two to tango"



- Some 80-95% of doctors regularly see drug reps despite evidence that their information is overly positive and prescribing habits are less appropriate as a result.
- Many doctors receive multiple gifts from drug companies every year, yet most doctors deny their influence despite considerable evidence to the contrary.

BMJ 2009;338 (5 Feb)

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"It takes two to tango"

Industry-doctor interaction correlates with:

- Doctors' preferences for new products that hold no demonstrated advantage over existing ones.
- Decreased prescribing of generic drugs.
- A rise in both and irrational and incautious prescribing.
- Rising prescription expenditures.

BMJ 2003;326 (31 May)

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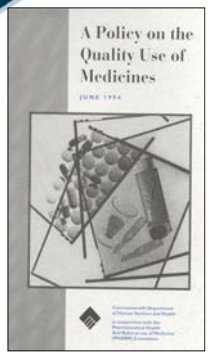
Quality Use of Medicines Policy



Strategies

- Policy development and implementation
- National facilitation and co-ordination (PHARM)
- Objective information
- Ethical behaviour
- Education and training
- Services and interventions
- Evaluation

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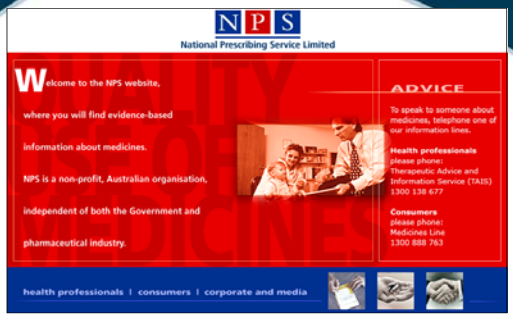
Ethical behaviour

QUM: Services and interventions



- Core curriculum
- Academic detailing
- Campaigns
- Drug audits
- Case studies
- Advice and information
- Practice incentive payments

http://www.nps.org.au/

NPS: Core curriculum

http://nps.unisa.edu.au/new/index.htm

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NPS: Academic detailing

Also: home medication review by pharmacists (Government-Guild agreement)

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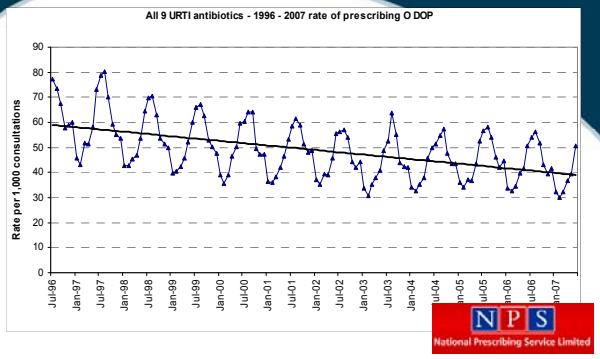
NPS: Consumer Campaigns

http://www.nps.org.au/site.php?page=2&content=/resources/ccncs/index.htm

Results: antibiotic scripts URTI 1996-2007



NPS
National Prescribing Service Limited

- The NPS initially received about $5 million per annum (for four years) in 1997/98.
- A evaluation of their activities showed that each dollar spent on independent education saved the PBS three dollars.
- Their budget has subsequently been increased and a consumer education moiety has been added.
- **Spending money on RDU activities saves money by reducing inappropriate drug use.**

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Quality Use of Medicines Policy

Partnership with:

- Health care consumers, their careers, and the general community;
- Health practitioners and health
- Educators;
- Pharmaceutical Industry;
- Media;
- Government.

http://www.health.gov.au/internet/wcms/publishing.nsf/Content/nmp-quality.htm

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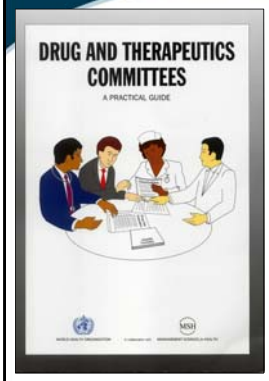
In Hospitals - DTCs:



- Select cost-effective drugs for the hospital formulary.
- Develop (or adapt) and implement standard treatment guidelines.
- Audit drug use to identify problems.
- Conduct interventions to improve drug use.
- Manage adverse drug reactions and medication errors.
- Educate staff about drug use issues, policies and decisions.

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Antimicrobial Stewardship Programs

- Effective hospital antimicrobial stewardship (AMS) programs have been shown to decrease antimicrobial use and improve patient care.
- Along with infection control, hand hygiene and surveillance, AMS is a key strategy in local and national programs to prevent the emergence of antimicrobial resistance and decrease preventable healthcare associated infection.

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Action steps for today[1]

- Vaccinate
  - have influenza vaccine yourself.
  - make sure all infants, children and adults receive a full schedule of vaccines (and boosters) provided free under the National Immunisation Program.
  - give influenza and pneumococcal vaccine to at-risk patients.
- Use *Antibiotic Guidelines*.
- Say "no" to patients asking for antibiotics for URTI you suspect are viral.

1. http://www.mja.com.au/public/issues/177_06_160902/col10836_fm.html

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Action steps for today

- Tell patients that:
  - The benefits of antibiotic therapy in:
    - pharyngitis,
    - tonsillitis,
    - non-suppurative otitis media and
    - sinusitis
  - are much more limited than previously thought and counterbalanced by the risk of drug side effects, such as rash.
    - Regular analgesia is more effective than antibiotics in decreasing symptoms for the above conditions.
  - It's best to keep antibiotics for serious infections when they are really needed.

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Action steps for today

- When prescribing antibiotics:
  - Select the narrowest spectrum agent possible.
  - Stop treatment when infection is unlikely (e.g. cultures are negative) or has responded.
  - Remove the cause of persisting infection such as indwelling catheters and undrained abscesses.
  - Restrict prophylactic antimicrobial therapy to situations in which it has been shown to be effective or the consequences of infection could be disastrous
    - e.g. colorectal surgery, prosthetic large joint replacement and cardiac valve replacement.
    - N.B. a single dose of an appropriate prophylactic antibiotic administered at the time of skin incision is usually adequate.

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Action steps for today

Finally, break the chain of contagion:

- Wash your hands between patients;
- Follow good infection control practices;
- Stay home when you are sick (and recommend that infectious patients also stay home from work);
- Set a good example!

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Practical problems –possible solutions?

Patient expectation	Explain diagnosis and reasons for not using antibiotics
Limited consultation time	Use nurses, pharmacists, provide printed materials
Diagnostic uncertainty	Encourage telephone review (give script in case needed)
Fear of litigation	Follow *Antibiotic Guidelines*, good communication with patient

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All counties have the same problem

Review Open Access
Rational antibiotic use in China: lessons learnt through introducing surgeons to Australian guidelines
Yan Zhang, Ken J Harvey
Australia and New Zealand Health Policy 2006, 3:5 (30 May 2006)
[Abstract] [Provisional PDF] [PubMed] [Related articles]

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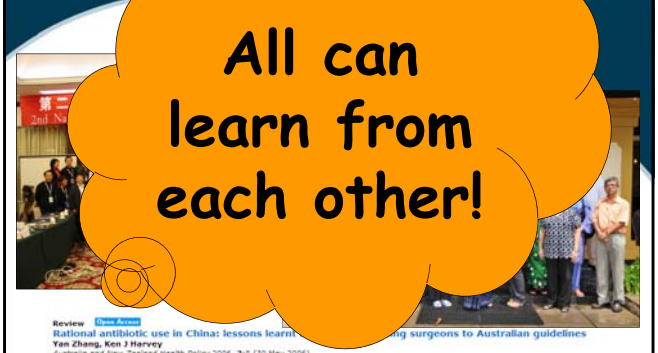
All can learn from each other!



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[Abstract] [Provisional PDF] [PubMed] [Related articles]

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- Australian Antimicrobial Resistance Summit 2011 http://www.antimicrobialsummit.com.au/
- So A, Gupta N, Cars O, Tackling Antibiotic Resistance. BMJ 2010;340:c2071 http://www.bmj.com/cgi/content/full/340/may18_2/c2071
- Alliance for the Prudent Use of Antibiotics (APUA) http://www.tufts.edu/med/apua/
- Reaction on antibiotic resistance (REACT) http://www.reactgroup.org/

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