20 INDEPENDENT REVIEW OF THE LITERATURE

20.1 INTRODUCTION

As part of the process of preparing our Report, the Sub-Group on Antimicrobial Resistance commissioned an independent review of the literature to determine the nature and quality of the evidence that changing prescribing patterns could result in reduction or limitation of the spread of antimicrobial resistance.

20.2 AIMS

To assess the evidence that inappropriate use of antibiotics leads to increased levels of antimicrobial resistance.

To assess the quality of evidence that antimicrobial resistance levels can effectively be reduced or reversed.

To examine the evidence that effective implementation of changes in prescribing practices will result in reduction of antimicrobial resistance levels.

To provide independent confirmation, or otherwise, that the conclusions reached in the main report are justified.

20.3 METHODOLOGY

MEDLINE searches were carried out to identify relevant studies published in the last 10 years. A search of the BIDS database was also employed. Searches used both appropriate keywords and MeSH terms such as ‘Drug resistance, microbial’ and ‘Prescriptions, drug’. Additional papers were identified from the reference lists of these papers, grey literature including conference reports, and the work of key authors. The main focus was Western Europe and North American studies.

The quality of the research was critically appraised and graded using a slightly modified version of the criteria developed in the NHS Centre for Reviews and Dissemination, University of York, in conjunction with the Cochrane Collaboration.

The grading was that of the independent reviewers.

Grade I (Strong evidence)
Randomised controlled trial or review of randomised controlled trials

IA: Calculation of sample size and accurate and standard definition of outcome variables
IB: Accurate and standard definition of outcome variables
IC: Neither of the above

Grade II (Fairly strong evidence)
Prospective study with a comparison group, (non-randomised) controlled trial or good observational study

IIA: Calculation of sample size and accurate, standard definition of outcome variables and adjustment for the effects of important confounding variables
IIB: One of the above
IIC: None of the above

Grade III (Weak evidence)
Retrospective study

IIIA: Comparison group, calculation of sample size and accurate and standard definition of outcome variables
IIIB: Two of the above criteria
IIIC: None of the above

Grade IV (Weak evidence)
Cross-sectional study

In addition several papers were reviewed which involved *in-vitro* experimental techniques, using bacterial cultures. There is no standard grading for the quality of such evidence. It was, therefore, divided into three grades (using Arabic numbers)

1. Good *in-vitro* evidence
Standardised prospective experimental procedures with good controls and clearly defined conditions

2. Fairly good *in-vitro* evidence
Good controls and clearly defined conditions in retrospective or non-standard procedures

3. Weak *in-vitro* evidence
Poorly controlled or defined experimental conditions.

20.4 SEARCH RESULTS

The basic MEDLINE search using the terms ‘Drug resistance, microbial’ and ‘Prescriptions, drug’ yielded 65 references over the last 10 years. However, eight of these were in a variety of languages other than English (Scandinavian or other European languages) and few had abstracts available in English. There was a preponderance of papers in journals which were not readily available.

Other key words were tried: ‘Eradication’ yielded references almost exclusively on *Helicobacter pylori*. ‘Reduction’ brought up many general references on infection control, while ‘reversal’ generated mainly articles on leprosy, HIV and several *in-vitro* molecular experiments, including the identification of resistance mechanisms and use of inhibitors. The limitations of MEDLINE were revealed by the failure to include the work of the Finnish Study Group for Antimicrobial Resistance (FIRE) until both ‘Finland’ and ‘Erythromycin’ were used as search terms.

A search of the BIDS database was less specific, but did yield about 12 relevant papers (out of over 200) including an editorial comment on the Finnish results.

In general the quality of the evidence was not high. No good randomised controlled trials were identified and few controlled prospective studies. This is not surprising as randomised controlled trials are not feasible in this field. Research designs normally regarded as of relatively poor quality for evaluation of clinical interventions may be the best available in this case. Such findings have been noted before in other areas of service delivery. Many papers were non-systematic reviews, conference reports and editorial comments rather than original studies and, therefore, contributed little to the overall body of evidence. The exceptions to this were in the field of guideline implementation, where there have been randomised controlled trials and systematic reviews, and the studies of prescribing in primary care.

In contrast, much of the *in-vitro* evidence results from experiments performed in standardised conditions where well-controlled experiments can be designed. However, it is difficult to relate the value of such evidence to clinical situations and there appears to be no standard methodology for doing so. Mathematical modelling in bacterial population genetics is even more difficult to evaluate, but has the potential to provide answers unobtainable in any experimental situation.

The difficulties noted in undertaking this systematic review were compounded by the limited time available. It is also of note that similar problems – the paucity of good evidence and the difficulty of adapting scoring schemes devised for clinical trials – were encountered by the review being undertaken by the Advisory Committee on the Microbiological Safety of Foods.

20.5 PAPERS APPRAISED

20.5.1 IN VITRO CONTROLLED EXPERIMENTS AND MATHEMATICAL MODELS

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
222	Lenski RE 1997	The cost of antibiotic resistance – from the perspective of a bacterium	Review of *in-vitro* experiments	Costs of antibiotic resistance in bacteria are subject to evolutionary change and reduce over time due to natural selection	1
224	Bouma JE, Lenski RE 1988	Evolution of a bacterial / plasmid association	*In-vitro* controlled experiment	New plasmid-bearing *E. coli* inferior competitor to plasmid-free strain in absence of antibiotic. After 500 generations in presence of chloramphenicol genetic adaptation had occurred in chromosome so evolved plasmid-bearing bacteria had competitive advantage even in absence of antibiotic	1
278	Lenski RE, Simpson SC, Nguyen TT 1994	Genetic analysis of a plasmid-encoded, host genotype-specific enhancement of bacterial fitness	*In-vitro* controlled experiment	Tetracycline resistance is actually beneficial to the evolved host bacteria in the absence of antibiotic, making it competitively superior to its plasmid-free counterpart	1
279	Modi RI, Adams J 1991	Co-evolution in bacteria-plasmid populations	*In-vitro* controlled experiment	After 800 generations cost of carriage of a plasmid encoding resistance for ampicillin and tetracycline in *E. coli* significantly reduced, due to changes in both bacterial and plasmid genomes	1

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
218	Schrag SJ, Perrot V 1996	Reducing antibiotic resistance	*In-vitro* controlled experiment	Chromosomal mutations in rpsL gene of *E. coli* confer resistance to streptomycin, but at cost of altered ribosomes and slower protein synthesis. After >200 generations this cost is reduced due to secondary mutations elsewhere, without change in streptomycin resistance	1
280	Cohan FM *et al* 1994	Amelioration of the deleterious pleiotropic effects of an adaptive mutation in *Bacillus subtilis*	*In-vitro* controlled experiment	Mutations causing rifampicin resistance occur in gene coding for RNApolymerase, reducing competitive fitness. Cost varies with both mutation and strain of *B. subtilis*, so should be reduced over time due to natural selection	1
281	Sundin GW, Bender CL 1996	Dissemination of the strA-strB streptomycin resistance genes among commensal and pathogenic bacteria from humans, animals and plants	*In-vitro* controlled experiment	Resistance persists widely in nature. The genes encoding for streptomycin resistance have been recently disseminated by transfer between human-, animal- and plant-associated bacteria	2
282	Roberts M, Elwell LP, Falkow S 1977	Molecular characterization of two β-lactamase-specifying plasmids isolated from *Neisseria gonorrhoeae*	*In-vitro* controlled experiment	Stability of penicillin resistance in *N. gonorrhoeae* plasmids increased over time	2
219	Schrag SJ *et al* 1997	Adaptation to the fitness costs of antibiotic resistance in *Escherichia coli*	*In-vitro* controlled experiment	Second site mutations compensate for fitness costs of streptomycin resistance in *E. coli* to produce a competitive advantage over sensitive strains. The resistance sequences had not changed over 10,000 generations	1
283	Borman *et al* 1996	Resistance of HIV-I to protease inhibitors. Selection of resistant mutations in the presence and absence of the drug	*In-vitro* controlled experiment	Resistant strains of HIV-1 did not revert to wild type when serially passaged in drug-free conditions. Secondary mutations continued to emerge, improving both replicative capacity and resistance	1
226	Levin BR, Lipsitch M, Perrot V *et al* 1997	The population genetics of antibiotic resistance	Mathematical modelling	Frequencies of resistant bacteria are related to antibiotic usage, but decline in rates after restrictions would be very slow and subject to rapid reversal on re-introduction	1
225	Bonhoeffer S, Paulous S, Clavel F 1997	Evaluating treatment protocols to prevent antibiotic resistance	Mathematical modelling	Long-term benefit from first use to high resistance levels is almost independent of pattern of use. When more than one antibiotic is used the optimum strategy is to use both drugs in combination	2

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
284	Lipsitch M, Levin BR 1997	The population dynamics of antimicrobial chemotherapy	Mathematical modelling	Model predicts resistance will not emerge during treatment if resistant mutants are not present initially and the average net rate of decline is comparable to rate of cell division, but sustained exposure to lower doses will select for resistance. Random non-adherence to regimen can be compensated for by more potent drug combinations	2

20.5.2 EFFECT OF ANTIBIOTIC USE ON RESISTANCE PATTERNS

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
228	Levy SB, Marshall B, Schluederberg S, Rowse D, Davis J 1988	High frequency of antibiotic resistance in human fecal flora	Cross-sectional survey	Seven agents in 600 subjects, healthy, ambulatory and hospitalised: high rate of resistance regardless of recent antibiotic therapy (10% of those with no recent history had one or more resistant strains, and >50% of those taking antibiotics). Frequent multi-resistance found	IV
285	Hart CA 1998	Antibiotic resistance: an increasing problem?	Editorial	Resistance problem is increasing, but genes and mechanisms existed before antibiotics were ever used. Inappropriate to apportion blame but should reconsider control of infection practice	
286	D'Amico R, Pifferi S, Leonetti C, Torri V, Tinazzi A, Liberati A 1998	Effect of antibiotic prophylaxis in critically ill adult patients: systematic review of randomised controlled trials	Systematic review and meta-analysis of RCTs	Prophylaxis with a combination of topical and systemic antibiotics can reduce respiratory tract infections and overall mortality in critically ill patients. No conclusion on risk of antibiotic resistance due to lack of valid data	IA
287	Working Party of the British Society for Antimicrobial Chemotherapy 1994	Hospital antibiotic control measures in the UK	Postal survey	Majority of responding hospitals had policies: 51% for prophylaxis, 62% therapy and 79% formulary, but compliance was monitored in only 40% and actively controlled in only 50% of these. Only 11% had formal audit	IV

20.5.3 IMPACT OF ANTIBIOTIC POLICIES ON RESISTANCE LEVELS

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
242	Betts RF, Valenti WM, Chapman SW *et al* 1984	Five-year surveillance of aminoglycoside usage in a university hospital	Prospective study	Following a change from gentamicin to amikacin as the primary aminoglycoside, resistance to gentamicin and tobramycin showed a statistically significant decrease in several gram-negative organisms	IIB
234	Kataja J, Huovinen P, Muotiala A *et al* 1998	Clonal spread of group A streptococcus with the new type of erythromycin resistance. Finnish Study Group for Antimicrobial Resistance	Retrospective survey	The new erythromycin resistance reported in Finland in the 1990s is mostly from a single clone	IIIC
233	Seppala H, Klaukka T, Vuopio-Varkila J *et al* 1997	The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococcus in Finland. Finnish Study Group for Antimicrobial Resistance	Retrospective survey	National policy reduction in macrolide antibiotics in community led to decrease in frequency of resistance in isolates	IIIC
288	Seppala H, Klaukka T, Lehtonen R, Nenonen E, Huovinen P 1997	Erythromycin resistance of group A streptococci from throat samples is related to age	Retrospective survey	Risk of resistance decreased significantly with increasing age by 1% a year, possibly due to different prescribing practices	IV
19	Huovinen P, Seppala H, Kataja J, Klaukka T 1997	The relationship between erythromycin consumption and antibiotic resistance in Finland. Finnish Study Group for Antimicrobial Resistance	Review of retrospective studies	Erythromycin resistance in isolates significantly linked to local consumption. 83% of isolates were a single clone. Following new prescribing guidelines macrolide consumption fell by 40%	IV
289	Seppala H *et al* 1995	Outpatient use of erythromycin; link to increased erythromycin resistance in group A streptococci	Cross-sectional survey	206 health authorities: proportion of isolates resistant to erythromycin in 1992 increased significantly with local out-patient consumption in 1991	IV
290	Cullman W 1996	Comparative evaluation of orally active antibiotics against community acquired pathogens: results of eight European countries.	Multi-centre cross-sectional survey	>13,000 isolates from 37 centres. For many species % resistant similar across Europe, but high levels of penicillin G-resistant *S. pneumoniae* in Spain and Hungary and ampicillin resistant *H. influenzae* in Spain	IV
291	Nissinen A, Gronroos P, Huovinen P *et al* 1995	Development of beta-lactamase-mediated resistance to penicillin in middle ear isolates of *Moraxella catarrhalis* in Finnish children 1978–1993	Cross-sectional survey	Bimodal increase in resistance; 0–60% up to 1983 and from 60–80% in 1988–90. Substantial increase in cephalosporin use in community coincided with second increase	IV

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
292	Nissinen A, Leinonen M, Huovinen P *et al* 1995	Antimicrobial resistance of *Streptococcus pneumoniae* in Finland 1987–1990	Cross-sectional survey	Isolates from middle ear fluid of children with otitis media and throat swabs from healthy children. Six multi-resistant strains identified, 85% from three common serogroups	IV
236	Manninen R, Huovinen P, Nissinen A *et al* 1997	Increasing antimicrobial resistance in *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* in Finland	Cross-sectional survey	Levels rose including erythromycin resistance in pneumococci, which increased from 0.6% in 1990 to 2.5% in 1995	IV
270	King JW, White MC, Todd JR, Conrad SA 1992	Alterations in the microbial flora and in the incidence of bacteremia at a university hospital after adoption of amikacin as the sole formulary aminoglycoside	Prospective study comparing low use with high frequency usage	Rates of resistance to gentamicin, tobramycin and amikacin in gram-negative isolates fell by ~50% following the intervention. Incidence of bacteraemia also decreased	IIC?
237	Stephenson J 1996	Icelandic researchers are showing the way to bring down rates of antibiotic-resistant bacteria	News report of conference paper by Kristinsson	Great increase in penicillin-resistant pneumococci (PRP) in Iceland to 1993 especially in children's day-care. Major publicity campaign to public and physicians. Parents encouraged not to send sick children. Sales fell from 1990 on. Resistance declined from 20% in 1992 to 15% in 1995 (not significant)	?
293	Asensio A, Guerrero A, Quereda C, Lizan M, Martinez-Ferrer M 1996	Colonisation and infection with methicillin resistant *Staphylococcus aureus*: associated factors and eradication	Retrospective case-control and cohort studies	Six factors associated independently with MRSA colonisation / infection: age, ward (OD surgical 1 / ICU 60) previous or long hospitalisation, coma and invasive procedures. Antibiotic therapy not independent risk factor. Reduce rates by identifying high risk, prompt discharge and control of infection in invasive procedures	IIIA
17	Muder RR, Brennen C, Drenning SD, Stout JE, Wagener MM 1997	Multiple antibiotic resistant gram-negative bacilli in a long-term care facility: a case-control study of patient risk factors and prior antibiotic use	Retrospective case-control study	Acquisition of resistance associated with prior antibiotic exposure	IIIC
294	Brennen C *et al* 1998	Vancomycin resistant *Enterococcus faecium* in a long-term care facility		24 of 36 patients with VREF had it on transfer from acute care. 17 also had MRSA. Treatment of VREF colonisation with antimicrobial agents prolonged carriage	IIIC

20.5.4 GUIDELINE IMPLEMENTATION AND CHANGING CLINICAL PRACTICE

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
268	NHS centre for Reviews and Dissemination, University of York and Nuffield Institute for Health, University of Leeds 1995	Effective Health Care Bulletin. Implementing clinical practice guidelines: can guidelines be used to improve clinical practice?	Systematic review of 91 guideline implementation evaluations	Practice guidelines can change professional behaviour and improve process and outcome of care. 81 showed improvements in care and 12/17 in outcome	IA
266	Grimshaw J, Russell I 1993	Effect of clinical guidelines on medical practice – a systematic review of rigorous evaluations	Systematic review	Review of implementation of 59 guidelines. 55 resulted in significant improvements in care	IA
269	Grol R 1997	Beliefs and evidence in changing clinical practice	Review / comment	Implementing change requires good planning and several interventions. Obstacles to change should be identified	
295	Weingarten SR, Riedinger MS, Hobson P *et al* 1996	Evaluation of a pneumonia practice guideline in an interventional trial	Prospective controlled trial	Guideline provided information on switching patients from parenteral to oral antibiotics and early discharge. No significant difference in care (majority conformed to guideline) or outcomes	IIB

20.5.5 IMPROVING HOSPITAL PRESCRIBING OF ANTIMICROBIAL AGENTS

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
250	Pestotnik SL, Classen DC, Evans RS, Burke JP 1996	Implementing antibiotic practice guidelines through computer assisted decision support: clinical and financial outcomes	Prospective descriptive epidemiology and financial analysis	Computer-assisted decision-support programmes using local clinically derived guidelines improved antibiotic use, reduced costs and stabilised resistance levels	IIB
251	Evans RS, Pestotnik SL, Classen DC *et al* 1998	A computer-assisted management programme for antibiotics and other anti-infective agents	Prospective interventional study in ITU with retrospective controls	Programme use reduced antibiotic susceptibility mismatches and excess doses. Full compliance caused shorter stays and lower drug and hospital costs	IIC
296	Evans RS, Classen DC, Pestotnik SL, Lundsgaarde HP, Burke JP 1994	Improving empiric antibiotic selection using computer decision support	Prospective controlled trial	The computer programme helped physicians to order the optimum regimen significantly more often	IIB

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
216	McGowan JE 1994	Do intensive hospital antibiotic control programs prevent the spread of antibiotic resistance?	Review	Most studies do not have susceptibility as an outcome and have problems of bias and confounding. Intensive control programmes for drug–organism pairs in a few hospitals were associated with increased susceptibility, which reversed rapidly when controls were relaxed. Properly conducted multi-centre studies are required	IIIC
16	McGowan JE 1996	Does antibiotic restriction prevent resistance?	Review	Association between antimicrobial usage and resistance is likely to be causal. Educational efforts alone have failed to be effective on a large scale or in the long term	
18	Shlaes DM, Gerding DN, John JF *et al* 1997	Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals	Review and guidelines	Appropriate usage including optimal selection, dosage and duration of treatment and control of use will prevent or slow emergence of resistance	IIC
58	Archibald L, Phillips L, Monnet D, McGowan JE, Tenover F, Gaynes R 1997	Antimicrobial resistance in isolates from inpatients and outpatients in the United States: increasing importance of the intensive care unit	Cross-sectional survey	% of resistant isolates decreased from ICU patients through other in-patients to out-patient samples over a range of antimicrobial agents and organisms in eight hospitals. Resources allocated to control should be focused on hospitals and especially ICUs	IV
188	Baquero F 1996	Antibiotic resistance in Spain: what can be done?	Review / health policy statement	Strategies for improving surveillance of resistance, monitoring antibiotic consumption and influencing producers, prescribers and consumers	–
297	Sturm AW 1990	Effects of a restrictive antibiotic policy on clinical efficacy of antibiotics and susceptibility patterns of organisms	Retrospective study following policy change	Restrictive antibiotic policy led to cure in 88% with initial therapy and further 7% with change of drugs, but failure in 5%. No change in resistance patterns over 2-month evaluation period	IIIC
298	Goldmann DA, Weinstein RA, Wenzel RP *et al* 1996	Strategies to prevent and control the emergence and spread of antimicrobial resistant micro-organisms in hospitals	Consensus statement and review	Highlights excessive prescribing and failure to use basic infection control techniques. Provides strategies to optimise usage and monitor development of resistance in a hospital, with suggested process and outcome measures	–

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
271	Pear SM, Williamson TH, Bettin KM, Gerding DN, Galgiani JN 1994	Decrease in nosocomial *Clostridium difficile*-associated diarrhoea by restricting clindamycin use	Surveillance and retrospective case control	Nosocomial outbreak was controlled by analysis of antibiotic usage, identification of a clindamycin-resistant strain and then restriction of clindamycin. Frequency of isolation of this strain subsequently declined ($p < 0.001$)	IIIB
299	Moller JK 1989	Antimicrobial usage and microbial resistance in a university hospital during a seven-year period	Retrospective survey of hospital and community	Resistance in *S. aureus* and *E. coli* stable overall, but increased in *S. epidermidis* from 29% in 1981 to 43% in 1987. Correlation between specific usage and resistance when co-selection from other antimicrobial agents included	IIIC
300	Courcol RJ, Pinkas M, Martin GR 1989	A seven year survey of antibiotic susceptibility and its relationship with usage	Retrospective survey in hospital	Significant correlation between antibiotic usage and increasing resistance, especially in cephalosporin	IV
301	Olson B, Weinstein RA, Nathan C, Chamberlin W, Kabins SA 1984	Epidemiology of endemic *Pseudomonas aeruginosa*: why infection control efforts have failed	Detailed survey in ICU	Many patients arrived colonised, but this was unrecognised, despite frequent throat and rectal cultures. Cross-infection rare	IIIB
15	Chow JW, Fine MJ, Shlaes DM *et al* 1991	Enterobacter bacteremia: clinical features and emergence of antibiotic resistance to therapy	Prospective multicentre observational study	Previous administration of third-generation cephalosporins more likely to be associated with resistance than other antimicrobial agents	IIC
20	Manian FA, Meyer L, Jenne J, Owen A, Taff T 1996	Loss of antimicrobial susceptibility in aerobic gram-negative bacilli repeatedly isolated from patients in intensive-care units	Prospective observational study	Loss of sensitivity in repeat AGNB isolates is common and related to prior antibiotic use. Minimising use of antibiotics in ICUs is important to help reduce risk of resistance development	IIC
127	Vincent JL, Bihari DJ, Suter PM *et al* 1995	The prevalence of nosocomial infections in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study	1-day point prevalence study	ICU infection is common and often associated with resistant strains. Risk factors include length of stay, ventilation, trauma and catheterisation	IV
302	Johnson AP, Speller DC, George RC, Warner M, Domingue G, Efstratiou A 1996	Prevalence of antibiotic resistance and serotypes in pneumococci in England and Wales: results of observational surveys in 1990 and 1995	2-week observational surveys of PHLS laboratories	Resistance to penicillin and erythromycin increased. No change in other organisms. No resistance to rifampicin or vancomycin detected during study periods	IV

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
303	Baquero F 1996	Trends in antibiotic resistance of respiratory pathogens: an analysis and commentary on a collaborative surveillance study	Retrospective multicentre survey: resistance vs prescription data for 1992 and 1993	Complex situation but in general countries with highest per capita consumption also have highest resistance levels. Definite stages of development from susceptibility to very high resistance	IIIB
144	McNulty C, Logan M, Donald IP 1997	Successful control of *Clostridium difficile* infection in an elderly care unit through use of a restrictive antibiotic policy	Observational study of antibiotic usage and infection rates	Outbreak controlled by combination of infection control measures and strict prescribing	IV
304	Acar JF 1997	Consequences of bacterial resistance to antibiotics in medical practice	Review	Costs of resistance include extra bed days and diagnostic tests in addition to higher antibiotic costs	–
305	Barie PS 1998	Antibiotic-resistant gram-positive cocci: implications for surgical practice	Review	Use of broad-spectrum antibiotics selects for resistance. Rampant inappropriate use of vancomycin must be curtailed and infection control precautions tightened	IV
306	Rho JP, Yoshikawa TT 1995	The cost of inappropriate use of anti-infective agents in older patients	Review	High levels of inappropriate prescribing found in several studies. Likely consequences are poor compliance, adverse reactions and selection for resistance	IV
307	Sutherland R 1991	Beta-lactamase inhibitors and reversal of antibiotic resistance	Review	Development of clavulanate and other similar inhibitors (not reduction in prevalence of resistance)	–
308	Rubin LG, Tucci V, Cercenado E, Eliopoulos G, Isenberg HD 1992	Vancomycin-resistant *Enterococcus faecium* in hospitalised children	Survey and case control study	High prevalence of VRE amongst paediatric oncology patients, associated with length of stay and administration of vancomycin and other antibiotics. Prevention associated with contact isolation and restriction of vancomycin use	IV
309	Evans ME *et al* 1996	Vancomycin in a university medical centre: comparison with hospital infection control practices advisory committee guidelines	1-month prospective survey of all patients given vancomycin	Only 35% of prescriptions conformed to guidelines. Main reason was failure to obtain cultures	IV
310	Harbarth S, Rutschmann O, Sudre P, Pittet D 1998	Impact of methicillin resistance on the outcome of patients with bacteremia caused by *Staphylococcus aureus*	Cohort and case control studies	Methicillin resistance in patients with *S. aureus* bacteraemia had no significant impact on mortality after adjustment for major confounders (age and length of stay)	IIIB

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
21	Parry MF, Panzer KB, Yukna ME 1989	Quinolone resistance. Susceptibility data from a 300-bed community hospital	Prospective survey over 4 years	Resistance levels rose with increasing usage and 72% of isolates were from patients who had had a fluoroquinolone in the previous month	IV
311	Zakrzewska-Bode A, Muytjens HL, Liem KD, Hoogkamp-Korstanje JA 1995	Mupirocin resistance in coagulase-negative staphylococci, after topical prophylaxis for reduction of colonization of central venous catheters	Survey plus small prospective series	After 5 years of routine application, resistance was observed in 42% of isolates from NICU – fell to 21% after 5 mupirocin-free months and 13% after 1 year	IV
312	Conus P, Francioli P 1992	Relationship between ceftriaxone use and resistance of *Enterobacter* species	Retrospective survey	Compared consumption and evolution of resistance over 4 years. Consumption trebled and resistance in isolates rose from 10 to 27%. No changes in hospital hygiene and no epidemics during study period	IV
313	Bergmans DC, Bonten MJ, Gaillard CA *et al* 1997	Indications for antibiotic use in ICU patients: a one-year prospective surveillance	Prospective survey	53% of infections were ICU-acquired, 99% in intubated patients. 59% of antibiotics were prescribed for bacteriologically proven infections. Prevention of RTI most effective mode of reduction of antibiotic use	IV
314	Boyce JM, Opal SM, Potter-Bynoe G, Medeiros AA 1993	Spread of methicillin-resistant *Staphylococcus aureus* in a hospital after exposure to a health care worker with chronic sinusitis	Retrospective study	Cases in an epidemic of MRSA were found to be significantly more likely to have had contact with a respiratory therapist with chronic sinusitis with the same strain. Plasmid DNA of isolates had the same digestion pattern. Eradication of the sinusitis and nasal carriage, and implementation of general control measures terminated the outbreak	IIIC
14	Fish DN, Piscitelli SC, Danziger LH 1995	Development of resistance during antimicrobial therapy: a review of antibiotic classes and patient characteristics in 173 studies	Review	Resistance was most common in intensive care units or ventilated patients, and in studies in teaching hospitals	III
315	Anglim AM, Klym B, Byers KE, Scheld WM, Farr BM 1997	Effect of a vancomycin restriction policy on ordering practices during an outbreak of vancomycin resistant *Enterococcus faecium*	Audit of vancomycin use pre- and post-policy implementation	Use compared with HICPAC guidelines from CDCP, Atlanta. Initially 61% inappropriate according to criteria, falling to 30% at follow-up. Overall use fell by 50%	IIIB

20.5.6 RESISTANCE IN THE COMMUNITY

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
238	Kristinsson KG 1995	Epidemiology of penicillin resistant pneumococci in Iceland	Review	Rapid spread of PRP in Iceland may have been facilitated by high antimicrobial consumption in day-care centres for small children. Most resistant infections came from a clone originating in Spain	IV
239	Kristinsson KG 1997	Effect of antimicrobial use and other risk factors on antimicrobial resistance in pneumococci	Review	Propaganda against overuse, led to reduction in usage and subsequent reduction in PRP	IV
316	van den Bogaard AE 1997	Antimicrobial resistance – relation to human and animal exposure to antibiotics	Letter / survey	Antimicrobial agents for animal use much cheaper than for humans so expenditure unreliable guide to usage. In 1990 human dosage in Holland was 100 mg active substance / kg body weight / year in contrast to 125 mg / kg / year for poultry and 430 mg / kg / year for pigs, mostly in animal husbandry rather than veterinary medicine	IV
240	Arason VA, Kristinsson KG, Sigurdsson JA, Stefansdottir G, Molstad S, Gudmundsson S 1996	Do antimicrobials increase the carriage rate of penicillin resistant pneumococci in children? Cross-sectional prevalence study	Cross-sectional prevalence study	Antimicrobial use (individual and total) is strongly associated with nasopharangeal carriage in children	IV
272	McCaig LF, Hughes JM 1995	Trends in antimicrobial drug prescribing among office-based physicians in the United States	National sample survey on prescribing patterns	Increasing trend towards more expensive broad-spectrum antimicrobial agents and away from penicillins. This has impact on all patients due to higher costs and emerging resistance	IV
317	Stuart JM, Robinson PM, Cartwright K, Noah ND 1996	Antibiotic prescribing during an outbreak of meningococcal disease	Survey of GP prescribing rates in areas of high and low incidence	Erythromycin prescribing significantly higher in high incidence towns, possibly due to increased consultations for URTI, but may have contributed to increased acquisition	IV
318	Hammond ML, Norriss MS 1995	Antibiotic resistance among respiratory pathogens in preschool children	Survey in socio-demographically matched areas of Melbourne and Sydney	Resistance in pre-school children significant and possibly increasing	IV
154	Nyquist AC, Gonzales R, Steiner JF, Sande MA 1998	Antibiotic prescribing for children with colds, upper respiratory tract infections and bronchitis	Representative national survey	Outcomes were principal diagnoses and prescriptions. Antibiotics were prescribed for 44% children with colds, 46% with URTIs and 75% with bronchitis	IV

20.5.7 PRIMARY CARE PRESCRIBING BEHAVIOUR

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
155	Macfarlane JT, Holmes WF, Macfarlane RM 1997	Reducing reconsultations for acute lower respiratory tract illness with an information leaflet: a randomised controlled study of patients in primary care	Randomised controlled trial	Informing previously well patients about LRTI reduced reconsultations. It is also likely to reduce antibiotic usage and future consultation habits	IA
156	Holmes WF, Macfarlane JT, Macfarlane RM *et al* 1997	The influence of antibiotics and other factors on reconsultation for acute lower respiratory tract illness in primary care	Prospective study	Reconsultation is common in acute LRTI, associated with previous consulting habit, illness or dyspnoea, but not prescription of antibiotics at the index visit	IIB
157	Macfarlane J, Lewis SA, Macfarlane R, Holmes W 1997	Contemporary use of antibiotics in 1089 adults presenting with acute lower respiratory tract illness in general practice in the UK: implications for developing management guidelines	Prospective study	115 GPs prescribed antibiotics to three-quarters of patients. In addition to underlying disease and clinical factors, other factors influencing prescribing were patient pressure and social factors, and GP work pressure and previous experience of the patient, especially if the GP felt antibiotics were not indicated clinically	IIC
158	Macfarlane JT, Holmes WF Macfarlane R, *et al* 1997	Influence of patients' expectations on antibiotic management of acute lower respiratory tract illness in general practice: questionnaire study	Prospective study	Patients presenting with acute lower respiratory tract illness expect antibiotics and have significant influence on prescribing, even when antibiotics are not indicated	IIB
273	Ekedahl A, Andersson SI, Hovelius B, Molstad S, Liedholm H, Melander A 1995	Drug prescription attitudes and behaviour of general practitioners. Effects of a problem-oriented educational programme	Controlled prospective evaluation of educational programme	Producer-independent, problem-oriented group education programme did change attitudes and produced significant and sustained changes in prescribing and drug sales	IIB
275	Molstad S, Ekedahl A, Hovelius B, Thimansson H 1994	Antibiotics prescription in primary care: a 5-year follow-up of an educational programme	Controlled prospective evaluation of educational programme	Overall enduring reduction in prescriptions especially for broad-spectrum antibiotics. GPs were also aware that computer records of diagnosis and treatment enabled individual audit	IIB
277	Little P, Gould C, Williamson I, Warner G, Gantley M, Kinmonth AL 1997	Reattendance and complications in a randomised controlled trial of prescribing strategies for sore throat: the medicalising effect of prescribing antibiotics	Randomised controlled trial	Complications and early return resulting from no or delayed prescription are rare. Current and previous antibiotic prescribing for sore throat increases likelihood of reattendance	IA

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
164	Little P, Williamson I, Warner G, Gould C, Gantley M, Kinmonth AL 1997	Open randomised trial of prescribing strategies for managing sore throat	Randomised controlled trial	Prescribing antibiotics enhances patients' belief in them and intention to consult in future, compared with no or delayed prescription	IA
319	Britten N, Ukoumunne O 1997	The influence of patients' hopes of receiving a prescription on doctors' perceptions and the decision to prescribe: a questionnaire survey	Prospective survey of patients and retrospective survey of doctors in SE London	In area of low prescribing and high expectations, doctors' perceptions of patients' expectations was strongest predictor of prescribing decision	IIIC
276	Armstrong D, Reyburn H, Jones R 1996	A study of general practitioners' reasons for changing their prescribing behaviour	Qualitative analysis of semi-structured interviews	Interviewees identified recent specific changes. Major factors included: evidence, willingness to change and a challenging clinical event	IV
159	Bradley CP 1992	Factors which influence the decision whether or not to prescribe: the dilemma facing general practitioners	Focused interviews of GPs	Decision hardest for respiratory disease, skin problems and psychiatric conditions. Patient factors included socio-economic factors and doctor–patient relationship. Doctor factors included previous clinical experience, logistics, peer- and self-expectations	IV
160	Bradley CP 1992	Uncomfortable prescribing decisions: a critical incident study	Focused interviews of GPs	Main reasons for decision: patient expectations, clinical appropriateness, GP–patient relationship and precedents	IV
161	Webb S, Lloyd M 1994	Prescribing and referral in general practice: a study of patients' expectations and doctors' actions	Prospective survey of patients and retrospective survey of doctors	GP actions strongly associated with patient expectations, both in prescribing and hospital referral	IIIC
164	Steffensen FH, Schonheyder HC, Sorensen HT 1997	High prescribers of antibiotics among general practitioners – relation to prescribing habits of other drugs and use of microbiological diagnostics	Retrospective survey of prescriptions and use of diagnostics	15-fold range between GPs. Positive predictors were high prescribers of other drugs, and high users of cultures and urine tests. High use of throat cultures was a negative predictor	IV
163	Macfarlane J, Prewett J, Rose D *et al* 1997	Prospective case-control study of role of infection in patients who reconsult after initial antibiotic treatment for lower respiratory tract infection in primary care	Prospective observational study with nested case-control	Active infection is rare at reconsultation and another antibiotic prescription thus not indicated. Patient perception is more important than infection – two-thirds obtained another antibiotic	IIB

20.5.8 OTHER REFERENCES:

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
320	Solomkin JS 1996	Antimicrobial resistance: an overview	Editorial	Lack of documentary evidence that resistance harms individual patients in ICU. Conflict between individual and wider good. Compliance with basic hygiene very poor	–
321	Bohnen J 1998	Antibiotic therapy for abdominal infection	Clinical review	Little information on promotion of resistance in this condition	–
274	Webster J, Faoagali JL, Cartwright D 1994	Elimination of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit after handwashing with triclosan	Survey of new MRSAcases after policy change	No other procedural changes. No new isolates reported after discharge of last colonised infant. Cost-saving due to reduction in vancomycin use	IV
322	Haley RW, Cushion NB, Tenover FC *et al* 1995	Eradication of endemic methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit	Retrospective survey	Triple dye applied to cords of neonates in intermediate care but not NICU, and rate of MRSA decreased in intermediate care only. Extension to NICU and dedicated infection control nurse led to near zero colonisation and infection in both areas	IIIB
323	Payne DN *et al* 1998	Antiseptics; a forgotten weapon in the control of antibiotic resistant bacteria in hospital and community settings	*In-vitro* experiment	4 antiseptics tested against various strains: all showed some effect against *E. coli*, *E. coli* O157, *S. aureus*, MRSA, *E. hirae* and VRE	3
324	Hancock RE 1997	The role of fundamental research and biotechnology in finding solutions to the global problem of antibiotic resistance	Conference presentation	Outlines variety of novel approaches including recombinant cationic peptides	
325	Bax RP 1997	Antibiotic resistance: a view from the pharmaceutical industry	Conference presentation	Development influenced by market opportunities. All new products since 1960 are modifications of existing structures. Problems with clinical trials of antimicrobial agents due to patients' needs. Need to develop more sophisticated outcome measures than cure and eradication	
326	Couper MR 1997	Strategies for the rational use of antimicrobials	Conference presentation	WHO preparing to assist countries to develop rational policies. Need to monitor drug use and resistance patterns	

REF. NO.	AUTHOR(S) AND YEAR	TITLE	STUDY TYPE/ DESIGN	RESULTS	GRADE
327	O'Brien TF 1997	The global epidemic nature of antimicrobial resistance and the need to monitor and manage it locally	Conference presentation	Over 1000 resistant genes now identified. May delay emergence by using fewer antimicrobial agents, and delay spread by good hygiene, infection control and avoidance of agents likely to select for resistant strains. Global problem requires local solutions	
328	Goldmann DA, Huskins WC 1997	Control of nosocomial antimicrobial resistant bacteria: a strategic policy for hospitals world wide	Conference presentation	Emphasises need for better basic hygiene precautions; thorough hand-washing and use of gloves, etc. Multidisciplinary efforts supported by management should be fully monitored	
329	Hughes JM, Tenover FC 1997	Approaches to limiting emergence of antimicrobial resistance in bacteria in human populations	Conference presentation	Prevention and control will require sophisticated surveillance, using epidemiological, statistical and molecular techniques	
330	Helmuth R, Protz D 1997	How to modify conditions limiting resistance in bacteria in animals and other reservoirs	Conference presentation	Antimicrobial agents should be used only by a doctor or vet, and are not suitable for eradication of a pathogen from an environment or to replace poor hygiene	
331	Spratt BG, Duerden BI, *et al* 1997	Antibiotic resistance; the threat to international health	Conference report		
332	Michel M, Gutmann L 1997	Methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci: therapeutic realities and possibilities	Review	Proposed schemes for medical management, based on preventive measures for colonisation / carriage.Vancomycin alone or in combination (depending on site and strain) for MRSAand various combinations including amoxycillin and / or gentamicin depending on susceptibility	III
333	Levin BR, Antia R, Berliner E *et al* 1998	Resistance to antimicrobial chemotherapy: a prescription for research and action	Conference workshop report and update	Even with more prudent use resistance will not decline quickly if at all. Need to husband existing drugs and implement other means of infection control	

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22 LIST OF RECOMMENDATIONS

PRESCRIBING IN THE COMMUNITY

Patients with minor infections mostly present to GPs; consequently, 80% of UK human prescribing is in the community. This Report, therefore, concentrates on community prescribing of antimicrobial agents.

There should be a national Campaign on Antibiotic Treatment (CAT) in primary care on the theme of: 'Four things you can do to make a difference' (see Box). The CAT must be matched by a National Advice to the Public (NAP) campaign aimed specifically at supporting the initiative in primary care. A key feature of the NAP campaign should be to highlight the benefits of 'cherishing and conserving your normal bacterial flora'. Further support for appropriate prescribing in primary care should be provided by developing and promulgating evidence-based national guidelines for the management of certain infections, under the aegis of the National Institute for Clinical Excellence. Such national guidelines should be adapted for local use during the development of Health Improvement Plans. To make the incorporation of the guidelines into everyday practice as effort-free as possible they should be integrated within computerised decision-support systems.

FOUR THINGS YOU CAN DO:

- no prescribing of antibiotics for simple coughs and colds
- no prescribing of antibiotics for viral sore throats
- limit prescribing for uncomplicated cystitis to 3 days in otherwise fit women
- limit prescribing of antibiotics over the telephone to exceptional cases

PRESCRIBING IN HOSPITALS

Hospital prescribing accounts for c. 20% of human prescribing of antimicrobial agents in the UK; nevertheless, resistance problems are greatest in hospitals and infections may be life-threatening. Although prescribing in hospitals poses some different issues from those in primary care, hospital clinicians would benefit as much as GPs from the availability of computer-aided decision-support systems.

Studies should be undertaken in selected hospitals to develop and test one or more prototype decision-support systems. Systems should include information from local antimicrobial sensitivity profiles, these, in turn, should feed into regional and national surveillance databases.

PRESCRIBING GUIDELINES

Prescribing guidelines should be quality evidence-based documents. They are often the first source of information for inexperienced prescribers. National guidelines, suitably adapted in response to local resistance patterns, could be integrated into decision-support systems.

Local prescribing information should, wherever possible, be harmonised with prescribing information in the British National Formulary (BNF) and other formularies.

Guidelines and formularies should also take account of the proposed national evidence-based guidelines to be produced under the aegis of the National Institute for Clinical Excellence.

Local prescribing guidelines should take their cue from these national guidelines.

All such local guidelines should include, as a minimum, advice on drug, dose, frequency and duration.

INTERNATIONAL CO-OPERATION

Resistant bacteria spread between countries, the UK is not isolated from the greater resistance problems that exist in other parts of the world, for example, Southern Europe.

Every effort should be made by the Government in international fora, particularly in the European Union, to raise the profile of antimicrobial resistance as a major public health issue meriting priority action.

SURVEILLANCE OF RESISTANCE

Effective surveillance is critical to understanding and controlling the spread of resistance. Not only is surveillance essential for monitoring the existing situation, it allows the effects of interventions to be evaluated.

A national strategy for resistance surveillance should be developed and implemented as swiftly as possible, covering the whole of the UK.

RESEARCH

Antimicrobial resistance has been of low priority for Research Councils and scored poorly in the recent Research Assessment Exercise.

Research into antimicrobial resistance should become a high priority for all funding bodies concerned with health care and biomedical research.

EDUCATION

The development of guidelines and their widescale introduction into clinical practice will have important and beneficial spin-offs for the education of health care professionals involved in antimicrobial prescribing. The whole population would benefit from enhanced education about the benefits and disadvantages of antimicrobials.

Greater emphasis should be placed on teaching about antimicrobial prescribing in medical and dental schools as well as in the undergraduate curricula for pharmacists and nurses.

Teaching about antimicrobials should be better integrated with teaching about the infections for which they are used.

This enhanced emphasis on education in antimicrobial use should be carried over into continuing medical, dental and professional education and development.

Similar concepts apply in the field of veterinary medicine.

In addition to health education material aimed at adults, teaching about antibiotics should be included as part of health education in the National Curriculum.

HYGIENE, INFECTION CONTROL AND CROSS-INFECTION

Infection control, although intimately bound up with problems of antimicrobial resistance – particularly in health care environments – was outside the Terms of Reference of the Sub-Group. Nevertheless, it is fundamental to preventing the spread of resistant organisms, not only in hospitals but also in the community.

Consideration should be given to producing guidance on infection control in the community, especially in nursing and residential homes, similar to that which exists for hospitals.

VETERINARY AND AGRICULTURAL USE

Antimicrobials are used in therapy and prophylaxis, and as growth promoters/enhancers in animals

The use of antibiotics in veterinary practice should be guided by the same principles as for human prescribing – namely, they should be used only for clinical conditions where their use is likely to provide a genuine health benefit.

Alternative means of animal husbandry should be developed so that the use of antibiotics as growth promoters can be discontinued.

IMPLICATIONS FOR INDUSTRY

If our recommendations are followed, they should have the effect, *inter alia*, of reducing antibiotic usage. There may be financial implications for the pharmaceutical industry, upon whose profitability the development of new antibiotics depends.

Consideration should be given by the appropriate bodies to finding ways – through pricing and other mechanisms – of ensuring that investment in the development of new antibiotics remains commercially viable. Industry should be encouraged to undertake studies of optimum prescribing regimens for new antimicrobial agents, for each indication and in adults and children as appropriate. Licensing authorities should have due regard to an antimicrobial agent's potential to select for resistance as well as to its safety and efficacy.

22.1 IMPLEMENTATION OF RECOMMENDATIONS

The aim of this Report has been to produce recommendations that can constitute the first phase of a national strategy for minimising the development of antimicrobial resistance.

As part of this phase a small National Steering Group (NSG) should be established, charged with ensuring that these recommendations are implemented and that their effects on prescribing practice and on the development of resistance are monitored.

The NSG, which might need to establish a small number of expert groups to take forward specific aspects of the recommendations, should report to the Chief Medical Officer within a year on progress.

Thereafter the CMO may wish to consider asking SMAC to reconvene this Sub-Group, to provide a suitable inter-disciplinary forum for the development of the next phase of the strategy.

23 GLOSSARY OF TERMS

Acquired resistance	resistance to antimicrobial agents that develops in micro-organisms that were previously sensitive
Acute otitis media	inflammation of the middle ear commonly caused by infection
Analgesic	a drug that reduces or relieves pain
Analogue	corresponding or similar to
Antibacterial spectrum	the range of bacteria that are susceptible to a particular antibiotic
Antibiotic	a substance produced by or derived from a micro-organism, that selectively destroys other micro-organisms or inhibits their growth
Antibiotic policy	written guidance that recommends antibiotics and their dosage for treating of specific infections
Antifungal agent	an agent that can be used to treat infections caused by fungi
Antimicrobial agents	any compound that at low concentrations exerts an action against microbial pathogens and exhibits selective toxicity towards them
Antimicrobial chemotherapy	the use of to prevent or treat microbial disease
Antiseptic	a non-toxic chemical that can be used to clean skin before an operation so as to prevent infection or applied to skin to cleanse dirty wounds
Appendicectomy	surgical removal of the appendix
Asymptomatic	not showing any symptoms of a disease, although it is present
Audit	organised review by staff of current practices and comparison with predetermined standards. Action is then taken to rectify any deficiencies that have been identified in current practices. The review is repeated to see if the predetermined standards are being met
Bacilli	rod-shaped bacteria
Bacteraemia	presence of bacteria in the bloodstream
Bacteriophage	a virus that survives and multiplies in bacteria. Each type of bacteriophage attacks a particular type of bacterium
Bacterium	a single-celled micro-organism that is simpler and usually smaller than protozoa (q.v)
Blood culture	sample of blood taken from a patient with a serious infection, such as meningitis, and investigated in the laboratory to try to determine the pathogen causing infection
CCDC	Consultant in Communicable Disease Control, a doctor who is appointed by each Health Authority and who has a responsibility for the surveillance, prevention and control of infections in the community
Chromosome	the structure containing nucleic acid (DNA) that carries the genetic information of an organism
Clinical microbiologist	a person who studies the science of the isolation and identification of micro-organisms that cause disease in humans and applies this knowledge to treat, control and prevent infections in humans
Cocci	round bacteria
Cohort nursing	placing patients with the same infection together in an area of a ward to reduce the risk of the infection spreading to other patients. This is often done when there are more infected patients than single rooms available for isolation
Colonisation	the ability of some pathogens to live on or in a host without causing disease
Commensal	a member of the normal bacterial flora

Communicable disease	a disease caused by a micro-organism that can be passed from a person, animal or the environment to another susceptible individual
Community	populations, diseases or health services outside of hospitals
Compliance	the degree to which patients follow the instructions for taking a course of treatment
Concordance	the aim of concordance is to optimise health gain from the best use of medicines, compatible with what the patient desires and is capable of achieving
Contact	a person who has been exposed to a source of infection
CSF	cerebrospinal fluid: the clear watery fluid that surrounds the brain and spinal cord
Cystic fibrosis	an inherited disease in which respiratory tract infections are very common and often cause death
Denominator	the population considered to be at risk, eg the total number of people admitted to a hospital or receiving a particular antimicrobial agent. This is used to calculate rates such as incidence and prevalence
Disinfectant	a chemical that destroys or removes bacteria and other micro-organisms. Used to cleanse surgical instruments and surfaces of equipment or furniture
DNA	deoxyribonucleic acid: the genetic material of most living organisms
Efficacy	the effectiveness of an agent or a preparation or a treatment
Empirical treatment	treatment based on past experience or observation rather than the result of laboratory investigations
Endocarditis	infection of the heart valves
Enzyme	a protein that, in small amounts, speeds up the rate of a biological reaction without itself being used up in the reaction
Epidemiology	the study of the occurrence, cause, control and prevention of disease in populations
Febrile	feverish
Flora	see normal bacterial flora
Formulary	a compendium often used in hospitals to list the drugs readily available for prescribing. Some indicate the seniority of medical staff who may prescribe individual drugs
Fungus	a simple plant which lacks the green pigment chlorophyll. Some fungi cause local infections such as thrush or athlete's foot, but may also cause serious infections in immunocompromised people
Ganglion	an aggregation of nerve cell bodies
Gene	the basic unit of genetic material
Genomics	technique involving sequencing the entire chromosomes of bacteria
GP	general practitioner
Gram's stain	a dye that is used to stain bacteria to aid identification when viewed with a microscope
Gram-negative	bacteria that are stained red by Gram's stain
Gram-positive	bacteria that are stained violet by Gram's stain
ICU	intensive care unit
Immunocompetent	a person who has normal immune responses
Immunocompromised	a person who has impaired immunity due to disease (eg cancer) or treatment (eg corticosteroid drugs or radiotherapy)
Impermeable	does not allow the passage of fluids or solutes, eg bacteria may be impermeable to an antimicrobial agent so that it cannot get into the bacteria

Incidence	the number of episodes of a disease that occur in a specified period of time in a specified group of people, eg the number of infections in people admitted to a hospital or in people undergoing a particular procedure in a given time
Inflammation	the response of tissues to damage caused by physical, chemical or biological agents
Inherent resistance	resistance to an antimicrobial agent that is due to the basic nature of the organism, eg all gram-negative bacteria are impermeable to glycopeptides and are therefore resistant to them
Interferons	a group of chemicals produced by mammalian cells that increase their resistance to viral infection
In vitro	tests undertaken in laboratory equipment, eg test tubes and not in a living human or animal
In vivo	tests undertaken within a living human or animal
IT	information technology such as computers
Local Health Care Group	the equivalent in Wales of Primary Health Care Groups
Meningitis	inflammation of the membranes (meninges) that envelope the brain and spinal cord. Bacteria that cause meningitis include *Neisseria meningitidis*
Meta-analysis	statistical analysis that combines results from several studies to obtain an overall estimate, eg the effectiveness of antibacterial agents to treat acute otitis media
MIC (minimum inhibitory concentration)	the lowest concentration of an antimicrobial agent that can inhibit the growth of a micro-organism. A micro-organism with a low MIC is susceptible to that antimicrobial agent, one with a high MIC is resistant
Micro-organism	any organism that is too small to be visible to the naked eye, eg bacteria, fungi, viruses and protozoa
Monotherapy	treating an infectious disease with one antimicrobial agent
Morbidity	the state of having a disease
Mortality	death
Multi-resistance	a micro-organism that is resistant to two or more unrelated antimicrobial agents
Mutation	a change in the genetic material of an organism, or the resultant change this causes in a characteristic of the individual, caused by an alteration to the nucleic acid structure
Myocardial infarction	sudden loss of the blood supply to the heart muscle (myocardium) followed by death of the muscle. Popularly known as ‘heart attack’
Neutropenia	a reduction in the number of white cells in the blood, because of disease or treatment, that renders patients more susceptible to infections
NICE (National Institute for Clinical Excellence)	a new national institute that will give coherence and prominence to information about clinical effectiveness and cost-effectiveness
Normal bacterial flora	the bacteria that normally live on and in the skin, gut, mouth and upper respiratory tract of humans. Also called commensal organisms, they do not normally cause disease, and provide some protection from infection. When antimicrobial agents are used to treat infectious disease they can affect the normal bacterial flora and their ability to provide protection from infection
Opportunist pathogen	a pathogen that infects immunocompromised people but rarely infects immunocompetent people
Optimum duration	the best duration of treatment, not too long or too short
Parenteral	giving drugs by intramuscular or intravenous injection
Pathogen	a micro-organism capable of causing disease

PHLS	Public Health Laboratory Service. An organisation of public health laboratories based in district general and teaching hospitals in England and Wales, and a central facility at Colindale in North London which houses the headquarters, national Reference Laboratories and Communicable Disease Surveillance Centre. Its purpose is to protect the population from infection
Plasmid	a piece of genetic material (DNA) often found in bacteria that is independent of the chromosome
Prevalence	the number of instances of a particular disease or other condition at a particular time, eg the number of people with tuberculosis, or the number infected with a pathogen resistant to antimicrobial agents
Primary Health Care Groups	group of GPs in England who will be responsible for commissioning health services for their populations or patients
Prophylaxis (or chemoprophylaxis)	using an antimicrobial agent to prevent infection, eg giving antimicrobial agents before gut surgery in order to prevent micro-organisms in the gut spreading into the abdomen and producing peritonitis
Protozoan	a single-celled micro-organism, that is more complex and usually bigger than a bacterium and may be free living or parasitic
Quality issues	issues about the quality of health services delivered to patients in hospitals and the community
Randomised control studies	an experimental method for comparing different treatments by randomly assigning people to groups which receive different treatments and comparing outcomes, eg how many people in each group were cured or improved by each treatment
Reactivation	restore to a state of activity. Certain viruses, eg herpes simplex virus, produce recurrent episodes of disease such as cold sores, or genital infection. The virus survives in nervous tissue between episodes of disease and can be reactivated to produce disease
Reference laboratory	a laboratory that carries out more specialised tests on samples received from other laboratories and is usually involved in research relating to its particular area of interest
Replication	the process of making an exact copy of a molecule or an organism
Resistance	the ability of a micro-organism to withstand an antimicrobial agent. See also acquired resistance, multi-resistance and inherent resistance
Respiratory tract infection (RTI)	infection of the respiratory tract including upper respiratory tract infections such as colds, sinusitis, and lower respiratory tract infections such as pneumonia
Reverse transcriptase	an enzyme that makes a DNAcopy of an RNA molecule, and is essential in the replication of viruses such as HIV that use RNAas their genetic material
Ribosome	a particle, consisting of RNA and protein, that occurs in cells and is the site of protein synthesis in the cell
RNA(ribonucleic acid)	one of the two types of nucleic acid in organisms. RNAis a chemical messenger in all organisms and some viruses, eg influenza and HIV, use RNAto carry their genetic information
Selection pressure	environmental conditions that favour the survival and replication of certain individuals, eg the presence of an antimicrobial agent favours the survival of micro-organisms that are resistant to it
Sensitive	organisms that are unable to replicate or are killed by an antimicrobial agent
Septicaemia	severe general infection caused by pathogens and their toxins
Sinusitis	inflammation of the sinuses of the nasal cavities that is commonly caused by infection

Surveillance of disease	the systematic collection and evaluation of data on all aspects of a disease that are relevant to its prevention and control
Tertiary hospital	teaching or specialised hospital that provides specialised care
Topical treatment	drug applied directly, or locally, to the surface of the part being treated, eg the skin or eye
Transmission	passing infectious disease from one person to another or a plasmid from one bacterium to another
Transposon	a piece of DNA(often containing genes for resistance) that can move from one DNA molecule to another
Vaccine	a preparation that can be used to stimulate the development of immunity against one or more pathogens to prevent infections including measles, mumps, polio, rubella, whooping cough, diphtheria, hepatitis A, hepatitis B and rabies
Virulence	the ability of a pathogen to cause disease
Virus	a very small micro-organism that can only survive and multiply within a living host cell
Zoonosis	an infectious disease of animals that can be transmitted to humans, eg brucellosis and rabies

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