Psychosexual counsellors are medical practitioners, usually women, who have attended training seminars run by the Institute of Psychosexual Medicine. Their therapy is psychodynamically oriented and focuses on the individual rather than the relationship. Such counsellors are particularly suitable for women with vaginismus. A list of psychosexual counsellors may be obtained from the Institute of Psychosexual Medicine, 11 Chandos Street, London W1M 9DE.

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Prescribing in Pregnancy

Antibiotics

RICHARD WISE

Young women often develop infections, particularly of the urinary tract. Therefore pregnant women commonly require antimicrobial treatment. Bacteriuria occurs in about 5% of pregnancies, and if it is not treated between a quarter and a third of patients may develop pyelonephritis with consequent danger to their own health and an increased incidence of fetal loss.[1] Because pregnant women are often in an environment with young children they are at greater risk of developing the more trivial upper respiratory infections, which may require treatment. Occasionally, pregnant women need treatment for more serious infections. It is therefore necessary to know which antimicrobial agents can be used with negligible risk for the minor infections and to have some appreciation of the balance of risks for more serious cases.

In assessing the risk to the fetus several points should be considered. For many antimicrobial agents we now have more than 25 years' experience of freedom from congenital abnormality. Many studies have been performed in animals, but, although important, their results should be viewed with some reservation. For example, sulphonamides can cause gross fetal malformations when given in high doses to mice and rats,[2] but 50 years of use would surely have shown a teratogenic propensity in humans, which, to my knowledge, has not been recorded. One of the reasons why laboratory animals make poor models for studying fetal damage is the profound effect large doses of antimicrobial agents have on the animal's gastrointestinal flora and consequently on the animal's metabolism. On the other hand, certain drugs should definitely be avoided. For example, streptomycin causes neonatal ototoxicity after long term treatment of maternal tuberculosis.[3,4] It therefore follows, by implication rather than by hard information, that the other aminoglycosides, such as gentamicin, tobramycin, netilmicin, and amikacin, should be avoided for minor infections. In the treatment of serious maternal infection, however, their undoubted efficacy should be balanced against these theoretical risks.

Pregnant and non-pregnant women differ considerably in the way in which they handle antimicrobial agents, and this may influence treatment. Philipson showed that serum concentrations of ampicillin in women who were 9-36 weeks' pregnant were half the values found in the same women when they were not pregnant.[5] Low maternal concentrations have been described after ingestion of most antimicrobial agents, including aminoglycosides. The therapeutic implications of these low concentrations are difficult to assess. Failure of antibiotic treatment might incorrectly be blamed on the wrong choice of antibiotic and the drug might be replaced by a potentially more toxic agent. This could be particularly dangerous when treating a serious infection with an agent such as an aminoglycoside, when the natural caution of the doctor against giving what he might consider to be high doses will in fact cause more problems. In general, full adult doses should be used when treating infections in pregnant women. When serious infections are to be treated with an aminoglycoside, for example, assays should be performed to ensure that the patient is receiving sufficient drug and that neither she nor her fetus is being exposed to unacceptably high levels. Similarly, the length of treatment should be dictated by the disease and not be influenced unduly by the fact that the patient is pregnant. Inadequate treatment, which may be followed by further courses of antibiotics, is likely to put mother and fetus at greater risk than a full course of the correct antimicrobial agent. In the case of bacteriuria in pregnancy a 7-14 day course of treatment is usually prescribed, but some investigations suggest a single dose[6,7] or high dose short course.[8]

Antimicrobial agents

Table I lists various antimicrobial agents together with their possible toxic effects on the fetus in early or late pregnancy. I have attempted to give a safety rating: "probably safe" indicates that no significant risk to the fetus has been documented and hence such agents constitute a first choice if an antimicrobial agent has to be used; "caution" indicates that effects on the fetus have been recorded with the agent (or a chemically related compound) or that its mode of action suggests a theoretical risk, but there may well be times when the balance of risks suggests that such compounds should be used. "Avoid" indicates that the agent carries a definite risk and its use might imply negligence (unless there was an overwhelming reason to the contrary). Such division of the compounds is obviously somewhat subjective.

Treatment of common conditions

Table II lists some of the common infections likely to be encountered in pregnancy. The first choice of treatment is usually

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an agent listed as probably safe in table I, although not necessarily so. A second choice agent might have to be used if (*a*) the patient is allergic to a first choice compound or (*b*) the bacteria responsible are resistant to the first choice agent. In this context it is particularly important to take cultures from pregnant patients before treatment so that a safe and efficacious change can be made to treatment if the patient does not respond or the causative organism proves resistant to initial treatment. The dose chosen should be that indicated for the condition in the *British National Formulary* and the clinician should eschew the temptation to use too low a dose. If the infection needs treating at all it needs full dosage.

URINARY TRACT INFECTION

The most common reason for pregnant women to take antibiotics is for acute cystitis or covert bacteriuria. The choice of treatment is between ampicillin (or its close relative amoxycillin) and cephalexin (as the oral cephalosporin with which there is more experience). Cephalexin is probably more suitable because about one third of the common Gram negative bacteria which cause urinary tract infections are resistant to ampicillin. Although a combination of amoxycillin and clavulanic acid (Augmentin) has been used in pregnancy and it would overcome the problem of resistance, this combination might best be reserved for difficult cases until more evidence about its safety has accumulated. Women who are allergic to β lactams can be given a short course of trimethoprim with or without sulphamethoxazole in the first, and probably the second, trimesters; in the third trimester nitrofurantoin would be an acceptable alternative.

PHARYNGITIS AND TONSILLITIS

Most sore throats are caused by viruses and are therefore not susceptible to treatment. Patients with signs of systemic infection such as tachycardia, fever, and enlarged cervical lymph nodes should be given penicillin. If the infection is severe this should be given parenterally, followed by phenoxymethylpenicillin. Patients allergic to penicillin should receive erythromycin base.

BRONCHIAL AND PULMONARY INFECTIONS

An acute bacterial bronchial infection after a viral bronchitis is not uncommon in a previously healthy young woman. The first choice of treatment is either ampicillin or amoxycillin. A specimen for culture should be taken, however, because 5-10% of *Haemophilus influenzae* are resistant to these two drugs. If the patient fails to respond this might be a reasonable indication for a course of treatment with a combination of amoxycillin and clavulanic acid.

The commonest cause of lobar pneumonia in a previously well young women is *Streptococcus pneumoniae*, and this should be treated with benzylpenicillin, or erythromycin if the patient is allergic to benzylpenicillin. Legionnaires' disease is a common

TABLE I—*Antimicrobial agents and their possible adverse effects*

Agent	Use	Adverse effects on the fetus: First trimester	Adverse effects on the fetus: Second and third trimesters	Comments
Penicillin (benzylpenicillin and phenoxymethylpenicillin)	Probably safe		Allergy; possibility of sensitising the fetus	All the commoner β lactams may be described as safe
Long acting penicillins	Probably safe		Allergy; possibility of sensitising the fetus	Little information available but no suggestion of increased toxicity
Ampicillin	Probably safe		Allergy; possibility of sensitising the fetus	
Ampicillin prodrugs: Talampicillin, pivampicillin, bacampicillin				Little information available. Reasonable to avoid prodrug formulation and use the parent ampicillin
Amoxycillin	Probably safe		Allergy; possibility of sensitising the fetus	
Amoxycillin and clavulanic acid (Augmentin)	Probably safe		Allergy; possibility of sensitising the fetus	Little information available. Best avoid until more experience reported
Antipseudomonal penicillins: Carbenicillin, mezlocillin, azlocillin, ticarcillin, piperacillin	Probably safe		Allergy; possibility of sensitising the fetus	Little information available. Reserve for treatment of serious infections caused by susceptible bacteria
Mecillinam	Probably safe		Allergy; possibility of sensitising the fetus	Little information available. Reserve for treatment of serious infections caused by susceptible bacteria
Antistaphylococcal penicillins: Flucloxacillin and cloxacillin	Probably safe		Allergy; possibility of sensitising the fetus	
Cephalosporins:				
Oral—cephalexin, cefaclor, cephradine	Probably safe		Allergy; possibility of sensitising the fetus	Little information available
Injectable	Probably safe		Allergy; possibility of sensitising the fetus	Little information available. These agents are probably safe and might well be reasonable choices in treatment of severe infection. Agents containing *N*-methyl tetrazole side should be avoided on theoretical grounds—that is, interference with vitamin K metabolism (latamoxef and cefamandole in the United Kingdom)
Sulphonamides:				
All agents	Probably safe in first trimester. Avoid within two days of delivery		Avoid (within two days of delivery), kernicterus	Risk is greater for more highly protein bound agents, such as sulphafurazole, rather than sulphamethoxazole
Trimethoprim	Probably safe			Theoretical tetratogenic risk of folic acid antagonist. Risk of megaloblastic anaemia preventable by folinic acid
Co-trimoxazole (trimethoprim and sulphamethoxazole)	Probably safe (but see sulphonamide above)		Kernicterus	Considerable experience of safety in first trimester
Tetracyclines:				
All agents	Avoid		Discoloration and dysplasia of teeth and bones, cataracts	Possible hepatotoxicity in mother
Aminoglycosides:				
Streptomycin	Avoid		Ototoxicity	Little reason to be used. A better choice can be made in tuberculosis and serious sepsis
Gentamicin, tobramycin, netilmicin, amikacin	Caution		Theoretical risk of ototoxicity suggested	Effective in serious sepsis; regular assay required
Spectinomycin	Probably safe			Reserve for treatment of gonorrhoeae when penicillin resistance or allergy is a problem
Fusidic acid	Probably safe			
Quinolones:				
Nalidixic acid	Caution			Wide experience suggests safety. Deposition in growing bones in certain animals. Interferes with bacterial DNA; theoretical risk to humans

Continued on page 44

TABLE I—*Antimicrobial agents and their possible adverse effects*—continued

Agent	Use	Adverse effects on the fetus		Comments
		First trimester	Second and third trimesters	
Recently developed drugs:				
Ciprofloxacin, norfloxacin, enoxacin, ofloxacin, pefloxacin	Avoid			No experience in pregnancy—see nalidixic acid
Nitrofurantoin	Probably safe			Theoretical risk of haemolysis in glucose-6-phosphate dehydrogenase deficiency
Vancomycin	Caution			Safety data not available in humans. Reserve for treatment of serious staphylococcal sepsis
Macrolides and lincosamides:				
Erythromycin base/stearate	Probably safe			
Erythromycin estolate	Avoid			Maternal hepatoxicity in late pregnancy
Lincomycin and clindamycin	Avoid			Maternal pseudomembranous colitis. Avoid unless no other suitable agent available
Metronidazole	Caution	Theoretical risk of teratogenesis		No evidence of teratogenicity in man. Benefit will probably outweigh risk in serious anaerobic sepsis
Chloramphenicol	Avoid		Grey baby syndrome	Little evidence of ill effect to fetus in early pregnancy. Remember possible maternal blood dyscrasias. Usually a safer choice can be made
Antituberculous agents:				
Rifampicin	Caution		Postnatal bleeding	Avoid in mothers with liver disease. High dosage teratogenicity in animals. Benefits probably outweigh risks. Vitamin K should be given to mother and neonate
Isoniazid	Probably safe			
Ethambutol	Probably safe			Observe mother for jaundice
Para-aminosalicylic acid	Probably safe			Now little used
Pyrazinamide	Caution			Little information available
Antifungal agents:				
Amphotericin	Caution			Limited information; safety not established
Flucytosine	Avoid	Teratogenic in animals		
Ketoconazole	Caution			Limited information; safety not established
Miconazole	Caution			Absorbed from vaginal topical use
Griseofulvin	Avoid	Teratogenic in animals		
Nystatin (topical)	Probably safe			
Antimalarial drugs:				
Chloroquine	Probably safe			Safety established in low dose, except for rare reports of hearing loss in children
Quinine	Avoid	Possible abortifacient		
Proguanil	Probably safe			
Pyrimethamine and dapsone (Maloprim)	Avoid			Teratogenicity reported in rats, but no convincing evidence in humans. Maloprim and Fansidar have been associated with fatalities
Pyrimethamine and sulphadoxine (Fansidar)	Avoid			
Primaquine	Avoid			
Antiparasitic agents:				
Piperazine	Probably safe			
Mebendazole	Avoid	Possibly teratogenic		
Thiabendazole	Caution			Safety not established
Praziquantrel	Caution			Safety not established
Antiviral agents:				
Amantadine	Avoid	Embryotoxic in animals		Unless there is a life threatening infection in the mother it is probably best to avoid antiviral agents in pregnancy
Acyclovir	Caution	Theoretical risk		
Vidarabine	Avoid	Teratogenic in animals		

TABLE II—*Common infectious conditions in pregnancy with recommended treatment*

Condition	First choice treatment	Second choice treatment	Comments
Asymptomatic bacteriuria or simple cystitis	Ampicillin, amoxycillin (if isolate sensitive), or cephalin by mouth	Nitrofurantoin, sulphonamide, or trimethoprim (or co-trimoxazole)	In asymptomatic bacteriuria treatment should probably last 7-10 days Simple acute cystitis may respond to a single dose or short course
Acute pyelonephritis	Cefuroxine, ampicillin intravenously (if isolate sensitive)	Gentamicin intravenously	
Pharyngitis	Benzylpenicillin intravenously, procaine penicillin intramuscularly, or phenoxymethylpenicillin by mouth	Erythromycin base	Note: 70-80% of cases of pharyngitis are caused by viruses
Bronchitis	Ampicillin by mouth or amoxycillin	Erythromycin	
Lobar pneumonia	Benzylpenicillin	Erythromycin	If not pneumococcal change in treatment may be required
Legionnaires' disease	Erythromycin plus rifampicin		
Endocarditis prophylaxis	Amoxycillin by mouth	Erythromycin	Follow recommendations of working party[8]
Endocarditis treatment:			
Streptococcal	Benzylpenicillin+gentamicin		
Staphylococcal	Flucloxacillin+fusidic acid	Vancomycin	
Gonorrhoea	Benzylpenicillin intramuscularly	Cefuroxime or spectinomycin	Spectinomycin if patient is β-lactam allergic
Infection caused by *Chlamydia trachomatis*	Erythromycin by mouth		Erythromycin should be given for 7-10 days
Prophylaxis for abdominal operations:			
Gastric or biliary	1 dose cefazolin	1 dose co-trimoxazole	
Appendicectomy or colonic	1-3 doses amoxycillin and clavulanic acid (Augmentin)	1-3 doses gentamicin plus metronidazole	
Tuberculosis	Rifampicin+isoniazid+ethambutol		Rifampicin and isoniazid should be given for 9 months and ethambutol for 3 months. Pyridoxine supplements should be given with isoniazide
Malaria prophylaxis	Chloroquine		See text
Serious undiagnosed sepsis	Gentamicin intravenously+antipseudomonal penicillin intravenously, possibly plus metronidazole	Broad spectrum cephalosporin intravenously (such as cefuroxime or ceftazidime)	On establishing causative pathogen it may be possible to omit gentamicin if (*a*) organisms susceptible to antipseudomonal penicillin and (*b*) patient has made a satisfactory response

cause of community acquired pneumonia. There is still some doubt about the best treatment for this condition, but present knowledge suggests erythromycin. In seriously ill patients rifampicin may be added; however, this agent does not have a licence in the United Kingdom for legionella infections.

SURGICAL PROPHYLAXIS

Although elective operations are avoided in pregnancy, emergency operations may be necessary. The same guidelines for the choice of the correct prophylactic antibiotic should be followed—namely, that a short course of an appropriate agent should be given. If there is no evidence of established intra-abdominal sepsis (such as an appendix abscess) one to three doses of a parenteral cephalosporin such as cefuroxime plus metronidazole should be given (or possibly cefoxitin or amoxycillin and clavulanic acid alone). If there is abscess formation then three to four days' treatment is required.

For patients who need antibiotic prophylaxis because of a pre-existing heart disorder the guidelines of the British Society for Antimicrobial Chemotherapy working party should be followed.[9]

SEPTICAEMIA

Happily, it is rare to have to treat a pregnant patient with a microbiologically undiagnosed possible septicaemia. In such instances the risks to the patient outweigh the risks to the fetus and broad spectrum antimicrobial agents in full dosage should be prescribed. Parenteral cefuroxime would be a good first choice, possibly with the addition of metronidazole if there is evidence of intra-abdominal sepsis. Once a pathogen and its antimicrobial susceptibilities have been determined treatment can be directed at that organism.

TUBERCULOSIS

Because of the chronic nature of tuberculosis it is not uncommon to encounter this infection in pregnancy. Young women who are not pregnant should be warned of the increased risk of failure of the contraceptive pill if, as is likely, rifampicin is prescribed.

Opinions differ on the treatment of infections with *Mycobacteria tuberculosis* in pregnant women. This difference is mainly concerned with the risks associated with rifampicin, which readily crosses the placenta; teratogenicity has been suggested but not confirmed. Treatment should not be appreciably different from that in non-pregnant patients and should be of full duration. Streptomycin is rarely used in tuberculosis and should certainly be avoided in pregnant women. Treatment by a physician who specialises in respiratory medicine is advisable.

MALARIA PROPHYLAXIS AND TREATMENT

Malaria is an important cause of abortion, premature labour, and perinatal death, as well as affecting the mother. Hence both prophylaxis and treatment are required during pregnancy. Prophylaxis should be started one week before visiting a malarial area and continued for one month after leaving. For travel to north Africa and the Middle East, where chloroquine resistance has not been reported, chloroquine 300 mg weekly is advised. Travel to a country where chloroquine resistant *P falciparum* is found presents a problem. Pyrimethamine and sulfadoxine (Fansidar) and pyrimethamine and dapsone (Maloprim) are now considered to carry sufficient risk of Stevens-Johnson syndrome and neutropenia respectively to almost outweigh their benefits, not only in pregnant women but in any individual. Pregnant women should therefore be advised not to visit an area where chloroquine resistant *P falciparum* is found (such as east and central Africa, South East Asia, and South America). For women who intend to visit a major urban centre only (where the risk is smaller) chloroquine 300 mg a week plus proguanil 200 mg a day should be prescribed.

In the treatment of benign malaria (caused by *P vivax*, *P ovale*, and *P malariae*) chloroquine should be used; radical cure with primaquine should not be undertaken until after pregnancy to avoid the possibility of haemolysis due to glucose-6-phosphate dehydrogenase deficiency. *P falciparum* malaria should again be treated with chloroquine except when the patient comes from an area where chloroquine resistance is known. In such cases quinine should be used. Quinine will reduce the numbers of parasites in the blood and after a three day course a single dose of three tablets of Fansidar is warranted. Then, if asexual parasites are still present in a blood smear a seven day course of erythromycin should be given.

OTHER PARASITIC INFECTIONS

Toxoplasmosis—Fetal infection in the first trimester is relatively uncommon, but in most of the cases that do occur the disease is severe. In the last trimester, however, infection of the fetus by an infected mother is more usual, but most babies will have no overt disease at birth. The treatment suggested is as follows: pyrimethamine 50 mg twice weekly, plus folic acid 5 mg daily, plus sulphadiazine 50 mg/kg twice daily. Patients should have treatment for two weeks followed by four weeks without treatment; this should be repeated throughout pregnancy. Anyone considering treating a pregnant patient with possible toxoplasmosis should liase with an expert in this disease.

Amoebiasis—Metronidazole 800 mg three times daily should be given for five days followed by diloxanide furonate 500 mg three times daily for five days (to eliminate trophozoites from the gut lumen).

Giardiasis—Metronidazole 400 mg three times daily should be given for seven days. Relapses are not uncommon.

Helminthiasis—Most infections with ascaris and trichuris are asymptomatic and are best left alone in pregnancy. Occasionally, a 4 g dose of piperazine may be required. Heavy hookworm infections should be treated with 5 g of bephenium or 10 mg/kg of prantel pamoate if anaemia is severe.

VENEREAL DISEASES

As penicillin forms the basis of the treatment of both gonorrhoea and syphilis there is no need for any change in treatment in pregnancy, and both conditions should be treated vigorously and followed up (in both mother and infant). A problem can arise in the treatment of syphilis in pregnant women who are allergic to penicillin. It is doubtful if erythromycin is satisfactory in eradicating spirochaetes from the fetus. In such cases it might be reasonable to use tetracycline because the effect of congenital syphilis on the teeth (not to mention other sites) would be more severe than the effect of tetracycline. Chlamydial infections causing non-specific urethritis during pregnancy should be treated with erythromycin.

PELVIC INFLAMMATORY DISEASE

Pelvic inflammatory disease is not uncommon in pregnancy, and treatment is difficult. Patients should be given erythromycin together with metronidazole (except in the first trimester).

Antibiotics and lactation

Both mother and general practitioner are often anxious that antimicrobial agents being used to treat the mother are being transferred to the infant. Although most antibiotics are found in breast milk in low concentrations, they are unlikely to affect the

child. This is because appreciable amounts of the agent will not be absorbed from the infant's gastrointestinal tract—for example, the aminoglycosides and injectable cephalosporins—or, if the agents are absorbed, the concentrations reached in the infant are extremely low—for example, ampicillins. Concern has been expressed, however, over a few agents.

Chloramphenicol—Although grey baby syndrome is most unlikely (as concentrations are too low), the possibility of infant marrow toxicity necessitates either avoiding this agent or stopping breast feeding.

Tetracyclines—Tetracylines should be avoided because of the theoretical, rather than real, risk of teeth discoloration. Chelation of the tetracycline by the calcium ions in milk probably overcomes this problem.

Sulphonamides (including co-trimoxazole)—Although the risk of kernicterus is low, it should be borne in mind especially if a highly protein bound sulphonamide—for example, sulphadimethoxine—is being used. In glucose-6-phosphate dehydrogenase deficiency there is the risk of haemolytic anaemia.

Isoniazid—There is a theoretical risk of convulsions with isoniazid. Both mother and baby should be given pyridoxine.

Metronidazole—Mothers who start taking metronidazole after they have started breast feeding may find that it has an adverse effect on the taste of the milk.

Conclusion

A wide range of antimicrobial agents are now available and harmful effects on the fetus have been proved in relatively few. Infection in pregnant women usually requires treatment and the choice of agent should not be a major problem.

I thank Dr C Ellis for his advice on the treatment of parasitic infections.

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Portraits from Memory

1—Fifty years of microbiology: first steps

JAMES HOWIE

This is the first of a series of short articles by Sir James Howie. The complete collection will be published as a book.

John Cruickshank, first professor of bacteriology in the University of Aberdeen, stimulated my interest in the subject when I attended his class in 1928. He was then a bright lecturer, expert at selecting the newsworthy parts of bacteriology—how the plague commission, for example, not only proved the route of transmission from rat to man by way of the flea, but also devised simple, humorous, and convincing experiments to prove the point with such clarity that even the hard-headed owners of slum property in Bombay reluctantly came to accept that the rat infested hovels had to be burned down. Previously they had argued for a selective capture and killing of enough female rats to create a situation of polyandry in the rat population. This, they argued with feeling, would inevitably so enfeeble the species that rats would soon become extinct by reason of the fighting among males for an ever diminishing number of females.

Professor John Cruickshank.

John did not weary us with details of the technical methods used to identify microbial species but showed us by good examples how bacteria established themselves, spread around, and could be interrupted by measures of hygiene and immunisation. At that time successful generalised chemotherapy was only an aspiration and a dream in spite of the work of Ehrlich. John Cruickshank also saw to it that his practical classes were supported by a large enough team of demonstrators to ensure that every student really saw what was being handled, so that bacteria and bacteriological diagnostic methods became realities and not mere textbook abstractions. We were not taught actually to become practical bacteriologists but we certainly saw and came to know how bacteriologists worked and thought. During the practical classes demonstrators, and the professor himself, regularly and provocatively challenged individual students by embroiling them in argument for and against current clinical dogmas and popular beliefs. Attendance at lectures was voluntary; absences from the practicals were easily noticed in a class of only 50 students and were firmly discouraged on the basis that you cannot think sensibly about bacteria if you have never even seen them.

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