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# Staircase pharmaceuticals

*especially in relation to low income countries*

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# Staircase Pharmaceuticals

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The majority of patients who present to a medical officer or other health worker with some complaint will get better spontaneously provided they get supportive care (Cochrane of Evidence-based-medicine fame estimated 80%, Franz J. Ingelfinger, the former editor of the New England Journal of Medicine estimated 85%). But in the minority who will not improve spontaneously some form of drug therapy is likely to be needed.
Thus it is important first to make the right diagnosis and decide whether drug therapy is indicated. Then it is essential to choose a drug which has been proved to be clinically efficacious as well as affordable to both patient and the community. Whatever drug is chosen, it should always be combined with good supportive therapy in order to maximize its effect.

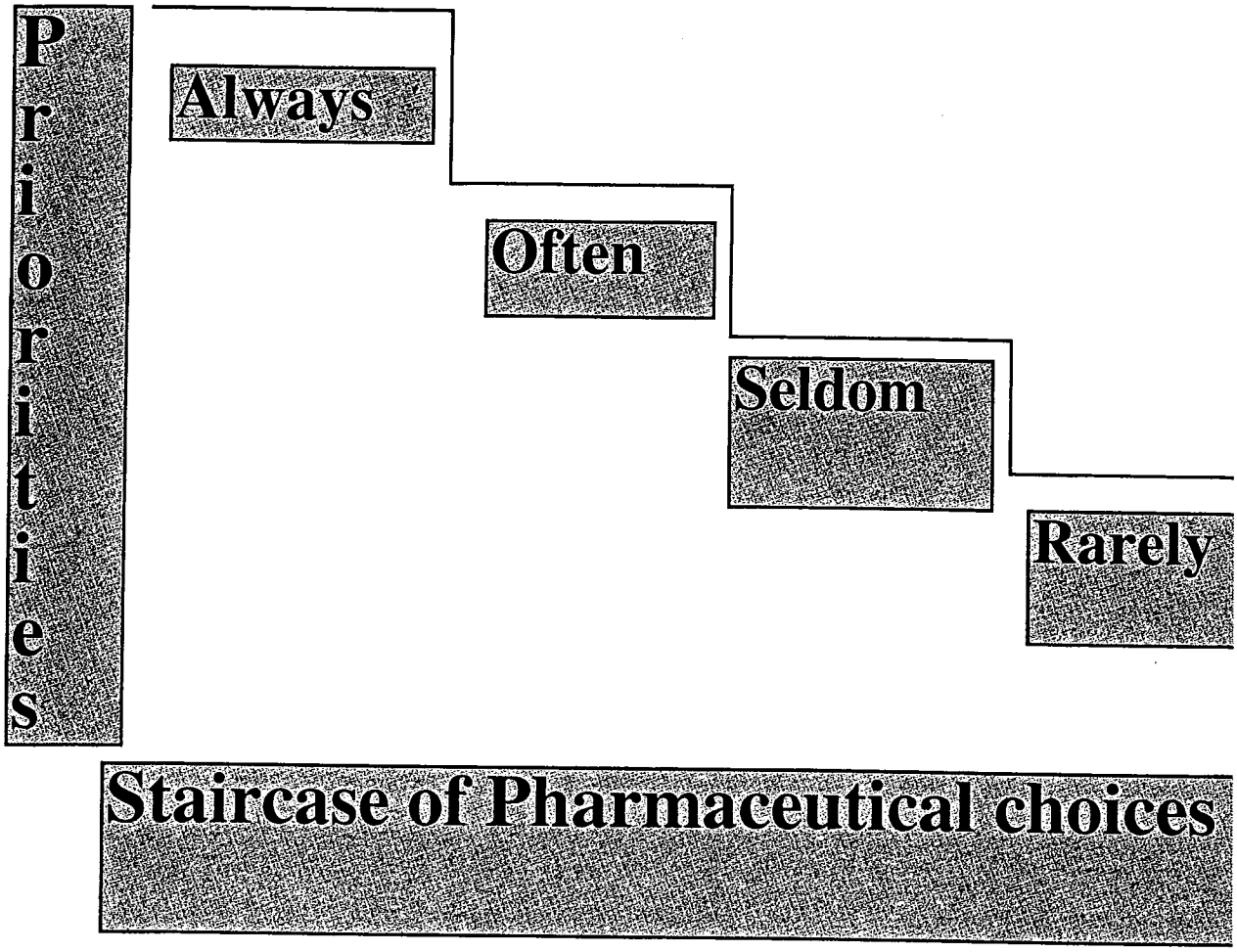
Wherever there is competition between the clinical efficacy of a pharmaceutical preparation and its cost these two major criteria have to be weighed against each other. In certain settings and especially in low-income-countries the cost becomes the major factor. There is a role for recommending a staircase approach to pharmaceuticals where the first level is often cheaper than the next level.
There exist many pharmaceutical preparations that are possibly seen as old-fashioned but that are sound and well established in scientific studies. These may be chosen in preference to more modern preparations that cost much more, even though they may have marginally better clinical efficacy or slightly less side-effects. The more expensive drugs could prove necessary in certain settings when cheaper drugs are either not effective or their side-effects are too significant. However very few breakthrough drugs for major diseases have been discovered in the last 30 years in contrast with the Golden Era in the preceding 30 years.

At various levels of clinical care the resources that are available for diagnosis and treatment will vary very widely. Thus it seems logical to provide a selection of acceptable and efficacious drugs with varying cost and varying pattern of efficacy and side-effects. **These are presented as four steps of acceptable therapy and three forms of therapy which at present are not recommended.**

The choice of drug for specific defined diseases at various levels can be discussed and decided upon in district Drug and Therapeutic Committees (DTCs) and the model encourages updating as time moves on.

In the following tables suggestions are given of the range of seven options that may be available to such committees. These should be seen as only suggestions and examples and the DTCs will have flexibility to choose other options and update these options at regular intervals. The method of Staircase pharmaceuticals is to be seen as an instrument in promoting the **rational use of drugs** and not a straight-jacket to stifle independent thinking.

The model was first presented at a workshop for looking at the National Formulary and Treatment Guidelines under the National Drug Policy Development of the Ministry of Health at Lilayi Lodge, Lusaka, Zambia in May 1997. It was modified after discussions in June 1997 with the Infectious Disease Clinic at Ryhov County Hospital, Jönköping in Sweden and later in discussions with the Department of Pharmacology at Huddinge Hospital, Stockholm as part of their Janus project. The author acknowledges the help and encouragement of the participants at these gatherings but takes the full responsibility for the contents of this document. The author is in receipt of funding from **Sida**, collaborating with the **Ministry of Health**, Zambia, with the Division of **International Health Care Research** at Karolinska Institute, and with the Department of Pharmacology at Huddinge Hospital, Stockholm.




**In the following examples of Titrating Pharmaceutical choices the number given next to each disease entity refers to the relevant section in the Oxford Texbook of Medicine Third Edition, 1996, whose sequence of diseases we follow. Dosages suggested are often starting doses for adults and may need adjusting. Check with local drug regimens.**

# Contents

# Staircase Pharmaceuticals

## HIV infection including anti-viral therapy 7.10.29

*Caused by two viruses, HIV[1] and HIV[2] but the former is the dominant throughout the world. Treatment as with all primarily sexually transmitted disease should be given in the context of health promotion (reducing number of partners or ideally lifelong mutual monogamy), disease prevention (encouraging the use of condoms where health promotion fails) illness management (given below) and disability rehabilitation.*

**Always.** Acceptable medical practice that is available at all levels and is cheap.

Start with ensuring adequate treatment of opportunistic infections at all levels.

Cotrimoxazole 960mg 12hrly PO for 7 days or amoxycillin 500mg 8hrly PO for bacterial respiratory infections metronidazole 500mg 8hrly PO for 7 days for bowel infections, local clotrimazole 10mg x 5 daily for fungal infections of mouth and oesophagus, codeine max. 0.5mg/kg 6hrly PO for pain and diarrhoea. When indicated tuberculosis therapy using pyrazinamide, isoniazid, rifampicin and ethambutol (alt. in extreme resource constraint streptomycin) by DOTS 3 times a week (see TB p. 10 for details).

**Often.** Consider when resources are available wider treatment and prophylaxis.

Add to the above in later HIV infection dapsone prophylaxis 100mg twice weekly PO against PCP, good analgesia in painful tumours or infections, adequate anti-diarrhoeal therapy with codeine (see above) or loperamide 4-8mg daily in divided doses, fluconazole 50-100mg daily PO or where resources are scarce ketoconazole 200-400mg daily PO for mucosal fungal infections. Treat initially for 14-30 days but likely to nee repeating and may need to remain on prophylactic dose. Add when resources are available prophylaxis in HIV+ delivering women to prevent mother-to-child transmission: nevirapine single dose to mother during labour and single dose to newborn after delivery combined with strict exclusive breast feeding for 3-6 months.

**Seldom.** Best medical practice for anti-HIV effect when resources are available.

When CD4 cells fall below 500/ml or viral load above 10 000/ml consider anti-HIV treatment with triple ora therapy e.g. lamivudine 150mg 12hrly, zidovudine 500mg daily in 2 divided doses, indinavir 800mg 8hrly + early treatment of bacterial infections including TB + early antiviral treatment for herpes, CMV, disseminat VZV + prophylaxis for PCP (and possibly for HSV, MAC and TB however cost-effectiveness varies**). Fluconazole 200-400mg daily for 6-8 weeks for cryptococcal meningitis.

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## *Not recommended therapy*

a. Therapy that is still being developed.

New protease inhibitor nelfinavir, non-nucleoside reverse transcriptase inhibitors delaviridine, nevirapine, Interleukin-2, chemokine AOP-RANTES, N-acetylcysteine to replace Glutathione, anti-oxidants such as Vitamin-E, anti-Tumour-necrosis-factor-α with pentoxiphylline or thalidomide

b. Poor medical practice which is now obsolete. Long-term single line treatment with AZT alone

c. Contra-indicated therapy. Thiacetazone therapy in Tuberculosis

### References

Lipsky J.J. Antiretroviral drugs for AIDS Lancet 1996; 348:800-803

Report of the NIH Panel to define Principles of Therapy of HIV Infection. 1997. Office of AIDS Research, National Institute of Health, United States.

Guidelines for the use of Antiretroviral agents in HIV-infected adults and adolescents, 1997. Dept of Health and Human Services, USA, and Henry J. Kaiser Family Foundation.

Morris, K. Never say never to a cure for HIV-1 infection Lancet 1997; 349:1371

Perelson, A., Ho, D. et al Nature 1997; 387:188-191

*Freedberg KA et al The cost-effectiveness of preventing AIDS-related opportunistic infections. JAMA 1998, 279:130-135

Coutsoudis A. et al Influence of infant-feeding patterns on early mother-to-child transmission of HIV-1 in Durban, South Africa: a prospective cohort study. Lancet 1999; 354: 471-76

# Staircase Pharmaceuticals

## Gonorrhoea in the presence of PPNG 7.11.6

*Caused by Neisseria gonorrhoeae and complicated by appearance of resistant strains with Penicillinase Producing Neisseria gonorrhoeae (PPNG). Treatment to be in the context of Health Promotion, Disease Prevention (see under HIV), illness Management as given below and disability rehabilitation e.g. for blindness and infertility.*

**Always.** Acceptable medical practice that is available at all levels and is cheap. Ensure widespread availability of diagnosis (e.g. using Syndromic approach) and treatment e.g. cotrimoxazole 480 mg x 10 tabs daily for 3 days, with gentamicin 240mg i.m. single dose as back-up in treatment failure. NB increasing resistance in some countries to cotrimoxazole.

**Often.** When resources are available increase treatment efficacy by starting with: gentamicin 240mg i.m. single dose. Where cheaper good quality ciprofloxacin is available, this is recommended at this level: 500mg PO single dose.

**Seldom.** Back-up medical practice when resources are available:
Start with ciprofloxacin 500mg PO single dose or ofloxacin 400mg PO single dose or ceftriaxone 250mg i.m. single dose or cefotaxime 1g i.m. single dose or cefixime 400mg PO single dose.

**Rarely.** In high income countries disregarding cost use:
spectinomycin 2gms i.m. single dose.

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## *Not recommended therapy*

a. Therapy that is still being tested.
   Sparfloxacin, grepafloxacin
b. Poor medical practice which is now obsolete.
   Procaine penicillin
c. Contra-indicated therapy.
   Herbal medicine

### References

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 323-349 W.B.Saunders. London.
Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Conte J.E. Manual for antibiotics and Infectious Diseases. 1995. 8th Ed. Williams and Wilkins. Baltimore

## Staircase Pharmaceuticals

### Dysentery 7.11.7

*Usual organisms: Shigella, salmonella, campylobacter, vero cytotoxin producin E.coli VTEC (also called enterohaemorrhagic E. coli EHEC), less acute Entamoeba histolytica*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Ensure priority treatment at all levels e.g. rehydrate all patients, orally if possible; selective chemotherapy for the toxic cases: cotrimoxazole 480mg x 2 tabs twice daily PO for 7 days where resistance is still rare; otherwise nalidixic acid 1g thrice daily PO for 5 days . In amoebic dysentery: metronidazole 500mg thrice daily PO for 5 days.

**Often.** When resources are available increase treatment efficacy by starting with:

Rehydration as above. Give nalidixic acid 1g thrice daily PO for 5 days, alt. norfloxacin 400mg twice daily for 7 days. Where cheaper good quality ciprofloxacin is available, this is recommended at this level: 500 mg twice daily for 5 days.

In amoebic dysentery metronidazole 500mg thrice daily PO for 5 days.

**Seldom.** Back-up medical practice disregarding cost.

Rehydrate as above. Ciprofloxacin 500 mg twice daily for 5 days.

In amoebic dysentery tinidazole 2g daily for 3 days

In all dysentery avoid anti-motility drugs. In VTEC watch out for haemolytic uraemic syndrome.

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## *Not recommended therapy*

a. Therapy that is still being tested.

Grepafloxacin

b. Poor medical practice which is now obsolete.

Tetracycline

c. Contra-indicated therapy.

**Anti-diarrhoeal medicine;** inadequate rehydration

### References

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 835-840 W.B.Saunders. London.

Bell R.B. Lecture notes on Tropical Medicine. 4th. Ed. 1995. Blackwell Science. Oxford.

## Staircase Pharmaceuticals

### Typhoid fever 7.11.8

*Cause: Salmonella typhi or parapythi types A,B and C spread by contaminated water, food or person to person with poor personal hygiene.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
Chloramphenicol 500-750mg 6-hrly PO for 14 days or cotrimoxazole 480mg x 2 tabs twice daily for 14 days or amoxycillin 1g 6-hrly PO for 14 days unless resistance in area is high

**Often.** When resources are available increase treatment efficacy by starting with:
alternative to chloramphenicol if resistance has been proved: ciprofloxacin 500mg -1g PO twice daily for 14 days or norfloxacin 800mg twice daily PO for 14 days.

**Seldom.** Back-up medical practice disregarding cost.
If resistance to ciprofloxacin has been proved start with cefixime 20mg/kg PO twice daily for 14 days or ceftriaxone 50-60mg/kg i.m. twice daily for 7-10 days or cefotaxime 1g i.v. thrice daily for 14 days

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## *Not recommended therapy*

a. Therapy that is being developed.
Grepafloxacin

b. Poor medical practice which is now obsolete.

c. Contra-indicated therapy.
Tetracycline.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 854-855 W.B.Saunders. London.
Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.

# Staircase Pharmaceuticals

## Cholera 7.11.11

*Cause: Enterotoxin fromVibrio cholerae which is transmitted through contaminated water or food.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Oral rehydration with ORS in water. If initiated early in the disease this may obviate need for i.v. therapy. However more serious disease may need intial resuscitation with i.v. fluids. Can make this up locally from 4g NaCl + 6.5g sodium acetate + 1g KCl in a litre of sterile, pyrogen-free distilled water.

Protection of the community with improved quality and quantity of water and better sanitation. Isolation of all cholera patients in special units.

**Often.** When resources are available increase treatment efficacy by adding to the above:

antibiotic treatment to shorten the illness e.g. doxycycline 300mg PO as a single dose or tetracycline 250mg x 4 PO for 3-5 days. Alt in resistance: furazolidone 400mg PO daily for 3 days, or erythromycin 250mg 6-hrly PO for 3 days, or cotrimoxazole 480mg x 4 tabs twice daily for 3 days . Single dose ciprofloxacin 1gm PO may be considered in certain circumstances especially if a cheaper generic drug of good quality is available.

Oral rehydration is still the corner-stone of milder cases. In more severe dehydration give i.v. Ringer's lactate. In a setting of multi-drug resistance, rehydration alone will be effective in most cases.

**Seldom.** Back-up medical practice disregarding cost.

Add to the above multiple dose ciprofloxacin 500mg twice daily PO for 3 days. Alternative mecillinam 400mg thrice daily PO for 3 days.

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## *Not recommended therapy*

a. Therapy that is being developed.

Substitute rice starch for glucose in ORS.

L-glutamine based solution which has better intestinal cotransport than glucose

b. Poor medical practice which is now obsolete.

Putting all cholera patients automatically onto long-term i.v. rehydration

c. Contra-indicated therapy.

Use of antacids and other acid-suppressing therapy (especially proton pump inhibitors) in those with immediate risk of exposure to Vibrio cholerae.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 854-855 W.B.Saunders. London.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Lima, A.A.M. Cholera: molecular epidemiology, pathogenesis, immunology, treatment and prevention. Current opinion in Infectious Diseases 1994. 7:592-601

Khan, W.A. et al. Randomized controlled comparison of single-dose ciprofloxacin and doxycycline for cholera caused by Vibrio cholerae 01 or 0139. Lancet. 1996. 348: 296-300

## Staircase Pharmaceuticals

### Chancroid 7.11.13

*Caused by Haemophilus ducreyi, a sexually transmitted disease. Treatment to be in the context described under HIV. This is the commonest cause of genital ulcer disease in some African countries. It is particularly prone to increase the risk of HIV spread.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
ensure widespread availability of e.g. cotrimoxazole 2 tabs x 2 for 7 days, with erythromycin 500 mg x 3 PO for 7 days as back-up in treatment failure

**Often.** When resources are available increase treatment efficacy by substituting with: Ciprofloxacin 500 mg PO as a single dose

**Seldom.** In high income countries disregarding cost use:
azithromycin 1 gm PO as a single dose or ceftriaxone 250 mg i.m. as a single dose

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## *Not recommended therapy*

a. Therapy that is still being tested.
   Sparfloxacin, grepafloxacin
b. Poor medical practice which is now obsolete.
   Tetracycline
c. Contra-indicated therapy.
   Herbal medicine

### References

Conte J.E. Manual for antibiotics and Infectious Diseases. 1995. 8th Ed. Williams and Wilkins. Baltimore

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 323-349 W.B.Saunders. London.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

## Staircase Pharmaceuticals

### Tuberculosis 7.11.22

*Caused by Mycobacterium tuberculosis spread mainly by droplets in air-borne transmission. Follow as far as is possible National TB Therapy guidelines.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
Ensure widespread availability of diagnosis and treatment i.e. 2-months streptomycin 15mg/kg im daily + isoniazid 5mg/kg PO daily + pyrazinamide 25mg/kg PO daily + rifampicin 10mg/kg PO daily followed by 4 months isoniazid 5mg/kg PO daily + ethambutol 15mg/kg PO daily (or thiacetazone 3mg/kg PO daily where HIV has been ruled out).

**Often.** When resources are available increase treatment efficacy by substituting:
6-months treatment consisting of: **3-times-weekly** DOTS*. with rifampicin 10mg/kg PO, isoniazid 10mg/kg PO, pyrazinamide 35mg/kg PO and ethambutol 30mg/kg PO *for 2 months*, followed by 4 *months* of 3-times-weekly isoniazid 10mg/kg PO and ethambutol 30mg/kg PO.

**Seldom.** In high income countries disregarding cost use:
6-months of 3-times-weekly DOTS* with rifampicin 10mg/kg PO, isoniazid 10mg/kg PO, pyrazinamide 35mg/kg PO and ethambutol 30mg/kg PO.

**Rarely.** Back-up in **multi-drug resistance** of ethionamide 15mg/kg daily PO, ofloxacin 15mg/kg PO daily, or ciprofloxacin 500mg twice daily PO, amikacin 15mg/kg daily i.m., capreomycin 1g daily i.m., pyrazinamide 25mg/kg PO daily, cycloserine 250mg twice daily PO, PAS 10-12g daily PO in 2 divided doses, kanamycin 15mg/kg daily i.m. (N.B. prognosis is poor even with best therapy).

**Suggested regime:** amikacin + pyrazinamide + ethionamide + ofloxacin until sensitivity results available or for at least 3-4 months and then ethionamide and ofloxacin for 18 months. Consider surgery if only one area of lung is affected

***DOTS = Directly Observed Treatment Short-course where a volunteer lay person or a community health worker administers and observes each dose being taken to ensure 100% compliance.**

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## *Not recommended therapy*

a. Therapy that is still being developed.
   Rifabutin, grepafloxacin

b. Poor medical practice which is now obsolete.
   Long-term isolation of TB patients in special units. 18-month treatment with Streptomycin (first two months), isoniazid and thiacetazone or PAS.

c. Contra-indicated therapy.
   Thiacetazone therapy in the presence of HIV

### References

Crofton,J. et al. Clinical Tuberculosis. 1992. Macmillan Education Ltd. London.
Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 997-1006 W.B.Saunders. London.

# Staircase Pharmaceuticals

## Leprosy 7.11.25

*Caused by Mycobacterium leprae spread mainly by droplets in airborne transmission. Reactions after starting treatment are common and are of two types: reversal reactions in BT,BB,BL where the immune response seems to increase with local inflammation and nerve damage; erythema nodosum leprosum (ENL) in LL (rarely BL). In reversal reactions give high steroid doses early to save the nerve function e.g. 60mg prednisoslone daily in 3 divided doses and reduce each 1-2 wks when inflammation starts to settle down and stop after 12 weeks. In ENL give thalidomide 200mg bd in men and in women who cannot become pregnant. Reduce to 50-100 mg nightly when there is improvement. Alternatives in women in a fertile age is a combination of prednisolone 40mg daily with clofazimine 300m daily reduced after 3 months.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Ensure widespread availability of diagnosis and treatment e.g. 6-month treatment for **paucibacillary** with rifampicin 600mg PO once monthly supervised and dapsone 100mg daily PO, or for **multi-bacillary leprosy** 2 years treatment with rifampicin 600mg once monthly supervised, clofazimine 300 mg PO once monthly supervised and 50mg daily PO, and dapsone 100mg daily PO .

Alt. where lab. facilities are inadequate use simpler classification, i.e. up to 5 patches, paucibacillary (6 months therapy); more than 5 patches **multibacillary** (may be possible to reduce treatment from the usual minimum 2 years to 18 months).

**Often.** When resources are available increase treatment efficacy by substituting:

in patients with a single lesion only a single dose of rifampicin 600mg PO + ofloxacin 400mg PO + minocycline 100mg PO.

**Seldom.** Back-up medical practice disregarding cost.

in multibacillary leprosy: alternative when rifampicin cannot be used : together with clofazimine 50mg daily PO add ofloxacin 400mg daily PO + minocycline 100mg daily PO or clarithromycin 500mg daily PO.

Alternative when clofazimine is unacceptable: ofloxacin 400mg daily PO or monocycline 100mg daily PO.

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## *Not recommended therapy*

a. Therapy that is still being tested.

Trial is underway of treating paucubacillary with rifampicin 600mg PO daily + ofloxacin 400 mg daily for 1 month and multibacillary leprosy with daily clarithromycin 500mg PO + ofloxacin 400 mg PO + minocycline 100mg PO + rifampicin 600mg daily for 1 month.

b. Poor medical practice which is now obsolete.

Monotherapy with dapsone

c. Contra-indicated therapy.

Stopping anti-leprosy treatment during reactions

### References

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 1037-1041 W.B.Saunders. London.

Smith, Cairns. Personal communication. 1996.

## Staircase Pharmaceuticals

### Genital Chlamydia 7.11.41

*Caused by a specific strain of Chlamydia trachomatis other strains of which produce several other completely different diseases. Spread by sexual transmission or mother to child.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
Ensure widespread availability of diagnosis (e.g. using syndromic approach) and treatment e.g. doxycycline 100 mg x 2 for 7 days (preferred) or tetracycline 500 mg x 4 for 7 days but these cannot be used in pregnancy or childhood.

**Often.** When resources are available broaden scope of those who can be treated:
i.e. in pregnancy and childhood use erythromycin 500 mg x 4 for 7 days

**Seldom.** Back-up medical practice in resistance disregarding cost.
azithromycin 1 gm orally as a single dose or ofloxacin 300 mg x 2 for 7 days

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## *Not recommended therapy*

a. Therapy that is still being tested.
   Sparfloxacin, grepafloxacin

b. Poor medical practice which is now obsolete.

c. Contra-indicated therapy.
   Use of doxycycline or tetracycline in pregnancy or childhood or ofloxacin in pregnancy.

### References

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 323-349 W.B.Saunders. London.
Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Conte J.E. Manual for antibiotics and Infectious Diseases. 1995. 8th Ed. Williams and Wilkins. Baltimore

## Staircase Pharmaceuticals

### Malaria prevention where P. falciparum dominates 7.13.2

*Bed-nets impregnated with permethrin are recommended at all levels in both semi-immunes and non-immunes. However on a wider scale must be community based to be sustainable. Drug prophylaxis may be inappropriate in a highly endemic malariasetting since it may lead to severe malaria at a later age. It may be called for in an epidemic situation for short-term use. Antimalarial drugs act at various stages of the malaria cycle: 1. Sporontocidal: proguanil, pyrimethamine, atovaquone. 2. Hypnozoitocidal: primaquine. 3. Tissue schizontocidal: proguanil, pyrimethamine. 4. Blood schizontocidal: chloroquine, quinine, artemisinin. 5. Gametocytocidal: primaquine*

**Always.** Acceptable medical practice that could be available at all levels and is cheap:
For non-immunes ensure widespread availability of impregnated bed-nets and possibly pyrimethamine 12.5mg/dapsone 100mg : 1 tab. weekly. For semi-immunes impregnated bed nets and occasionally weigh up need for same drug prophylaxis as a short-term intervention in an epidemic malaria situation.

**Often.** When resources are available increase treatment efficacy by adding to impregnated bed-nets drug prophylaxis in non-immunes with: proguanil 100mg daily PO plus chloroquine 150mg base PO once weekly.

**Seldom.** In those from high income countries when resources are available:
with high malaria risk add to impregnated bed-nets drug prophylaxis with mefloquine 250mg PO once weekly.

**Rarely.** In those from high income countries disregarding cost use:
with high malaria risk use drug prophylaxis with atovaquone 250mg + proguanil 100mg daily after a fatty meal (US$ 4/ day; SEK 30/day prices March 2000).

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### *Not recommended therapy*

a. Therapy that is still being developed. Tafenoquine as prophylactic. Preventive immunization.

b. Poor medical practice which is now obsolete. e.g. doxycycline as prophylactic except in exceptional circumstances, chloroquine alone in widespread chloroquine resistance. Use of unimpregnated bed-nets.

c. Contra-indicated therapy. Double dose i.e. pyrimethamine 25mg/dapsone 200mg weekly, combination of pyrimethamine 500mg-sulphadoxine 25mg and chloroquine as prophylactic, amodiaquine as prophylactic. Tetracycline prophylaxis in pregnancy or in childhood.

### References

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 1145-1146 W.B.Saunders. London.

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. 860-861. OUP . Oxford.

Fryauff D.J. et al Randomized placebo-controlled trial of primaquine for prophylaxis of falciparum malaria. Lancet 1995; 346:1190-1193

Lobel Ho et al. Long term malaria prophylaxis with weekly mefloquine Lancet 1993; 341: 848-851

Westeyn JCFM et al Is mefloquine prophylaxis ineffective for short-term travellers? Lancet 1995; 346: 574

Hill D.R. and Bia F.J. Tropical and travel-associated diseases. Current opinion in Infectious diseases 1994, 7:525-528

Bradley, D.J. and Warhurst, D.C. Malaria prophylaxis: guidelines for travellers from Britain. BMJ 1995; 310: 709-714

Barrett, P.J et al Comparison of adverse events associated with use of mefloquine and combination of chloroquine and proguanil as antimalarial prophylaxis. BMJ 1996; 313:525-528

Jones, M. Report from 14th International Congress on Tropical Medicine and Malaria. Nagasaki, Japan. 17th-22nd November 1996

## Staircase Pharmaceuticals

### Acute malaria treatment (P. falciparum with moderate CQ resistance) 7.13.2

*Antimalarial drugs act at various stages of the malaria cycle: 1. Sporontocidal: proguanil, pyrimethamine, atovaquone. 2. Hypnozoitocidal: primaquine.*
*3. Tissue schizontocidal: proguanil, pyrimethamine. 4. Blood schizontocidal: chloroquine, quinine, artemisinin. 5. Gametocytocidal: primaquine*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
Ensure availability of diagnosis and treatment e.g. pyrimethamine 500mg-sulphadoxine 25mg: 3 tablets single dose PO, or amodiaquine 600mg daily PO for 2 days then 300 mg on 3rd day

**Often.** When resources are available increase treatment efficacy by combining amodiaquine 600mg daily PO for 2 days then 300 mg on 3rd day with pyrimethamine 500mg-sulphadoxine 25mg: 3 tablets single dose PO. If recrudescence of malaria after this add doxycycline 200 mg daily for 7-10 days.

**Seldom.** In high income countries disregarding cost consider use of:
atovaquone 1000 mg daily plus proguanil 400mg daily PO after fatty meal for 3 days.
Alternative oral artesunate 4 mg/kg daily for 3 days then doxycycline 200 mg PO daily for 7 days,
Alt. quinine 10mg salt/kg PO thrice daily for 3 days then doxycycline 200 mg daily PO for 7 days,
Alt. mefloquine 15mg base/kg PO first dose followed by 10mg/kg 8 hrs later

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## *Not recommended therapy*

a. Therapy that is still under trial.

Chloproguanil/dapsone (LapDap®) likely to be cheap and effective in chloroquine resistant malaria (available by 2002), arte-ether for severe malaria, pyronaridine, , nitric oxide in ARDS of malaria, desferrioxamine in cerebral malaria

b. Poor medical practice which is now obsolete.

Mepacrine, use of chloroquine treatment in non-immunes.

c. Contra-indicated therapy.

Combination therapy of quinine and mefloquine, Halofantrine in arrythmic heart disease.

### References

Cochrane review from Liverpool: efficacy and safety of amodiaquine
Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 1121-1147 W.B.Saunders. London.
Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Gilles H.M. Management of severe and complicated malaria. 1991 WHO Geneva
Brasseur P. et al. Sensitivity of Plasmodium falciparum to amodiaquine and chloroquine in central Africa: a comparative study in vivo and in vitro. Trans Roy Soc Trop Med&Hyg 1995; 89:528-30
Nevill C.J. et al. A comparison of amodiaquine and chloroquine in the treatment therapy of falciparum malaria in Kenya. East African Med J 1994 71:167-170
Olliaro P et al Systematic review of amodiaquine treatment in uncomplicated malaria. Lancet 1996; 348:1196-1201
Radloff P.D. et al. Atovaquoine and proguanil for Plasmodium falcipaurm malaria. Lancet 1996; 347: 1511-1514
Staedke S.G. et al. Amodaiquine, sulfadoxine/pyrimethamine and combination therapy for treatment of uncomplicated falciparum in Kampala, Uganda: a randomized controlled trial. Lancet 2001; 358: 368-74

## Staircase Pharmaceuticals

### Mixed intestinal nematode infection 7.14.4

*Usual intestinal nematodes: Ascaris, necator, ancylostoma, trichuris, strongyloides*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
Ensure widespread availability of diagnosis and treatment e.g. levamisole 2.5 mg/kg PO single dose esp for Ankylostoma duodenale and Ascaris.

**Often.** When resources are available increase treatment efficacy by substituting with: mebendazole 100mg PO twice daily for 3 days, or low-cost albendazole 400mg single dose PO or in pregnancy pyrantel 10mg/kg PO single dose.

**Seldom.** Best medical practice disregarding cost.
Start with albendazole 400mg single dose PO, but in strongyloides ivermectin 0.15mg/kg single dose PO or thiabendazole 25mg/kg PO twice daily for 3 days or albendazole 400mg twice daily PO for 3 days.

.....

*Not recommended therapy*

a. Therapy that is under trial at present.

b. Poor medical practice which is now obsolete.
Piperazine, Tetrachloethylene, bephenium hydroxnaphthoate

c. Contra-indicated therapy.
Mebendazole or albendazole in pregnancy (these are still recommended contra-indications but both are now being questioned as no evidence has yet been shown for toxicity in pregnancy in humans)

**References**

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 1369-1402 W.B.Saunders. London.
Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

## Staircase Pharmaceuticals

### Schistosomiasis: S. haematobium and S. mansoni 7.16.1

*Ideally treatment should be in the context of improving sanitation and reducing risk of contact with contaminated water but these are long-term objectives. Mass treatment in heavily infected communities is sometimes warranted. Anti-snail measures can be effective but are rarely sustainable unless based on locally available biological agents.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
Ensure widespread availability of diagnosis and treatment. In S. haematobium, can use single dose combination metrifonate 12.5 mg + niridazole 25 mg* followed up after 3 months. Only those with live eggs on follow-up treated with praziquantel 40mg/kg PO single dose. In S. mansoni oxamniquine 10mg/kg twice PO on same day.

**Often.** When resources are available increase treatment efficacy by substituting with: metrifonate 10mg/kg PO weekly for 3 doses for S. haematobium, oxamniquine 10mg/kg twice PO on same day for S. mansoni. If low-cost praziquantel is available substitute this for both.

**Seldom.** Best medical practice disregarding cost.
Praziquantel 40mg/kg PO single dose for S. haematobium; praziquantel 30mg/kg PO for 2 or 3 doses for S. mansoni.

*This combination gives almost as good results as three separate doses of metrifonate a week apart with better compliance but since niridazole is now no longer widely available because of its side-effects as a montherapy it is becoming obsolete.

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## *Not recommended therapy*

a. Therapy that is contemplated and may be developed.
   Vaccination against schistosomiasis
b. Poor medical practice which is now obsolete.
   Stibophen and astiban, monotherapy with niridazole.
c. Contra-indicated therapy.
   Herbal medicine

### References

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 1443-1447 W.B.Saunders. London.
Adams and Maegraith. Maegraith, B. Clinical Tropical Diseases 1984. 8th Edition ; 396-399 Blackwell. Oxford

# Staircase Pharmaceuticals

## Insulin Dependent Diabetes Mellitus (IDDM) 11.11

*This is one of the most difficult clinical conditions to deal with in Africa especially in a rural setting. The most important advice is for the patient to move home as soon as the diagnosis has been made to live near to a health unit where regular supervision and regular supplies of insulin are available.* ***Enthusiastic, continued health education is crucial in all diabetes control.***

*Diabetes definition: any symptomatic patient with a random plasma glucose of 11.1 mmol/L (200 mg/dl). or a fasting plasma glucose >6.7 mmol/L and/or a 2 hour postglucose level >10.0 mmol/L. IDDM defined as any patient who without insulin injection becomes ketoacidotic within days. Usually in younger people. more common in white Caucasians.*

**Always.** Acceptable cheap medical practice to be made available at all levels.

Ensure widespread availability of diagnosis and treatment e.g. once daily dose of long-acting insulin e.g. lente insulin aiming at blood glucose levels < 12 mmol/L. Regular checks on urine glucose. Extra viscous fibres in diet i.e. from legumes and fruit. Low level of saturated fats. Higher levels of polyunsaturated fats. Regular exercise. Good BP control.

**Often.** When resources are available increase treatment efficacy by substituting with: twice-daily injection with an intermediate-acting insulin such as isophane insulin (NPH) and checking the control on twice daily blood glucose levels aiming at fasting < 8 mmol/L, and 2 hours postprandial < 10 mmol/L, as well as monthly glycated haemoglobin GHb within 4 S.D. of normal. Extra viscous fibres in diet i.e. from legumes and fruit. Low level of saturated fats. Higher levels of polyunsaturated fats. Regular exercise. Good BP control.

**Seldom.** Best medical practice in settings of good resources.

Intensive therapy with 4 daily injections of human soluble insulin and 4 daily checks of self-monitored blood glucose aiming at preprandial levels of 3.9-6.7 mmol/l and a normal glycated haemoglobin (GHb) concentration. Alt continuous sucutaneous insulin infusion (CSII). However be prepared for more frequent episodes of hypoglycaemia with this intensive régime. Extra viscous fibres in diet i.e. from legumes and fruit. Low level of saturated fats. Higher levels of polyunsaturated fats. Regular exercise. Good BP control.

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## *Not recommended therapy*

a. Therapy that is currently being tested.

Transplantation of islets of Langerhans. Use of analogues of human insulin such as Lys (B28), Pro (B29). Use of immune modulators in the early stages of symptomatic illness to stop the immune destruction of Islet cells. ACE inhibitors in those with early evidence of renal damage.

b. Poor medical practice which is now obsolete.

c. Contra-indicated therapy.

More than minimal "rapid" carbohydrates (such as sugar) in the diet

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Page S.R. et al How to achieve optimal diabetic control... Postgrad Med J. 1994 70:675-681

Bashoff E.C. et al Insulin therapy and the reluctant patient. Postgraduate medicine 1995 97:86-96

# Staircase Pharmaceuticals

## Non Insulin Dependent Diabetes Mellitus (NIDDM) 11.11

*This is likely to become a major cause of ill-health in the future as more affluence and unhealthy diets come to certain sections of communities in many countries. In some communities e.g. those of Polynesian-Micronesian stock 40-50% of some groups have abnormal glucose tolerance tests.*
***Enthusiastic, continued health education is crucial in all diabetes control.***
*Diabetes definition: any patient with a fasting plasma glucose >6.7 mmol/L and/or a 2 hour postglucose level >10.0 mmol/L. The classic picture is of an older obese (90%) person who presents with polyuria and polydypsia or one of the complications of chronic hyperglycaemia.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
Ensure widespread availability of diagnosis and treatment. Start with calorie restriction to bring about weight reduction. Increased exercise. Extra viscous fibres in diet i.e. from legumes and fruit. Low saturated fats + higher levels of polyunsaturated fats. Strictly control hypertension if present. If diabetes control is still poor add metformin 500-1700 mg daily divided in 2-3 doses especially in the obese. If hyperglycaemia still present add chlorpropamide 100-500 mg as a once daily dose. Watch out for hypoglycaemia. Ensure good BP control.

**Often.** When resources are available increase treatment efficacy by substituting with: twice-daily glibenclamide 2.5-5mg 2 or 3 times daily or other second generation sulphonylurea. If this fails try "BIDS" approach at bedtime of NPH dose 0.1-0.2U/kg combined with glibenclamide during the day. If this fails go over to insulin therapy (see IDDM). Ensure good BP control.

**Seldom.** Best medical practice in settings of good resources.
Diet as above in *Always* but in failure give insulin for 4 weeks which makes the pancreas more effective in responding to physiological signals or to sulphonylureas. After this 4 week period taper the dose and continue with diet, calorie restriction and exercise. If this is not enough add metformin 500-1700 mg daily divided in 2-3 doses and if necessary supplement with glibenclamide 2.5-5mg 2 or 3 times daily as in step 2, BIDS and then go over to insulin alone therapy as under IDDM. Ensure good BP control with ACE inhibitors.

.....

## *Not recommended therapy*

a. Therapy that is currently being tested.

Alpha-glucosidase inhibitors e.g. acarbose especially in postprandial hyperglycaemia.
Thiazolidinediones to increase insulin-sensitivity reducing doses of insulin needed
Supplements of polyunsaturated fatty acids (omega W-6) as precursors of prostaglandins and thromboxanes to reduce microangiopathic damage.

b. Poor medical practice which is now obsolete.

Phenformin because of risk of lactic acidosis

c. Contra-indicated therapy.

More than minimal "rapid" carbohydrates (such as sugar) in the diet

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. OUP. Oxford.
Cefalu W.T. Treatment of type II diabetes Postgraduate medicine 1996 99:109-119
UK Prospective Diabetes Study Group with type 2 diabetes Lancet 1998; 352: 837-53, 854-65, 703-13

# Staircase Pharmaceuticals

## Hypertension in pregnancy 13.2

*Virtually all cases except those with pre-existing hypertension develop after week 24 of pregnancy. Defn. A rise of 30 mm systolic or 15 mm diastolic over baseline (or > 140/90 where baseline is unknown in the latter half of pregnancy). Severe cases may need urgent delivery especially those with early onset.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Ensure widespread availability of diagnosis and treatment e.g. methyldopa 250mg twice daily PO up to 1.5 g daily. Hydralazine 6.25mg iv slowly in acute severe hypertension; then continue with hydralazine 25mg thrice daily PO up to 50mg twice daily. Magnesium sulphate 10mls 50% i.m. in each buttock in threatened or actual eclampsia. Repeat 5mls i.m. in each buttock every 4 hrs while needed.

**Often.** When resources are available increase treatment efficacy by substituting with:

pindolol 5-10mg once or twice daily. Hydralazine 6.25mg iv slowly in acute hypertension. In threatened or actual eclampsia magnesium sulphate 10mls 50% i.m. in each buttock . Repeat 5mls i.m. in each buttock every 4 hrs while needed.

**Seldom.** Best medical practice in settings of good resources.

Start with calcium antagonists isradipin 2.5 mg PO twice daily or nifedipin 10mg twice daily PO, (Alt. labetalol 100mg twice dailyPO) and combination with β–blocker if necessary. Magnesium sulphate 20 mg of 20% solution (4gms) i.v. over 15 mins then 1 gm/hr i.v. infusion in threatened or actual eclampsia

.....

## *Not recommended therapy*

a. Therapy that is uncertain.

Aspirin therapy when there is a high risk of pre-eclampsia

b. Poor medical practice which is now obsolete.

Diuretic therapy for oedema and/or hypertension

c. Contra-indicated therapy.

ACE inhibitors.

### References

Consensus report of working group in Scandinavian drug policy review

Cochrane review of Maternal Health Care as described in Enkin, M. et al. A guide to effective care in pregnancy and childbirth. 2nd Ed. 1995. Oxford University Press. Oxford.

## Staircase Pharmaceuticals

### Peptic ulcer 14.7

*Usually associated with colonization of the stomach and duodenum with Helicobacter pylori; a useful screening test for this is serlogical or salivary test for antibody to H.pylori.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Ensure widespread availability of diagnosis and treatment e.g. metronidazole 400mg t.i.d PO + tetracycline 500mg q.i.d PO for 2 weeks + bismuth chelate (or bismuth subcitrate) 120mg PO q.i.d for 4 weeks (not yet well assessed in randomized controlled trials). One recent article* shows highly effective cure of H. pylori with 10 days bismuth subnitrate 150 mg PO t.i.d + oxytetracycline 500 mg PO t.i.d + metronidazole 400 mg PO t.i.d.

Alt. Sucralfate 1g PO q.i.d + metronidazole 400mg t.i.d PO + tetracycline 500mg q.i.d PO for 2 weeks

**Often.** When resources are available increase treatment efficacy by substituting with: cimetidine 400mg PO b.i.d or ranitidine 150 mg PO b.i.d for two weeks + amoxycillin 500mg PO q.i.d + metronidazole 400mg t.i.d PO for 1 week

**Seldom.** Best medical practice in settings of good resources.

Omeprazole 40mg PO daily or lansoprazole 30mg PO daily or pantoprazole 40mg PO daily for one to two weeks + clarithromycin 250 mg PO b.i.d + tinidazole 500mg PO b.i.d for 1 week

.....

### *Not recommended therapy*

a. Therapy that is being developed.

Vaccine against Helicobacter pylori

b. Poor medical practice which is now obsolete.

Simple antacids alone (excluding sucralfate), anticholinergics, sedatives, strict diets

c. Contra-indicated therapy.

Early surgery without trial of medical treatment first,

Use of aspirin or non-steroidal anti-inflammatory drug in patient with known peptic ulcer

### References


Bateson, MC. Helicobacter pylori and radical therapy for peptic ulcer. Postgrad. Med.J. 1995; 71:641-644

van der Linden, B. Helicobacter pylori in gastroduodenal disease. Current opinion in Infectious diseases. 1994; 7: 577-581

Hentschel, E. et al Effect of ranitidine and amoxicillin plus metronidazole on the eradication of Helicobacter pylori and the recurrence of duodenal ulcer. New Eng.J.Med. 1993, 328: 308-312

Graham,DY. Treatment of peptic ulcers caused by Helicobacter pylori. New Eng.J.Med. 1993, 328: 349-350

van Zwet,AA. et al Explanations for high rates of eradication with triple therapy using metronidazole in patients harboring metronidazole-resistant Helicobacter pylori strains, Antimicrobial Agents and Chemotherapy, 1995; 39: 250-252

Jaup,BH. and Norrby,A. Low dose, short-term triple therapy for cure of Helicobacter pylori infection and healing of peptic ulcers. Am. J.of Gastroenterology. 1995; 90: 943-945

Banerjee,S. et al. Sucralfate suppresses Helicobacter pylori infection and reduces gastric acid secretion by 50% in patients with duodenal ulcer. Gastroenterology 1996; 110: 717-724

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

*Lerang F. et al Simplified 10-day bismuth triple therapy for cure of H. pylori infection. Am. J. Gastroenterol. 1998 93: 212-216

## Staircase Pharmaceuticals

### Persistent diarrhoea 14.18

*Defn. Diarrhoea that starts acutely and persists for more than 14 days. Associated with malnutrition, zinc and magnesium deficiency. The most common pathogens found are enteroadherent and enteropathogenic E.coli, and cryptosporidium. Underlying HIV infection , cholera, septicaemia or urinary tract infections are common in some settings.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Oral rehydration and specific treatment for shigella, cholera, UTI or septicaemia needed when indicated (see relevant section).

Nutrition supplementation with zinc, magnesium.

**Diet 1 :** Rice or maize, milk or yoghurt with soy flour if available, sucrose or lentils, oil

**Often.** When resources are available increase treatment efficacy by substituting:

**Diet 2:** Rice, egg-white or chicken, glucose or sucrose and oil

In AIDS with persistent diarrhoea consider albendazole 800mg twice daily for 2 weeks.

**Seldom.** Best medical practice in settings of good resources.

Add ciprofloxacin 500mg b.i.d for underlying intestinal infection together with rehydration and diet as above Step 2.

In HIV infection consider anti-retroviral therapy and where indicated treat cryptosporidium (paromomycin 10mg/kg PO t.i.d for 5 days or azithromycin 500mg daily PO for 5 days).

.....

## *Not recommended therapy*

a. Therapy that is being developed.

Oral gentamicin or cholestyramine.

Bismuth subsalicylate.

Use of Anti-secretory factor to reduce outpouring of fluid from bowel.

b. Poor medical practice which is now obsolete.

Parenteral nutrition which gives slower recovery as well as higher complications.

c. Contra-indicated therapy.

Anti-motility drugs including codeine, diphenoxylate, or loperamide

### References

Black,R.E. Persistent diarrhea in children of developing countries. Pediatric Infect. Dis. J. 1993 12:751-761

Evaluation of an algorithm for the treatment of persistent diarrhoea: a multicentre study. Bull. of WHO 1996. 74:479-489

Persistent diarrhoea Update from CDD at WHO No 4 March 1989

Kelly, P. et al Albendazole chemotherapy for treatment of diarrhoea in patients with AIDS in Zambia: a randomized double blind controlled trial. BMJ 1996. 312:1187-1191

# Staircase Pharmaceuticals

## Chronic heart failure 15.6

*Treat specific causes e.g. anaemia, thyrotoxicosis, hypertension. Stop smoking.*
*There are four known treatments that affect prognosis and symptoms: ACE inhibitors, Angiotensin II type 1 receptor antagonists, oral nitrates plus hydralazine, and ß-blockers. On top of these diuretics and digoxin may improve symptoms.*
*In acute pulmonary oedema combine morphine and a loop diuretic.*

**Always.** Acceptable medical practice that is available at all levels and is cheap (at the level of least resources none of the above four definitive treatments is possible):

Ensure widespread availability of diagnosis and treatment e.g. start with thiazide diuretics such as bendrofluazide10 mg *, followed by loop diuretics such as furosemide 40-80mg daily ; may need to add combination of metolazone** 5-10mg daily and loop diuretics. Digoxin in atrial fibrillation (about 12% of patients with sinus rythmn benefit from digoxin). Start with 250-500µg daily and titrate dose according to response. The above diuretics need potassium supplementation or combination with e.g. amiloride 5-10mg daily, a potassium sparing diuretic.

**Often.** When resources are available increase treatment efficacy by starting with:

loop diuretics, followed by combination of metolazone** and loop diuretics. Next step: hydralazine 25mg b.i.d + isosorbide dinitrate 5-10mg sublingually daily in divided doses if needed. If response is poor may add low-dose ß-blocker e.g. metoprolol 5mg daily initially going up over 7 weeks to 100-150 mg daily.

**Seldom.** Best medical practice in settings of good resources.

ACE inhibitors (e.g. enalapril*** 2.5 mg daily increasing up to 20mg daily in divided doses) often combined with loop diuretics after ACE inhibitors have been stabilized in dose. Add if necessary metolazone** and loop diuretics (see above for other dosages). May add digoxin to ACE inhibitors and loop diuretics if response is poor. If there are significant side-effects with ACE inhibitors, try angiotensin II type 1 receptor antagonists e.g. losartan 50 mg daily.

If response is poor add low-dose ß-blocker e.g. metoprolol 5mg daily initially going up over 7 weeks to 100-150 mg daily. Alt. carvedilol (3.125 mg daily initially going up to 50mg daily over 7 weeks) or bisoprolol (1.25 mg daily initially going up to 10mg daily over 12-15 weeks).

Short-term dobutamine infusion over 48-72 hours can give weeks of improved output.

Cardiac transplantation may be necessary when available as a last resort.

*Thiazides have a flat dose response curve and there is no benefit in going above e.g. 10 mg bendrofluazide and most should after the initial effect be on a lower maintenance dose, e.g. 5 mg. They have less effect in older people and more side-effects.

** Metolazone 5-10mg daily is a very powerful diuretic in combination with loop diuretics, with a long effect. It is often given only 2 or 3 times a week because of the risk of over-diuresis. It is about 3 times the price of a loop diuretic.

***Enalapril is about 6 times the price of a loop diuretic but has a powerful effect on survival.

.....

## *Not recommended therapy*

a. Therapy that is still being developed.

α–Blocker carvedilol with vasodilator and antioxidant effect.

Implantation of artificial heart

b. Poor medical practice which is now obsolete.

Standard long-term digoxin therapy in cardiac failure with sinus rhythm and without monitoring (but note under *Always* above). Over-zealous use of diuretics without monitoring cardiac output.

c. Contra-indicated therapy.

High dose non-selective Beta-blockers (still valuable in Hypertrophic cardiomyopathy and can be used sometimes in low dosage in other cardiomyopathies).

Increasing thiazide dose to try to increase effect (flat dose-response curve).

Use of NSAID's unless unavoidable.

## References

Davies MK et al ABC of heart failure Management: diuretics, ACE inhibitors and nitrates BMJ 2000; 320: 428-431

Gibbs CR et al ABC of heart failure management: digoxin and other inotropes, ß-blockers etc. BMJ 2000; 320: 495-498

Sorretino, M.J. Drug therapy for congestive heart failure. Postgraduate medicine 1997; 101: 83-94

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press.

# Staircase Pharmaceuticals

## Myocardial infarction 15.10.4

*Much smaller problem in many low-income-countries except in the newly affluent segment of society where the incidence may be higher (esp. in Asia) than in developed countries. The most important preventive measures (effect in men > than in women) are to avoid smoking, donate blood regularly, have regular exercise and eat a diet low in saturated fats and high in unsaturated fats with plenty of fruit and vegetables, and increased intake of cereal fibre and fatty fish. These measures are better than the best cholesterol-lowering drugs available. Diagnosis: typical history of crushing central or retrosternal pain often radiating into neck and upper limbs, persisting >20 mins, accompanied by regional ST elevation or new Q-waves appearing on ECG. Doubling in level of CKMB in 3-6 hours after onset. However in older patients symptoms may be minimal, abnormal or absent.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

e.g. aspirin 150-300 mg immediately diagnosis is suspected unless contra-indicated. Atenolol 100mg daily or metoprolol 100mg b.i.d unless contraindicated (first dose i.v. 5 mg if possible and then gradually introduce oral dose). Morphine 5-10 mg i.v. (+cyclizine if needed for nausea) and sublingual trinitrate for pain

**Often.** When resources are available increase treatment efficacy by starting with:

above treament but adding when possible early thrombolysis (within 12 hrs) - i.v. streptokinase 1.5 million unit over 60 mins. once MI diagnosed (alt. in remote practice anistreplase 30 units over 5 mins in single i.v. bolus). Once stable on 1st day add ACE inhibitor lisinopril 5mg within 24 hrs. repeat after 24hrs. then 10mg daily for 6 weeks or captopril 6.25mg daily after 3 days. Gradually increase to 150mg daily in divided doses if needed.

**Seldom.** Best medical practice in settings of good resources.

Treat as above but in younger normotensive patients (<60yrs) with a large infarct in early stages use alteplase 15mg i.v followed by infusion 50mg over 30 mins etc. combined with i.v. heparin 5000 units loading dose etc. as alternative thrombolytic to streptokinase.

Alternative to thrombolytics is Percutaneous Transluminal Coronary Angioplasty (PTCA)

In high risk groups such as diabetes and those in cardiogenic shock, glucose-insulin-potassium (GIK) regime reduces mortality by 30% (see articles below for details of GIK regime).

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## *Not recommended therapy*

a. Therapy that is still being developed.

Alternative ACE inhibitor zofenopril

Acute angioplasty together with intra-aortic balloon therapy in shock

b. Poor medical practice which is now obsolete.

Lignocaine infusion for arrythmia prophylaxis (still useful treatment after VF). If needed consider amiodarone for recurrent ventricular arrythmias.

i.v. Magnesium sulphate, Calcium blocking agents.

c. Contra-indicated therapy.

Aspirin in those with known intolerance, active peptic ulcer or recent GI bleed.

### References

Saltissi, S. Mushahwar, S. The management of acute myocardial infarction. Postgrad Med J 1995 71:534-541

Banerjee A. Improving the early diagnosis of acute myocardial infarction. Postgrad Med J 1996 72:705-708

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press.

Diaz et al The ECLA glucose-insulin-potassium trial. Circulation 1998; 98: 2227-34

Apstein CS. Glucose-insulin-potassium for acute myopcardial infarction. Circulation. 1998; 98: 2223-26

# Staircase Pharmaceuticals

**Hypertension (defn: sustained diastolic > 100 mm on 3 readings each a week apart) 15.27**

*Substitution for, or supplementary to, drug-treatment: stop smoking, reduce alcohol intake, optimize weight, no added salt at table, reduce salt in cooking, increase intake of potassium in fruit and vegetables, increase intake of fish oils (ω–3 fatty acids), relaxation therapy. Aim to start therapy with a single agent. If this is ineffective add a second drug of a different class while maintaining optimal dosage of the first drug. In elderly up to 80 years a systolic over 180 is worthwhile treating even if the diastolic is normal.* ***Aim for 140/85 where the benefit is maximal;*** *especially beneficial in diabetes. Add low-dose 75mg/day aspirin.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Ensure widespread availability of diagnosis and treatment using a staircase approach to antihypertensive therapy: **Level 1** Low-dose thiazide diuretic* e.g. bendrofluazide 2.5mg daily or ß-blocker* e.g. atenolol 25mg PO once daily or propranolol 40mg PO twice daily, **Level 2** Add low-dose reserpine**250µg PO daily, **Level 3** Add hydralazine 25mg PO twice daily, **Level 4** Add calcium blocker e.g. nifedipine 10mg thrice daily PO.

**Often.** When resources are available increase treatment efficacy by:

starting antihypertensive therapy with low-dose thiazide diuretic* or ß-blocker* (less effective in blacks) and adding the two if response is inadequate, or adding calcium blocker to ß-blocker (see above for doses).

**Seldom.** Best medical practice disregarding cost.

Staircase approach adding each additional step as necessary: felodipin ($Ca^+$ blocker) 5mg daily, then add enalapril 5mg daily (ACE inhibitor) (or low-dose β–blocker), then combine all three i.e. $Ca^+$ blocker + ACE inhibitor + β–blocker. If necessary add thiazide diuretic.

When acute reduction of BP is needed (e.g. hypertensive encephalopathy) use oral nifedipine 10mg t.i.d. In diabetic patients use ACE inhibitors early.

*Low-dose thiazide e.g. bendrofluazide 2.5 mg /day is preferred in elderly and in black patients. β–blockers are preferred in younger and in white patients.

** Reserpine should never be the first or only drug. It should always be added to a Level 1. drug. Provided a dose of 0.3 mg/day is not exceeded, depression is not a measurable side-effect.

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## *Not recommended therapy*

a. Therapy that is still being developed.

Behavioural therapy for hypertension

b. Poor medical practice which is now obsolete.

Methyldopa as first line therapy (still of use in pregnancy), or clonidine

c. Contra-indicated therapy.

Thiazide diuretic in non-insulin diabetes and gout, or ß-blocker in asthma, peripheral vascular disease or heart failure. ACE inhibitors in pregnancy.

## References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press.

Mann S. Hypertension in the elderly: assessment and treatment. Patient Management 1990;19:17-26

Hansson L. et al Effects of intensive blood-pressure lowering...HOT randomized trial. Lancet 1998; 351: 1755-1762

## Staircase Pharmaceuticals

### Acute otitis media 17.7.1

*Usual organisms: Various viruses and Strep. pneumoniae, H. influenzae, group A Streptococci. The most common group affected is young children. When good supervision is possible many well-nourished children will not need antibiotics if they can be seen regularly. Give analgesia and possibly decongestant nose drops. In low-income-countries proportion due to bacteria is higher and the possibility of follow-up supervision minimal. Thus it is more appropriate with a more generous antibiotic policy in acute otitis media.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

amoxycillin 20-25mg/kg /day in two divided doses for 3-5 days; 3-10yrs amoxycillin 750mg b.i.d for 2 days.

Alt. cotrimoxazole 480mg tabs: 2-12 months 1/2 tab b.i.d; 12 months-5 yrs. 1 tab b.i.d; above 5yrs 2 tabs b.i.d all for 5 days.

Alt. high dose penicillin V: up to 1yr 125mg b.i.d, 1-5yrs 250mg b.i.d, 6-12 yrs 500mg b.i.d. Five day treatment is acceptable.

In neonates benzyl penicillin 50mg/kg daily in two doses + gentamicin 5mg/kg once daily i.m. Dry wicking of any discharging ear.

**Seldom.** When resources are available use as back-up in treatment failure:

Amoxycillin- clavulanic acid susp. 125mg/31mg per 5ml: <1yr. 0.8 mL/kg daily in 3 divided doses; 1-6yrs 5mL t.i.d; over 7 yrs 10mL t.i.d. all for 5 days.

**Rarely.** In treatment failure of above.

Loracarbef 15mg/kg /day divided in two doses for 5 days.

In neonates ampicillin 25-50mg/kg/day i.v. or i.m. in two divided doses + netilmicin 6mg/kg/day i.v. or i.m. in 2 divided doses for 5 days.

.....

## *Not recommended therapy*

a. Therapy that is technically possible but as yet unproven.

Grepafloxacin

b. Poor medical practice which is now obsolete.

Low-dose penicillin V

c. Contra-indicated therapy.

Tetracycline.

### References

Shapiro AM., Bluestone CD., Otitis Media reassessed. Postgraduate medicine 1995;97:73-82

Management of Childhood Illness. Treat the Child. WHO and UNICEF 1995 WHO/CDR/95.14.D

WHO Division of Diarrhoeal and Acute Respiratory Disease Control. Integrated management of the sick child. Bull World Health Organ. 1995;73:735-40

Glover G.W. Otitis media. Prescriber's Journal 1990; 30: 218-224

## Staircase Pharmaceuticals

### Community-acquired pneumonia in adults 17.7.2

*Usual organisms: Various viruses such as influenza virus, RSV.and bacteria such as Strep. pneumoniae, H. influenzae, Klebsiella spp, Staph.aureus. In younger adults or in family clusters consider Mycoplasma pneumoniae or Legionella spp. In low-income-countries proportion of pneumonia due to bacteria is higher (around 70%) and thus antibiotic therapy is a priority.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
e.g. Cotrimoxazole 480mg 2 tabs b.i.d or doxycycline 200mg stat; then 100mg daily especially if mycoplasma or chlamydia is suspected.

**Often.** When resources are available increase treatment efficacy by using:
amoxicillin 500 mg t.i.d or benzylpenicillin 120mg/kg /day i.v. or i.m. in 3 divided doses for 5-7 days. Add erythromycin 500mg t.i.d PO if legionella, mycoplasma or chlamydia is suspected. Add flucloxacillin 750-1500 mg b.i.d. if pneumonia follows influenza.

**Seldom.** Best medical practice in settings of good resources.
Add in treatment failure or start treatment with second or third generation cephalosporin (cefuroxime 1.5g i.v. t.i.d or cefotaxime 1g b.i.d i.v or i.m.); if legionella or chlamydia or mycoplasma is suspected give clarithromycin 250mg PO b.i.d for 7-10 days (in legionella add rifampicin 600mg daily PO).
Add ciprofloxacin 500mg b.i.d PO if pseudomonas is suspected.

.....

## *Not recommended therapy*

a. Therapy that is still being tested.
   Grepafloxacin
b. Poor medical practice which is now obsolete.
   Tetracycline alone in moderately severe pneumonia
c. Contra-indicated therapy.
   Widespread antibiotic therapy in acute respiratory infection without clinical assessment.

### References

Bartlett, JG., Mundy, LM. Community-Acquired Pneumonia. New Eng. J.Med. 1995; 333: 1618-1624
Cunha, BA. Community-acquired pneumonia. Postgraduate medicine 1996; 99: 109-119
Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

## Staircase Pharmaceuticals

### Community-acquired pneumonia in children beyond neonatal period 17.7.2

*In Integrated Management of Childhood Illness diagnosis is based on the respiratory rate and signs of indrawing. Signs of severe disease: cyanosis and inability to drink. Classified as very severe pn., severe pn. and pneumonia*

*Usual organisms: Strep. pneumoniae, H. influenzae, group A Streptococci, Chlamydia, Staph.aureus*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

In **very severe pneumonia** chloramphenicol 100mg/kg/day in 3 divided doses i.v. or i.m. and change to oral when possible for 7 days total. In **severe pneumonia** benzyl penicillin 100mg/kg/day in 4 divided doses i.v. or i.m. In **pneumonia** cotrimoxazole: 480mg tabs: 2-12 months 1/2 tab b.i.d; 12 months-5 yrs. 1 tab b.i.d; above 5yrs 2 tabs b.i.d all for 5 days; or amoxicillin 20-25mg/kg /day PO in two divided doses for 5 days. Add erythromycin <2yrs 125mg q.i.d; 2-8yrs 250mg q.i.d if atypical pneumonia (e.g. chlamydia) suspected.

**Often.** When resources are available increase treatment efficacy by using:

amoxicillin or benzylpenicillin (see doses above). Add erythromycin (see doses above) if chlamydia is suspected. Add flucloxacillin <2yrs 125mg b.i.d PO; 2-10 yrs. 250mg b.i.d if pneumonia follows measles or influenza.

**Seldom.** Best medical practice in settings of good resources.

Add in treatment failure or start with second or third generation cephalosporin (cefuroxime 60mg/kg/day in 3 divided doses i.v.or i.m. or cefotaxime 100-150mg/kg in 2 divided doses i.v.or i.m.); if legionella or chlamydia or mycoplasma is suspected give clarithromycin <8kg 7.5mg/kg twice daily; 8-11kg 62.5mg twice daily; 12-19kg 125mg twice daily PO (in legionella add rifampicin 15mg/kg/day).

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## *Not recommended therapy*

a. Therapy that is technically possible but as yet unproven.
b. Poor medical practice which is now obsolete.

c. Contra-indicated therapy.

Tetracycline. Widespread antibiotic therapy in acute respiratory infection without clinical assessment and in viral illness.

### References

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 1037-1041 W.B.Saunders. London.
Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
WHO Programme for the control of Acute Respiratory Infections. Management of the young child with an acute respiratory infection: supervisory skills. Geneva: WHO, 1991.
Management of Childhood Illness. Treat the Child. WHO and UNICEF 1995 WHO/CDR/95.14.D
WHO Division of Diarrhoeal and Acute Respiratory Disease Control. Integrated management of the sick child. Bull World Health Organ. 1995;73:735-40

Tuberculosis

## Staircase Pharmaceuticals

### Lung Abscess 17.7.3

*Predisposing causes: inadequately treated pneumonia esp. Staph., Klebsiella or in relation to aspiration, bronchial obstruction, pulmonary infarction, septic emboli, Spread from sub-phrenic or liver abscesses.*

*Usual organisms: Klebsiella, Staph. aureus, Strep milleri, Anaerobic Strep., Pseudomonas, Legionella. Following aspiration: Bacteroides, Prevotella intermedia and other P. species.*

*Postural drainage with vigorous percussion helps in clearing the pus.*

***Take several sputum samples to rule out PTB!***

**Always.** Acceptable medical practice that is available at all levels and is cheap:

High dose benzylpenicillin 2.4g daily in 4 divided doses i.v. or i.m. + chloramphenicol 50mg/kg/day PO in 4 divided doses + metronidazole 800mg stat, then 400mg t.i.d PO.

**Often.** When resources are available increase treatment efficacy by:

adding in treatment failure or starting with cefuroxime 1.5g t.i.d i.v. or i.m. + gentamicin 5mg/kg i.v. once daily + metronidazole (see dose above);.

**Seldom.** Best medical practice in settings of good resources.

Add in treatment failure or start with clindamycin 150-300mg q.i.d PO + cefotaxime 1g every 12 hrs i.m. or i.v.

alt. meropenem 500mg every 8 hrs i.v.

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## *Not recommended therapy*

a. Therapy that is being developed.

Grepafloxacin + metronidazole

b. Poor medical practice which is now obsolete.

c. Contra-indicated therapy.

Tetracycline alone.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 79-80 W.B.Saunders. London.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.

# Staircase Pharmaceuticals

## Asthma in adults (follow with serial peak exp. flow rates) 17.9.1

*Components in asthma attacks are mucosal swelling, increased mucus secretion and bronchial muscle contraction. Avoidance of allergens is difficult but work place could be changed, pets avoided and smoking prohibited. However incidence of asthma higher in very clean environments with clean air even though once asthma is present air pollution is a negative factor.*
*In severe attacks (resp. rate >25/min, pulse >110/min.) combine salbutamol or terbutaline with systemic steroids and oxygen. The steroids need 5 hours to act. Can add ipratropium 4-hourly if available. If anaphylaxis is likely give subcutaneous adrenaline 0.5-1ml of 1/1000 solution.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
First staircase approach: inhaled salbutamol in asthma attack. If > 2 puffs (200µg) are needed per 12 hours add beclamethasone inhaler 200µg b.i.d or budesonide inhaler 200µg b.i.d prophylaxis. In severe exacerbation add short-course oral prednisolone 30-60mg/day as single dose for 3-4 days.

**Often.** When resources are available substitute above when needed by:
Second staircase approach (start with one and add on where necessary): inhaled salbutamol 2 puffs (200µg) in attacks, + beclamethasone inhaler 200µg b.i.d (as preventive)+ ipratropium inhaler 40µg t.i.d (in attacks) + oral short-course prednisolone as back-up in acute exacerbation (see above for other doses).

**Seldom.** Best medical practice in settings of good resources.
Third staircase approach (where needed): salmeterol diskhaler 50µg b.i.d as **bronchodilator** (if necessary with terbutaline inhaler 250µg as back-up in exacerbation); inhaled steroid fluticasone diskhaler 100µg b.i.d (+- sodium cromoglycate inhaler 20mg q.i.d or nedocromil sodium 4mg q.i.d) as **preventive**, ipratropium or oxitropium 200µg b.i.d as **anticholinergic** the latter two given by nebulizer, oral prednisolone as **back-up in status asthmaticus.** (see above for other doses)

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## *Not recommended therapy*

a. Therapy that is still being developed.

Desentization, leukotriene receptor antagonists, methotrexate or cyclosporin or other immune modulators, frusemide inhalation as prophylactic, i.v. immunoglobulin, nitric oxide inhalation, antioxidants.

b. Poor medical practice which is now obsolete.

Salbutamol by mouth, continuous inhalations with short-acting β–2–stimulants, early continuous oral prednisolone for mild asthma, oral theophylline.

c. Contra-indicated therapy.

Avoid β-blockers (except in special circumstances in minimum dosage). Caution with NSAIDs and Aspirin. Alternatives are paracetamol and trilisate.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Ariyananda, P. et al. Aerosol delivery systems for bronchial asthma. Postgrad.Med.J 1996; 72:151-6
Calverley, PMA. Asthma. Postgrad. Med.J. 1995; 72:12-18
Fricker,J. Salmeterol efficacy against exercise-induced asthma. Lancet 1997; 349:1453
Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. OUP. Oxford.
Report from The Swedish Council on Technology in Health Care. 2000 Treatment of Asthma and Chronic Obstructive Pulmonary Disease. report No. 151

## Staircase Pharmaceuticals

### Chronic obstructive pulmonary disease 17.9.4

*Defn.: largely irreversible intrathoracic small airways obstructive disease and includes chronic bronchitis (sputum production on most days for 3 months of 2 successive years), emphysema and chronic incompletely reversible asthma. Mainly amongst smokers and ex-smokers but also after heavy air pollution including industrial pollution and indoor pollution from cooking over open fires. In some linked to specific disease such as $\alpha_1$ -Antitrypsin deficiency.*

***Main advice: stop smoking; remove sources of air pollution by better stoves and cleaner industries.***

**Always.** Acceptable medical practice that is available at all levels and is cheap:

In exacerbation use of bronchodilater, salbutamol inhaler 2 puffs (200μg) every 4 hours and trial of 2-3 weeks of prednisolone (30-40 mg/day) PO to see response. In those who respond to steroids consider continuing with inhaled steroids (see under asthma). In acute exacerbations usual organism H.influenzae and use antibiotics (amoxycillin 500 mg t.i.d), inhaled salbutamol, oral prednisolone, possibly mucolytic drugs in chronic bronchitis.

**Often.** When resources are available supplement above when needed by:

adding ipratropium inhaler 40μg t.i.d which is as effective as salbutamol..

**Seldom.** Best medical practice in settings of good resources.

Immunization against pneumococcus and influenza virus. Trial of continuous salmeterol diskhaler 50μg b.i.d as **bronchodilator** and ipratropium by inhaler but iof no response, abandon. When $PaO_2$ is less than 7.3 kPa in the long-term stable state consider long-term oxygen treatment except in blue bloaters who need their hypoxic drive to maintain respiratory effort. Consider venesection when haematocrit over 0.55. Special nutrition support in severe loss of weight. Physiotherapy to improve breathing technique and exercise performance. Some benefit from CPAP at night. Lung transplantation when medical therapy has failed. Possible value of volume-reducing lung surgery in severe COPD with emphysema.

.....

## *Not recommended therapy*

a. Therapy that is technically possible but as yet unproven.

b. Poor medical practice which is now obsolete.

The majority of cough mixtures are without effect. Possibly mucolytic drugs are useful in COPD with chronic bronchitis

c. Contra-indicated therapy.

β-Blocker drugs. Generally avoid sedative drugs and specifically morphine. Continued exposure to smoking or air pollution

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford

Report from The Swedish Council on Technology in Health Care. 2000 Treatment of Asthma and Chronic Obstructive Pulmonary Disease. report No. 151

# Staircase Pharmaceuticals

## Rheumatoid arthritis 18.4

*Diagnosis based on at least 4 ot the 7 following criteria: morning stiffness at least 1 hour, swelling of at least 3 joints, swelling of the wrist, m-p or proximal i-p joints, symmetrical swelling, typical Xray changes in the hand-joints, subcutaneous nodules, positive RA-factor. The first 4 of these must have been present for at least 6 weeks*

*In all cases arrange physiotherapy and occupational therapy as well as help with suitable household and work implements. Consider intra-articular steroids when indicated and even surgery to improve joint function.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Start with NSAID e.g. ibuprofen 400-800mg PO x 3. If no improvement after 6 months start disease modifying drug such as chloroquine phosphate up to 4 mg/kg/day PO.

**Often.** When resources are available substitute above when needed by:

starting with NSAID e.g. naproxen 250-500 mg/12 hrs PO. If no improvement after 6 months start disease modifying drug such as sulphasalazine 2 gms daily PO. Alt chloroquine as above

**Seldom.** Best medical practice in settings of good resources.

**( i) Older Régime:** start with NSAID e.g. diclofenac 25-50 mg/8h PO combined with misoprostol 200µg t.i.d PO (for ulcer protection). If no improvement after 6 months start disease modifying drug such as sulphasalazine (2gms/day) PO or low-dose methotrexate (7.5 weekly) PO.

**(ii) Standard new régime:** start immediately diagnosis is assured with sulphasalazine 500 mg/day PO going up to 2 gms/day over 3 weeks. Alt. methotrexate 7.5 mg. weekly. Supplement this with NSAIDs as above where necessary and even low-dose prednisolone 7.5 mg/day

**(iii) New intense régime:** start with prednisolone in successive weeks with daily oral dosage of: 60mg, 40mg, 25mg, 20mg, 15mg, 10mg, and 7.5mg until week 28 and then taper over 7 weeks and stop. Give concurrently methotrexate 7.5 mg weekly for 40 weeks and then taper over 6 weeks and stop. Give also concurrently sulphasalazine as in (ii) above and continue at the higher dose indefinitely.

.....

## *Not recommended therapy*

**a. New Therapy** that is still being tested.

Long-term anti-bacterial therapy in early RA trying to eliminate the immune modulating effects of e.g. Mycoplasma arthritidis using doxycycline, minocycline or erthyomycin.

Total lymphoid irradiation, lymphoplasmapheresis, or bone marrow transplantation with autologous cells administered after cytotoxic therapy.

Monoclonal antibodies to T cells and T-cell subsets.

Substitution of dietary ω-6-essential fatty acids with ω-3-fatty acids such as eicosapentaenoic acid (3g daily) found in some fish oils and docosahexaenoic acid (2g daily).

**b. Poor medical practice** which is now obsolete.

Early high dose steroids before disease modifying drugs have been adequately tried. Long-term high dose aspirin when associated with significant side-effects.

**c. Contra-indicated therapy.**

NSAID (with the exception of Arthrotec) in someone with a risk for developing peptic ulcers.

## References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press.

Harrison's Principles of Internal Medicine. Isselbacher et al 1994. 13th Ed. Mcgraw-Hill Inc. N.Y.

Boers M. et al Randomized comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone in early rheumatoid arthritis. Lancet 1997. 350:309-318

# Staircase Pharmaceuticals

## Osteoarthritis 18.6

*Characteristics: joint pain, tenderness, limitation of movement, crepitus, occasional effusion and variable degrees of inflammation without systemic effects. There are no disease modifying drugs.*Start with Patient education, physical and occupational therapy, weight reduction, exercise, assistive devices.

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Paracetamol up to 1g every 4-6hrs. PO, thereafter if necessary add ibuprofen 200-400mg x 3 PO. If this is not enough add naproxen 250-mg/12 hrs PO. Can add local NSAID or local capsaicin.

**Often.** When resources are available substitute above when needed by:

using diclofenac 25-50 mg/8h PO combined with misoprostol 200µg t.i.d PO (for ulcer protection) if stronger NSAID needed. Intra-articular steroid (triamcinolone hexacetonide) or hyaluronic acid when needed.

Intra-articular lavage with normal saline.

**Seldom.** Best medical practice in settings of good resources.

As above but consider replacement of joint if symptomatic relief is inadequate and disability is significant.

.....

## *Not recommended therapy*

a. New Therapy that is still being tested.

Selective cyclooxygenase-2 inhibitors to provide safer NSAIDs.

Use of chemically modified tetracyclines and other metalloproteinase inhibitors.

IL-1 receptor antagonists.

Autologous cartilage transplantation

b. Poor medical practice which is now obsolete.

Early high dose NSAIDs.

Use of analgesics and anti-inflammatory when pain is absent.

Use of indomethacin in therapy because of greater comparative toxicity

c. Contra-indicated therapy.

NSAID (with the exception of Arthrotec) in someone with a risk for developing peptic ulcers.

### References

Creamer P. and Hochberg M.C. Osteoarthritis. Lancet. 1997 350:503-508

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press.

# Staircase Pharmaceuticals

## Gout 18.7

*Deposition of monosodium urate monohydrate into joints causing acute and/or chronic arthritis of 1st metatarsal joint or ankle, knee, small hand joints, wrist or elbow associated with high serum urate levels. Men:Women=10:1 esp under 65 years. Some ethnic groups more at risk: Polynesians, Maoris Associated with alcohol, dietary excess, hypertension, diuretic therapy (esp. thiazides)*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

In acute attack treat with indomethacin 50 mg/4hourly PO or colchicine 1 mg stat PO then 0.5 mg every 6 hours until relief. However latter often causes diarrhoea and abdo cramps. Can get quick relief with aspiration of joint or intra-articular steroids.

Long term: reduce alcohol, stop thiazides, give allopurinol (start with 100-300 mg PO daily) until serum urate is normal. Never start within 72 hours of acute attack and then under indomethacin cover for 4-6 weeks. Otherwise start with small dose e.g. 50 mg daily and slowly increase. For those who cannot tolerate allopurinol and have no renal problems can give uricosuric agents instead e.g. probenecid 0.5-1gm PO twice daily with high fluid intake and alkalinization of urine in early weeks of treatment.

**Often.** When resources are available substitute above when needed by:

choosing naproxen 250-500 mg/12 hrs PO for those who have side-effects from indomethacin.

**Seldom.** Best medical practice in settings of good resources.

As above but substitute uricosuric NSAID e.g. azapropazone 1.8gms PO daily in divided doses in acute gout; then when acute symptoms subside, 1.2g daily in divided doses until symptoms resolved for those who cannot tolerate allopurinol.

.....

## *Not recommended therapy*

a. Therapy that is currently being tested.

b. Poor medical practice which is now obsolete.

Starting allopurinol early in acute gout attack

c. Contra-indicated therapy.

Uricosurics in those with renal impairment, urolithiasis or gross overproduction of uric acid.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press.

Emmerson, B.T. The clinical role of allopurinol. Australian prescriber 1992; 15:77-79

# Staircase Pharmaceuticals

## Urinary tract infection 20.8.1

*UTI is the commonest bacterial infection seen in general practice. 80% are due to E. coli. Only two organisms have the capacity for causing UTI without predisposing factors within the urinary tract i.e. they can act as primary pathogens namely E. coli and Staph. saprophyticus. There is a vast difference in treating* ***uncomplicated*** *lower UTI in women and girls and dealing with* ***complicated*** *UTI: in boys and men, those with abnormal urinary tract, diabetics, those with impaired defences or obstruction and those with upper UTI.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

**Uncomplicated lower UTI:** single oral dose cotrimoxazole (1.92g) or trimethoprim (600mg) or three da course of cotrim. (960mg 12 hrly) or trimethoprim (300mg 12 hrly).

**Complicated or upper UTI:** if serious at least 5 days treatment with gentamicin 6mg/kg (under 10yrs 7.5mg/kg) once daily i.m. or i.v. Alt. cotrimoxazole 960mg PO 12 hrly for 7-14 days depending on situation.

**Often.** When resources are available substitute above when needed by:

choosing pivmecillinam 200mg PO x 3 for 3 days for uncomplicated lower UTI, Alt. nitrofurantoin 50-100mg PO x 4 or nalidixic acid 1g PO x 3 for 3 days.

Complicated or upper UTI: norfloxacin 400mg PO 12 hrly

**Seldom.** Best medical practice in settings of good resources.

Complicated and/or upper UTI substitute tobramycin 3mg/kg i.m. as single daily dose or netilmicin 3-5mg/kg i.m. or i.v. as single daily dose or ciprofloxacin 500mg PO x 2 for at least 5 days. Alt. cefuroxir 750mg x 3 i.v. or cefotaxime 1g 12 hrly i.v. Alt. ceftibuten 400mg PO once daily for 5 days.

.....

## *Not recommended therapy*

a. New Therapy that is still being tested.

Drinking of cranberry juice as a prophylactic in repeated UTI.

b. Poor medical practice which is now obsolete.

Prolonged treatment of uncomplicated UTI with antibiotics. Widespread use of quinolones when equivalent substitutes are available because of ecological effects of quinolones which do not break dow in nature.

c. Contra-indicated therapy.

Long-term prophylactic antibiotics for catheter bearers. This merely guarantees antibiotic resistant strains.

### References

Orenstein R. Wong ES. Urinary tract infections in adults. Am Fam Physician 1999 59: 1225-34

Barnett BJ. Stephens DS. Urinary tract infection: an overview. Am J Med Sci 1997, 314: 245-9

Nicolle LE. A practical guide to the management of complicated urinary tract infection. Drugs. 1997, 53: 583-92

Coley AL. Todd MW. Harrington P. Treatment of serious urinary tract infections at a teaching hospital: a retrospective chart review. Hosp Formul 1990, 25: 548-52

Ferry S. Burman LG. Antibiotikaval vid UVI - pendeln svänger tillbaka. Läkartidningen. 1999, 96: 4216-9

Warren JW. Clinical advances in urinary tract infections. Curr Opin in Infect Dis. 1995, 8: 43-8

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press.

Oxford Handbook of Tropical Medicine.Eddelsten M. and Pierini S. 1999. 1st Edition. OUP

# Staircase Pharmaceuticals

## Epilepsy in adults 24.4.1

*Three main types: tonic-clonic seizures (grand mal), typical absences (petit mal) and partial seizures (focal) including temporal lobe and psychomotor seizures.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Phenobarbitone* (60-180mg PO at night - child 5-8mg/kg daily) as prophylaxis against grand mal seizures, Alt. phenytoin**(100mg PO every 6-8hrs). Diazepam 10-20mg by slow i.v. route or rectally 10-30 mg. Child 1mg per yr. of age i.v. or rectally: child 1-3 yrs 5mg. Paraldehyde 0.1ml/kg by deep i.m. injection for status epilepticus (paraldehyde esp for focal seizures). Phenytoin** or carbamazepine (start with 100-200mg PO 1-2 times daily) as prophylaxis against partial seizures.

**Often.** When resources are available substitute above when needed by:

carbamazepine (start with 100-200mg PO 1-2 times daily) as prophylaxis against partial and grand mal seizures. Alt. phenytoin** (100mg PO every 6-8hrs)

**Seldom.** Best medical practice in settings of good resources.

Sodium valproate: start with 600mg PO daily in 2 divided doses as first choice for grand mal prophylaxis and even for absences and myoclonus, carbamazepine for partial seizures. Alt. prophylaxis against grand mal seizures phenytoin.

For an average dose required for an adult: sodium valproate is 2.5 times the price of carbamazepine which is double the price of phenytoin which is double the price of phenobarbitone.

* phenobarb may cause depression and confusion in older people and excitability in children

** the dose of phenytoin is very variable and where serum levels cannot be measured, use a normogram to approximate the best dose. Once saturation level is reached a small increase in dose causes a large increase in serum level.

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## *Not recommended therapy*

a. New Therapy that is still being tested.

e.g. Vigabatrin, lamotrigine, gabapentin as additional drugs in prophylaxis for partial seizures.

The implanted NeuroCybernetic prosthesis to act as a pace-maker for the brain in patients with refractory partial seizures. These can be activated by the patient when an aura indicates that a seizure is impending.

b. Poor medical practice which is now obsolete.

e.g. Early prophylaxis with multiple drugs (at least two seizures before considering prophylaxis).

N.B. Distinguish febrile convulsions in children from true epilepsy.

c. Contra-indicated therapy.

e.g. Driving, working with machinery, working near fire or water unless good control of seizures is guaranteed. Isolation of patients. Rapid withdrawal of anti-convulsants.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. OUP. Oxford.

FDA approves first-ever epilepsy device. Lancet. 1997. 350:268

# Staircase Pharmaceuticals

## Stroke 24.6

*This is a major cause of ill-health in all communities with a significant older population. Hypertension is the strongest and most treatable risk factor. Others are smoking, diabetes, and high intake of saturated fatty acids. Black people are especially at risk of stroke in uncontrolled hypertension. In a population reducing salt intake by 50 mmol/L might reduce strokes by 22%.*

*Cause: 85% are thrombo-embolic, 5% are due to subarachnoid haemorrhage10% due to intracranial haemorrhage.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Prevention is the most important intervention by treating adequately hypertension (see separate page), reducing or eliminating smoking, reducing salt intake and treating all who have had a TIA* attack with continuous aspirin 75mg/day PO and control of hypertension if present.

After stroke: try to diffentiate between thromboembolic and intra-cranial haemorrhage. Suggesting haemorrhage: early loss of consciousness, early vomiting, bilateral extensor plantars, marked elevation of BP . **Start non-haemorrhage patients on aspirin 300 mg/day.** Aim to build up a network of carers who will supervize home-based-care of stroke patients. Aim for early discharge as soon as clinical situation is stable. Home physiotherapy is the best option carried out by carers after training with CBR** methods. Gentle reduction of BP in hypertensives if diastolic >130mm but do not lower to less than 110mm in the first 48 hours. If atrial fibrillation present consider warfarin to prevent new emboli. Rule out syphilis.

**Often.** When resources are available consider adding:

if conscious level is impaired treat cerebral oedema with glycerol 10% 500ml i.v. infused over 4 hours daily for 6 days.

**Seldom.** Best medical practice in settings of good resources.

As above but use CT to differentiate between thromboembolic and intracranial haemorrhage, and then when appropriate using aspirin as above. Consider endarterectomy for carotid stenosis, heparin/warfarin for emboli from heart. Small doses of amitriptyline in depression or excessive emotionalism.

*TIA Transient Ischemic Attack: focal CNS disturbance with e.g. some weakness or numbness, tingling or visual changes which resolves completely within 24 hours.

**CBR Community-based rehabilitation based on developing community responses to disability (WHO).

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## *Not recommended therapy*

a. Therapy that is currently being tested.

Oxpentifylline and vinpocetine

b. Poor medical practice which is now obsolete.

Rapid reduction of BP in hypertensives after stroke

c. Contra-indicated therapy.

Therapy with streptokinase or recombitant tissue plasminogen activator

## References

Internat. Stroke Trial Collab. Group IST: a randomized trial of aspirin etc Lancet 1997 349: 1569-1581

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press.

Humphrey,P.R.D. Management of transient ischaemic attacks and stroke. Postgraduate Med J 1995; 71:577-584

Bath,P.M.W. Treating acute ischaemic stroke. BMJ 1995 311:139-140

## Staircase Pharmaceuticals

### Bacterial meningitis after neonatal period 24.15.1

*Typical CSF picture: turbid fluid, high WBC with polymorphs, low glucose, high protein. Gram staining shows the organisms in 50-80% of cases.*

*Usual organisms: Children under 10 yrs. H.influenzae, meningococcus, pneumococcus; over 10 meningococcus, pneumococcus, H.influenzae, Staph. aureus, pseudomonas, Listeria in elderly or immunocompromized*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Initial therapy: short-course high dose steroid dexamethasone 0.4mg/kg i.v. 12 hrly for 2 days starting 10mins prior to antibiotic followed by chloramphenicol 1g 6hrly i.v. or even better combine with ampicillin 2g 4-6hrly i.v. with back-up in antibiotic failure of rifampicin 10-20mg/kg PO or NG tube up to max 900mg daily (especially for its anti-Staph.effect). N.B. If TBM is even remotely suspected never give TB monotherapy.

**Often.** When resources are available consider substituting as follows:

steroids as above followed by i.v. high dose cefuroxime 200mg/kg/day in 3 divided doses i.v. (in adults 3g every 8 hrs i.v.) + ampicillin 200mg/kg/day in 4 divided doses i.v. if Listeria possible.

**Seldom.** Best medical practice in settings of good resources.

Steroids as above followed by i.v. cefotaxime 200mg/kg/day in 4 divided doses i.v. (adults 2g i.v. 4hrly) or ceftriaxone 100mg/kg/day in single dose i.v. (adults 2g i.v. 12 hrly) or cefuroxime + ampicillin (see above for doses).

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## *Not recommended therapy*

a. Therapy that is still being tested.

Endotoxin antibody therapy as adjuvant to antibiotics

b. Poor medical practice which is now obsolete.

Single treatment with crystalline penicillin unless meningococcus certain

c. Contra-indicated therapy.

Tetracycline.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 875-885 W.B.Saunders. London.
Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.

## Staircase Pharmaceuticals

### Cerebral Abscess 24.15.4

*Predisposing causes: ear, sinus, dental or periodontal infections, skull fracture and focal osteomyelitis of the skull, congenital heart disease, sub-acute bacterial endocarditis, bronchiectasis.*

***Need, if possible, urgent neurosurgical assessment and where available surgical drainage***

*Usual organisms: Staph. aureus, Strep milleri, Anaerobic Strep., Pseudomonas, Bacteroides, Actinomyces, Proteus.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

High dose benzylpenicillin 2.4g i.v. 4hrly + chloramphenicol 1g 6 hrly i.v. + metronidazole 800mg t.i.d. PO if possible. Cloxacillin 2g i.v. t.i.d if Staph. is suspected.

**Often.** When resources are available consider substituting as follows:

Cloxacillin and rifampicin 10-20mg/kg PO or NG tube up to max 900mg daily if Staph. is suspected and TB is ruled out since in TB, monotherapy with rifampicin is contra-indicated.

**Seldom.** Best medical practice in settings of good resources.

Neurosurgical assessment and treatment. Cefotaxime 200mg/kg/day in 4 divided doses i.v. (adults 2g i.v. 4hrly) + metronidazole 800mg t.i.d. PO if possible. Nafcillin 1g every 4hrs i.v. or i.m. if Staph. suspected (e.g. endocarditis, trauma).

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## *Not recommended therapy*

a. Therapy that is technically possible but as yet unproven.

b. Poor medical practice which is now obsolete.

e.g. Tetracycline.

c. Contra-indicated therapy.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Manson's Tropical Diseases. Cook G.C. 1996. 20th Edition. 881 W.B.Saunders. London.

Oxford Handbook of Clinical Medicine. Hope, RA. et al. 1996. 3rd Edition. Oxford University Press. Oxford.

# Staircase Pharmaceuticals

## Depression 27.2.8

*Central features: low mood, reduced energy and activities, loss of enjoyment*

*Biological features: early morning wakening, diurnal mood variation, loss of appetite and weight, complaints about constipation, loss of libido, amenorrhoea*

*Cognitive features: pessimistic thoughts and feeling hopeless, guilty recollections, suicidal ideas*

*Structured problem solving treatment has recently been shown to be as effective as drug therapy.*

*In all drug treatment a delay of around two weeks before any improvement is the norm.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Tricyclic antidepressants e.g. amiptriptyline 75mg PO at bed time gradually increasing dose as needed or imipramine 75mg daily in divided doses/clomipramine 10mg PO daily starting dose increasing to 30-150mg daily in divided doses (less sedating) linked with **good social support from family and the community.** ECT if rapid effect needed.

Nurse based structured problem solving treatment without drug therapy may be a good alternative.

**Often.** When resources are available consider substituting as follows:

Dothiepin 75mg PO daily in divided doses or as single dose at bedtime or lofepramine 140-210mg PO daily in divided doses (esp. if suicidal) linked with **good social support from family and the community.** ECT if rapid effect needed.

**Seldom.** Best medical practice in settings of good resources.

Selective serotonin uptake antagonists e.g. fluoxetine 20mg PO daily or sertraline 50mg PO daily or fluvoxamine 100mg PO daily or paroxetine 20mg PO each morning or citalopram 20mg PO daily linked with **good social support from family and the community.** Alt. serotonin-noradrenaline reuptake inhibitor: mianserin 30-40mg PO daily in divided doses. In bipolar depression/mania lithium of value. ECT if deep depression where rapid effect needed.

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## *Not recommended therapy*

a. Therapy that is being tested at present.

Behavioural therapy

Reboxetine, a selective norepinephrine reuptake inhibitor is being tested at present with favourable results.

b. Poor medical practice which is now obsolete.

Monoamine oxidase inhibitors without careful monitoring.

c. Contra-indicated therapy.

Older tricyclics in patients with cardiac arrhythmias especially with tendency to heart block. Prescribing large quantities of tricyclics to patients with suicidal risk.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Textbook of Psychiatry. Gelder M. et al. 1989. 2nd Ed. Oxford University Press. Oxford.

First reboxetine trial results reported. Lancet. 1997. 350:36

Mynors-Wallis LM et al RCT of problem solving treatment, antidepresssive medication etc. BMJ 2000; 320: 26-30

## Staircase Pharmaceuticals

### Mania 27.2.8

***Principal features:*** *elevated mood, increased energy and activity, expansive ideas, impaired insight, reduced sleep, increased appetite, increased libido*

**Always.** Acceptable medical practice that is available at all levels and is cheap:
Haloperidol 1.5-3mg PO 2-3 times daily (preferred) or chlorpromazine 25mg PO 3 times daily as starting dose. ECT in selected cases.

**Often.** When resources are available consider substituting as follows:
in treatment failure carbamazepine (start with 200mg PO 2 times daily) for mood stabilizing effect.

**Seldom.** Best medical practice in settings of good resources.
Early treatment: haloperidol , carbamazepine in failure. Valproic acid start with 250mg t.i.d PO as alternative. After more than one episode: lithium carbonate with careful monitoring for long-term control. ECT in selected cases. In those who cannot tolerate lithium, carbamazepine (300-600 mg PO daily in divided doses) as mood stabilizer

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## *Not recommended therapy*

a. Therapy that is technically possible but as yet unproven.
Propranolol added to haloperidol in treatment failure. Zoclopentixol.

b. Poor medical practice which is now obsolete.
Physical restraint once effective treatment has been established.

c. Contra-indicated therapy.
Lithium without careful monitoring

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.
Oxford Textbook of Psychiatry. Gelder M. et al. 1989. 2nd Ed. Oxford University Press. Oxford.

## Staircase Pharmaceuticals

### Schizophrenia 27.2.9

*Two syndromes are common: an acute syndrome with delusions, hallucinations, and disordered thinking (positive symptoms) and a chronic syndrome with apathy, slowness, and social withdrawal (negative symptoms).*

*First rank symptoms: Hearing thoughts spoken aloud, "third person" hallucination, somatic hallucinations, thought withdrawal or insertion, thought broadcasting, delusional perception, feelings or actions experienced as made or influenced by others.*

**Always.** Acceptable medical practice that is available at all levels and is cheap:

Chlorpromazine 25mg PO 3 times daily as starting dose (sedating), or trifluperazine 5mg PO b.i.d starting dose (less sedating), or haloperidol 1.5-3mg PO 2-3 times daily , linked with good social support from family and the community. Antimuscarinic drugs may be needed e.g. benzhexol 1mg PO daily starting dose if extrapyramidal side effects are significant (more common where higher doses are used. More common in trifluperazine than chlorpromazine).

**Often.** When resources are available consider substituting as follows:

Depot injection of fluphenazine decanoate 12.5mg by deep i.m. injection starting dose. Repeat after 14-35 days;

or flupenthixol decanoate 20-40mg every 2-4 weeks linked with good social support from family and the community. Antimuscarinic drugs may be needed if extrapyramidal side effects are significant.

**Seldom.** Best medical practice in settings of good resources.

In treatment failure consider use of risperidone 2mg PO daily in 1-2 divided doses starting dose then gradually increase to average 4-8mg daily, linked with good social support from family and the community.

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## *Not recommended therapy*

a. Therapy that is technically possible but as yet unproven.

Behavioural therapy

b. Poor medical practice which is now obsolete.

Frontal lobotomy, routine addition of anticholinergics to all patients on neuroleptics, electroconvulsive therapy apart from specific indications: catatonia and depression.

c. Contra-indicated therapy.

Isolation of patients apart from short periods when violent patients are being stabilized on therapy.

### References

Oxford Textbook of Medicine. Weatherall et al. 1996. 3rd Edition. Oxford University Press. Oxford.

Oxford Textbook of Psychiatry. Gelder M. et al. 1989. 2nd Ed. Oxford University Press. Oxford.