

STOPPING SMOKING

Just recently there have been a number of superb articles on smoking from both sides of the Atlantic - the 'Human cost of tobacco' series in the New England Journal [1,2], and Doll, Peto and colleagues reporting of the 40-year follow up on British doctors [3], and associated commentaries [4,5]. *Bandolier* wanted to know the most effective way to stop current smokers from smoking, and this focus article centres on that issue.

The human cost of a cigarette

The human costs of using tobacco use are charted in admirable starkness by Robert Schrier and his colleagues from Colorado, prompted because the prevalence of smoking in the US has plateaued at 26% after two decades of decline. Their two reviews, containing 114 references mainly to the US literature, chart the health and economic costs.

Most people, especially health professionals, think they know the risks associated with tobacco smoking. Reading the first of these articles [1] and the report on mortality of British doctors [3], is likely to make all except the most expert think again.

These reports are not 'mindstretchers', but mindblowers. The way in which tobacco use constitutes the single largest

threat to the health of the nation has been consistently understated - the more studies are performed, the greater are the number of diseases where tobacco use makes an impact.

If cigarettes cost more, then fewer people will smoke them, especially women and members of the lowest socio-economic groups where smoking prevalence is still as high as 50% [6]. Reduce prices, as happened in the UK between 1977 and 1979, and smoking goes up; increase prices, as has generally been the case since the early '80s, and smoking falls. The commitment of government to steadily increase the tax on cigarettes year-by-year should have an impact.

The economic cost of a cigarette

In the US it has been estimated that the average lifetime medical costs for a smoker are \$6,000 greater than those for a non-smoker. The Congressional Office of Technology Assessment has estimated that the total financial cost of smoking to society in 1990 was \$2.59 per pack of cigarettes (about £1.70 per packet at current exchange rates). There are numerous ways in which the economic costs of smoking and smoking-related diseases can be calculated, but whichever way it is calculated, all the numbers are big.

Other big numbers are seen in tobacco company profits - Philip Morris made more money in 1992 than any other US industrial corporation - \$4,900,000,000. (Ironically some tobacco companies have diversified into insurance, which have higher charges for smokers than non-smokers.) Another large number is that of tobacco company spending on advertising - \$2,000,000,000 a year by Philip Morris alone.

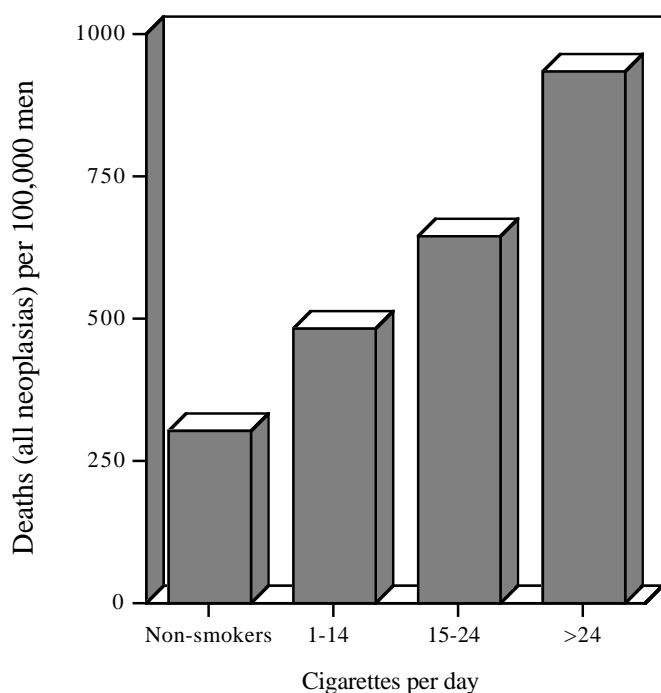
Tobacco advertising isn't Mickey Mouse!

When TV advertising of cigarettes was stopped in the US, the advertising revenue of magazines went up by an average of \$5.5 million a year, and smoking actually increased.

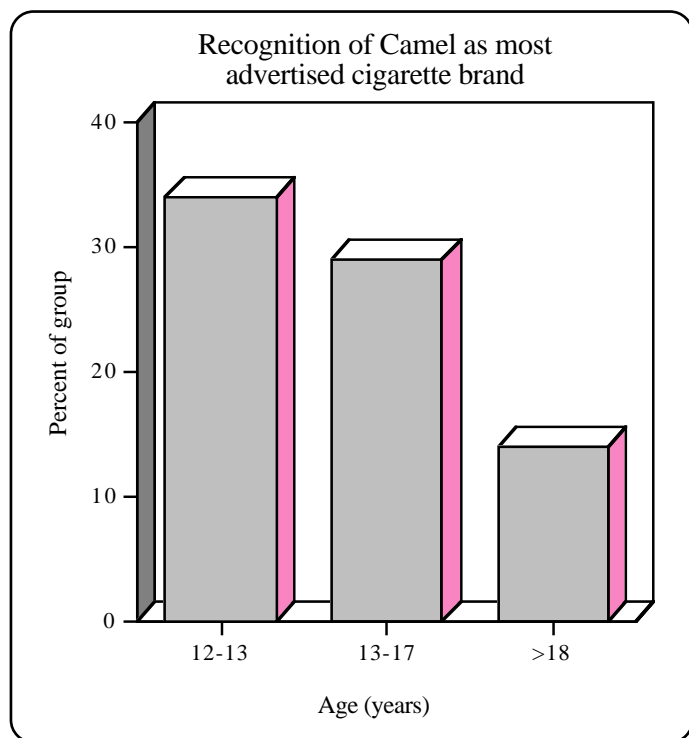
Buying sponsorship for sport is also very effective. During the 1989 broadcast of the Marlboro Grand Prix, lasting 93 minutes, the Marlboro name was mentioned 11 times and the logo shown a staggering 5,922 times, for a total of 46 minutes of exposure of which 18 minutes was "clear, in-focus air time".

The most chilling evidence of effectiveness of tobacco advertising relates to children recognising tobacco symbols. An RJR Nabisco campaign in 1988 featured a character, possibly modelled on James Bond, called Old Joe Camel. Three years into the campaign, Camel was recognised much more by children than adults as the most frequently adver-

Cancer deaths and cigarette smoking



tised brand. Over 30% of 3-year olds and over 80% of 6-year olds were able to associate a picture of Old Joe Camel with a packet of cigarettes - for 6-year olds about the same number who were able to associate the Disney logo with Mickey Mouse!



Campaigns to prevent tobacco use

The second of the NEJM articles [2] has a plethora of interesting facts on economics, advertising and issues relating to preventing tobacco use. Though these are directed at the US, most issues relating to reducing tobacco use are relevant, including:-

- increased taxation.
- comprehensive smoking bans.
- advertising and sponsorship bans.
- restricting sales to children.
- financial support for counter-advertising.
- community education programmes.

How to help the smoker

All of these issues are important parts of strategies to prevent smoking in populations. What about the individual smoker - what can be offered by healthcare professionals to help in giving up smoking, and what is effective?

Nicotine replacement therapy (NRT)

Nicotine replacement therapy is based on the idea that replacing nicotine in the body allows smoking behaviour to be stopped. A gradual weaning of the subject from nicotine follows without the pharmacological sequelae.

There have been three meta-analyses of nicotine replacement therapy published this year, looking mainly at nicotine chewing gum and nicotine patches [7-9]. Though slightly different in the range of studies included and meth-

ods used, they all had the same conclusion - that NRT is significant in helping smokers stop smoking.

Tang et al [7] analysed 28 randomised trials of 2 mg nicotine gum, six trials of 4 mg nicotine gum and six trials of transdermal patch. They used as a main outcome measure the difference between percent of control and NRT-treated patients who had stopped smoking at one year. The results showed that 2 mg nicotine chewing gum helped an extra 6% of smokers quit over controls, but this was as high as 11% in self-referred subjects and as low as 3% in invited subjects, suggesting that the desire to quit was essential.

When examined by dependency and whether patients were self referred or invited, the results showed that nicotine gum was helpful in highly dependent subjects.

Effects of NRT by degree of nicotine dependence		
<i>High Dependency</i>		
Group	No (%) who quit Gum	Control
Self referred	51/90 (57)	53/155 (34)
Invited	53/210 (25)	33/180 (18)
<i>Low Dependency</i>		
Group	No (%) who quit Gum	Control
Self referred	32/61 (52)	20/38 (53)
Invited	65/258 (25)	51/229 (22)

The meta-analysis by Silagy et al [8] examined 53 trials, 42 with gum, nine with patch, one with intranasal spray and one with inhaler. The results were generally similar, though expressed differently. The odds ratios for abstinence were increased with use of NRT, but differently for different forms. This report also looked at the numbers needed to be treated (NNT) to obtain one extra non-smoker at 12 months beyond the number who would achieve that with the control intervention: results are shown on the top of page 3.

The nicotine patch was the particular focus of the third meta-analysis [9]. Here 17 studies were identified, with nearly 5100 subjects. At six months 22% treated with patch had stopped smoking compared with 9% for placebo. The patch type (24 vs. 16 hours), patch treatment duration (more or less than 8 weeks), weaning, nor counselling format or intensity made no difference to result. There was some evidence that intensive behavioural counselling had a modest effect on increasing rates of smoking cessation.

Unaided smoking cessation

What about all the smokers who give up on their own, without medical help; how do they do it? Lennox and Taylor [10] used postal questionnaires in Aberdeen to investigate this. The simple finding was that light and heavy smokers found it easier to give up than did moderate smokers.

NRT preparations and abstinence				
NRT preparation (No. of trials)	% Quitting		OR (95%CI)	NNT
	Active	Control		
Gum (39)	18.2	10.6	1.6 (1.5-1.8)	13
Patches (9)	20.5	10.8	2.1 (1.6-2.6)	10
Nasal spray (1)	25.9	9.9	2.9 (1.5-5.7)	6
Inhaler (1)	15.2	5.0	3.0 (1.4-6.6)	10

Those who succeeded thought they had social support, and were more likely to have 'simply just stopped'. They were less likely to have used nicotine gum or believe that smoking was harmful. Failures experienced more withdrawal symptoms and were likely to be tempted by others smoking. Eleven percent had never tried to stop; these were older, but were more likely to stop for financial reasons.

What about other methods?

To find methods of smoking cessation which have used objective markers of smoking cessation, *Bandolier* performed a MEDLINE search from 1989-1994 using the words cotinine and urine. Cotinine is a metabolite of nicotine, and measurement of cotinine and hydroxyl metabolites of cotinine in urine (or blood or other body fluids) can be a useful objective test of nicotine intake. Obviously the use of gum or patch invalidates the test. While vegetables and other foods contain nicotine, huge amounts would need to be eaten to invalidate a cotinine test for active smoking, though that may not be so for passive smoking [11].

Measurement of urinary cotinine is likely to be helpful in determining the smoking behaviour in smoking cessation. Thus in a Japanese study of 49 patients who claimed to have stopped smoking, urinary cotinine concentrations one month after intensive instructions to stop smoking in a series of cardiac patients [12], only 30 had actually stopped smoking. There was a clear decrease of urinary cotinine in the quitters compared with no change in those who had not stopped.

Behaviour therapy

A German report [13] of an RCT of structured extensive behaviour therapy compared with a single unstructured antismoking advice session given by a physician in diabetic patients was disappointingly negative. Of 794 insulin-treated patients, only 89 consented to enter the study in which smoking cessation was measured objectively by urinary cotinine.

After six months, 2/44 patients randomised to the intensive behaviour therapy had stopped, compared with 7/45 who received the unstructured intervention.

Getting to mothers of infants

An attempt to use infants' cotinine levels was completely without effect [14] as a warning to mothers to reduce or stop smoking in a RCT where the physician telephoned the mother to report the urinary cotinine result and explain its meaning.

Smoking cessation in pregnancy

Because maternal smoking is associated with increased foetal risk and low birthweight, trying to prevent pregnant women smoking has top priority. One RCT [15] compared an immediate 20-minute intervention by a practice nurse with an evening class providing guidance on a self-help program for two hours on a group basis. Smoking cessation was confirmed by urinary cotinine measurement.

None of the women randomised to the intensive evening class attended, compared with 93% assigned to the immediate intervention. Rates of smoking cessation immediately after intervention, at 36 weeks gestation and postpartum were about 6% for the former and 14% for the latter.

However, there is one study which shows some success. Again, this was an RCT begun in early pregnancy, with randomisation between standard obstetric care and an intervention with self-help materials on smoking cessation in addition [16].

Self reported smoking behaviour was confirmed with a urinary cotinine test. This showed that 25% of women who said they were not smoking actually did smoke. The smoking cessation rates were not significantly different during pregnancy at about 24%, but at 8 weeks postpartum 29% of smokers had given up in the intervention group compared with under 10% in the non-intervention group. The cost of the intervention (self-help manual and audio-tapes) was \$50-111 per patient.

Conclusion

Nicotine addiction through cigarette smoking is recognised as the largest single cause of poor health in the UK. Nicotine replacement therapy has clearly been demonstrated to help people give up smoking, and directed government policies on issues like tax are also of great value in deterring smokers.

Strategies for smoking cessation seem not to be well developed, and though NRT is unequivocally helpful, this seems to be true to a limited extent in certain smokers. It is disappointing that more effective smoking cessation strategies have not been developed in the face of the enormity of the problem.

Bandolier recognises that effective smoking cessation strategies may have been missed by its limited search. Readers who are aware of strategies of proven success are invited to send details for publication in a future issue.

References:

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SHARED CARE FOR DIABETES - A SYSTEMATIC REVIEW

Medical writer Dr Trisha Greenhalgh was recently commissioned by North Thames RHA to prepare a comprehensive review of shared care systems for diabetes. The research, which has just been published as a book by the Royal College of General Practitioners [1], was performed according to standard methodology for systematic reviews produced by the UK Cochrane Centre in Oxford.

Methods

An extensive search of manual and electronic databases and personal communication with workers in the field revealed five RCTs, two comparative and three longitudinal, as well as 12 published descriptive studies and around 30 unpublished schemes in the UK. In her report Dr Greenhalgh highlights the main conclusions from the published trials, suggests areas for further research and makes some general recommendations for the implementation of new shared care initiatives.

Main findings

- 1: Both the randomised and non-randomised trials demonstrated clearly that structured care by GPs with an interest in diabetes and supported by an enthusiastic specialist liaison team produces comparable, and occasionally superior, levels of care to those provided in hospital. Unstructured care by disinterested and unsupported GPs is ineffective and wasteful of resources.

Structured care comprises systematic recall of patients, allocation of protected time, and adherence to a standard management protocol.

- 2: The three RCTs whose findings supported shared care had two common features: a centralised prompting system that recalled patients for appointments, and some form of structured checklist for the GP.

- 3: Established shared care schemes fell into two broad categories: firstly centralised, hospital-based and consultant-led, and secondly decentralised, community based and multidisciplinary. In all published successful schemes an enthusiastic key individual or close-knit steering group was clearly identifiable: the team was usually, but not always, led by a consultant diabetologist.
- 4: Three common features of successful district-wide shared care schemes were:
 - an extensive planning phase in which objectives were carefully defined and the facilities, expertise and commitment of individual general practices were assessed.
 - locally-developed written guidelines for diabetic management.
 - a well-developed outreach service, with a highly trained nurse-facilitator who could advise on practical problems, maintain enthusiasm and enable 'fast tracking' of patients for specialist review.
- 5: Maintaining standards was found to depend on regular audit, as has been shown before with chronic disease management programmes in general practice.

Recommendations

Like all good reviews, the work is not only useful as a description of what is known *now*, but is also a springboard for recommendations and new research to improve effectiveness in the *future*. The chief recommendations in Dr Greenhalgh's report are:-

- i) The central tenets of any shared care scheme are the "three Rs" of chronic disease management - registration, recall and regular review.
- ii) Setting up a shared care scheme is essentially an exercise in change management: success depends on ownership by the participants. GPs should be involved in standard-setting and strategic planning at the outset.
- iii) Extensive preliminary research is essential. Heterogeneity of needs and resources in general practice requires diversity of solutions.
- iv) Care should be shared rather than shifted. An efficient and effective outreach service will bring out the best in each primary care team.
- v) An audit cycle with clear, relevant and measurable objectives should be included in the scheme from the outset. Locally developed, district-wide audit guidelines will enable individual performance to be measured against common standards.

Future research

Possible areas for future research include:-

- longer-term follow-up of patients in trials already published or underway.

- exploration of the educational needs of the primary health care team and ways of meeting those needs.
- development of a simple audit dataset for use at the primary-secondary care interface.
- analysis of the practical problems associated with information transfer on large, centralised electronic databases.
- exploration of ways to involve less innovative practices in shared care systems.
- comparison of cost-effectiveness of different shared care systems.

An excellent and readable report with solid and workable advice.

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Reference:

- 1 PM Greenhalgh. Shared care for diabetes: a systematic review. RCGP Occasional Paper 67. London, Royal College of General Practitioners, October 1994.

CARDIAC REHABILITATION

Heart disease causes distress and impairs quality of life. Cardiac rehabilitation is a multidisciplinary approach to improve short-term recovery and promote long-term changes in lifestyle which help to correct adverse risk factors. It is a process by which patients are restored to and maintained in optimal physical, emotional, social, vocational and economic state.

Cardiac rehabilitation services usually include exercise training, risk factor modification, education and counselling. The principal justification for rehabilitation is the encouragement of return to full activities and a reduction in well-documented convalescence problems of lack of confidence and sleep, anxiety, depression fatigue and worry about non-specific physical symptoms together with excessive caution about everyday activities [1].

Where are we now?

The prevalence of ischaemic heart disease varies considerably, but for a district with a population of 250,000 between 25 and 750 patients a year will be suitable for cardiac rehabilitation.

Although efficacy and importance of cardiac rehabilitation is well recognised, the nature of existing hospital or community-based services in the UK varies considerably. Fewer than half of health districts have established programmes. Few of the programmes which do exist have been subject to careful audit, and there is little information on issues such as the type of service offered, characteristics of patients who use the service, the training and training needs of healthcare professionals involved, resources and outcome measures used.

Benefits of exercise?

Pooled data from several studies has indicated that exercise-based cardiac rehabilitation results in a reduction in overall and cardiovascular mortality of around 25% [2,3]; the first of these references analysed combined results of 10 RCTs involving 4347 patients, and the second overreviewed 22 RCTs.

Benefits of risk factor intervention?

Studies of risk factor intervention and psychological support have produced less dramatic but still impressive effects, not only for patients themselves, but also for their partners [4-6].

Benefits of psychosocial interventions?

There are no published reports of RCTs with convincing evidence for the benefits of psychosocial interventions.

Problems faced now?

There is a need for objective assessments of the physical, psycho-social and economic benefits of cardiac rehabilitation programmes. Programmes need to be developed which are evidence-based and which have on-going evaluation of a number of components of a comprehensive system, including graded exercise, education and support, and secondary prevention measures. The way in which service can be delivered effectively to special groups, like the elderly, women and ethnic minorities warrants special attention.

There are no accepted procedures for the assessment of quality of life during cardiac rehabilitation. What is required are standardised acceptable measures for use in individual patient care, audit of programmes, evaluation of interventions and examination of cost effectiveness.

Conclusion

The availability of cardiac rehabilitation programmes seems justified because it is cost effective [7], the financial benefits gained in terms of productivity and maintaining an occupational income by return to work are clear, and rehabilitation may result in lower costs of further hospital admissions [8]. Mechanisms for delivering a cost-effective service need greater definition.

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Checklist for Cardiac Rehabilitation

A cardiac rehabilitation programme should have most or all of the following, though the structure will depend upon available resources including people, equipment, patients and organisation and coordination of sessions.

People

An experienced coronary care nurse is ideal for taking responsibility for coordinating the programme. Services of a physiotherapist, dietician, clinical psychologist, pharmacist, vocational counsellor and social worker may be included to varying extents where appropriate.

Equipment

Resuscitation equipment including a defibrillator must be at hand and exercise equipment should be checked regularly and correctly maintained.

Patients

Inexpensive early routine care (exercise, advice, self-help materials) should be available for all patients. Monitoring during convalescence is necessary to identify those requiring extra continuing help for cardiac, social or psychological problems, whether or not they have attended a routine programme.

Organisation & Coordination

Close coordination between cardiac aftercare and rehabilitation services is important. A local full-time coordinator is essential to ensure that patients are identified, to liaise with other professionals and to monitor and audit activity in relation to agreed guidelines.

Content

The cardiac rehabilitation programme should offer a range of components, including a flexible menu of methods, and emphasise individual prescription of care. A programme usually includes exercise training, relaxation, risk factor modification, education and counselling. Programmes should begin from the cardiac event itself and should place emphasis on the patients resuming control of their recovery and future lifestyle.

Evaluation and audit

Each programme should keep a record of the numbers attending (including partners) and the drop out rate and reasons for non-attendance.

Outcome measures should include risk factor reduction outcomes (smoking, physical activity, blood pressure, weight, cholesterol), physical outcomes (mortality, reinfarction, cardiac arrest, ventricular function, myocardial ischaemia, physical working capacity, symptom limitations, task and activity performance), psychosocial outcomes (return to work, quality of life) as well as other outcomes (adverse events, non compliance, readmission).

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For many years the UK National External Quality Assurance Service (UKNEQAS) has been developing world-leading methods of ensuring that pathology results obtained in Cornwall are the same as those found in the Highlands of Scotland. Behind UKNEQAS is a raft of organisations which includes professional bodies and which ensures that any (rare) case of inadequate performance is put right. Professional organisations have followed the lead of UKNEQAS and have published detailed methodological reviews to aid the working scientist and pathologist.

UKNEQAS, though, is much more than proficiency testing; the organisers of the various schemes are skilled and knowledgeable people who spend much time and effort in helping laboratories which may have problems, in devising suitable ways of testing methods as well as laboratories for adequate performance, and in helping commercial suppliers to make products available which are scientifically sound.

Testing is not now confined to the laboratory. There are many circumstances in which testing is extra-laboratory, from ITUs and CCUs in hospitals, to testing for allergy and allergens, C-Reactive Protein (equivalent of ESR), or *Helicobacter pylori* in the doctor's surgery. While there are many excellent reasons why near patient testing is effective and worthwhile, those reasons only stand up where tests deliver the correct result. External Quality Assurance is one way of providing a high degree of comfort that such is the case.

UKNEQAS has yet to consider near patient testing and all the implications that widespread uptake would entail. The services presently offered are wide-ranging, and *Bandolier* this month publishes a full list of the schemes extant, their costs, and the names and contact numbers of their organisers on the Figure on page 8.

Laboratories performing any of these tests but not NEQAS members should rectify that.

Purchasers should ensure that laboratory services they buy are from laboratories which perform at least adequately in external quality assurance schemes.

UKNEQAS: TABLE OF ANNUAL CHARGES (UK CLINICAL LABORATORIES) FOR PARTICIPATION IN 1994-95

CLINICAL CHEMISTRY [a]	HORMONES	IMMUNOLOGY & IMMUNOCHEMISTRY [a]	MICROBIOLOGY & VIROLOGY [a]	HAEMATATOLOGY [v]
<p>Clinical Chemistry</p> <p>Lead & Cadmium in Blood</p> <p>Specific Proteins</p> <p>Glycated Haemoglobins</p> <p>Salicylate & Paracetamol</p> <p>Urinary Albumin</p> <p>Urinary Catecholamines & Metabolites</p> <p>Neonatal Screening (PKU, TSH)</p>	<p>PEPTIDE HORMONES [d]</p> <p>FSH and LH</p> <p>FSH or LH</p> <p>Prolactin, Growth Hormone</p> <p>All 4 analyses</p> <p>PTH, ACTH, Calcitonin</p> <p>All 3 analyses</p> <p>AFP, hCG, CEA</p> <p>All 3 analyses</p> <p>NTD AFP</p> <p>Downs Syndrome (AFP, hCG, E3)</p> <p>NTD and Downs Syndrome</p>	<p>AUTOIMMUNE SEROLOGY I</p> <p>Rheumatoid Factor</p> <p>Thyroid Antibodies</p> <p>Antinuclear Antibody</p> <p>AUTOIMMUNE SEROLOGY II</p> <p>ENA Antibodies</p> <p>Cardiolipin Antibodies</p> <p>Neutrophil Cytoplasmic Antibody</p> <p>AUTOIMMUNE SEROLOGY III</p> <p>Acetylcholine Receptor Antibody</p>	<p>General Bacteriology</p> <p>Mycology</p> <p>Syphilis Serology</p> <p>A/AFB Microscopy</p> <p>Rubella IgG Serology</p> <p>Rubella IgM Serology</p> <p>Hepatitis B Serology</p> <p>HIV Serology</p> <p>Virus Serology</p> <p>Virus Isolation</p> <p>Chlamydia Detection</p> <p>Hepatitis C Serology</p> <p>Toxoplasma Serology</p> <p>Mycobacteria Culture</p>	<p>Blood Count</p> <p>Blood & Parasite Films</p> <p>Reticulocytes</p> <p>Abnormal Hb/HbA2/HbF</p> <p>Red Cells G-6-PD</p> <p>Cytochemistry</p> <p>Vitamin B12 Absorption Test</p> <p>Red Cell Mass</p> <p>LEUCOCYTE IMMUNOPHENOTYPING [w]</p> <p>Immunofluorescence, -cytochemistry</p> <p>Immune Monitoring</p>
<p>300</p> <p>140</p> <p>140</p> <p>140</p> <p>140</p> <p>140</p> <p>140</p>	<p>230</p> <p>each 150</p> <p>each 150</p> <p>480</p> <p>each 150</p> <p>400</p> <p>each 150</p> <p>400</p> <p>100</p> <p>200</p> <p>250</p>	<p>90</p> <p>90</p> <p>90</p> <p>60</p> <p>60</p> <p>60</p> <p>90</p> <p>60</p> <p>110</p> <p>110</p> <p>60</p>	<p>440</p> <p>115</p> <p>110</p> <p>110</p> <p>110</p> <p>115</p> <p>143</p> <p>143</p> <p>143</p> <p>154</p> <p>143</p> <p>130</p> <p>130</p> <p>125</p>	<p>328</p> <p>52</p> <p>52</p> <p>52</p> <p>52</p> <p>52</p> <p>75</p> <p>270</p> <p>each</p>
<p>DRUGS OF ABUSE [b]</p> <p>Amphetamines, Barbiturates, Cannabinoids, Cocaine, Opiates, Opioids & Tranquilisers in urine</p> <p>Ethanol in serum</p> <p>(additional technique)</p>	<p>STEROID HORMONES [e]</p> <p>Annual Enrolment Fee</p> <p>Cortisol, 17aOH progesterone</p> <p>Progesterone, Oestradiol</p> <p>High-Level Oestradiol (IVF)</p> <p>Male & Female Testosterone</p> <p>Urinary Free Cortisol [f]</p> <p>Sex Hormone Binding Globulin [g]</p>	<p>PROTEINS & ANTIGENS</p> <p>CRP</p> <p>b2 Microglobulin</p> <p>AFP in amniotic fluid</p> <p>Acetylcholinesterase in amniotic fluid</p> <p>IgG Subclasses</p> <p>PSA</p> <p>Tumour Markers</p> <p>Fungal & related Antigens</p> <p>Monoclonal Protein Identification</p> <p>ALLERGY [p]</p> <p>IgE (serum)</p> <p>Allergen-specific IgE</p>	<p>PARASITOLOGY [j]</p> <p>Blood</p> <p>Faecal</p> <p>ANTIBIOTIC ASSAYS [s]</p> <p>Gentamicin, Tobramycin, Netilmicin</p> <p>Amikacin, Vancomycin, Chloramphenicol, Flucytosine.</p> <p>1 antibiotic</p> <p>2 or more antibiotics</p>	<p>HAEMATINICS [x]</p> <p>Vit B12, Folate, Ferritin, Red Cell Folate</p> <p>* 1-2 anls £100, 3 anls £150, 4 anls £200</p> <p>COAGULATION [y]</p> <p>LEVEL 1</p> <p>PT/INR</p> <p>PT Diagnostic (for anticoagulant control)</p> <p>APTT</p> <p>Thrombin Time</p> <p>Fibrinogen</p> <p>Fibrinogen Degradation Products</p> <p>Heparin Dosage</p>
<p>260</p> <p>150</p> <p>10</p>	<p>50</p> <p>each 180</p> <p>each 180</p> <p>144</p> <p>each 108</p> <p>120</p> <p>125</p>	<p>110</p> <p>110</p> <p>110</p> <p>60</p> <p>110</p> <p>110</p> <p>110</p> <p>110</p> <p>free</p> <p>215</p> <p>325</p>	<p>155</p> <p>242</p> <p>133</p> <p>143</p>	<p>330</p>
<p>Enrolment Fee</p> <p>Antiepileptic Drugs</p> <p>Respiratory Drugs</p> <p>Methotrexate</p> <p>Psycho-active Drugs</p> <p>Cardiac Drugs</p>	<p>THYROID HORMONES [h]</p> <p>T4, T3, free T4, free T3, TSH</p> <p>Neonatal Screening (PKU, TSH)</p>	<p>ALLERGY [p]</p> <p>IgE (serum)</p> <p>Allergen-specific IgE</p>	<p>ANTIBIOTIC ASSAYS [s]</p> <p>Gentamicin, Tobramycin, Netilmicin</p> <p>Amikacin, Vancomycin, Chloramphenicol, Flucytosine.</p> <p>1 antibiotic</p> <p>2 or more antibiotics</p>	<p>LEVEL 1</p> <p>PT/INR</p> <p>PT Diagnostic (for anticoagulant control)</p> <p>APTT</p> <p>Thrombin Time</p> <p>Fibrinogen</p> <p>Fibrinogen Degradation Products</p> <p>Heparin Dosage</p>
<p>50</p> <p>246</p> <p>107</p> <p>58</p> <p>78</p> <p>118</p>	<p>320</p> <p>140</p>	<p>215</p> <p>325</p>	<p>133</p> <p>143</p>	<p>330</p>
<p>TRACE ELEMENTS [c]</p> <p>Serum Copper, Zinc, & Gold</p> <p>Serum Aluminium & Selenium</p> <p>Urine Mercury & Cadmium</p> <p>Water Aluminium</p>	<p>HISTOPATHOLOGY</p> <p>Immunocytochemistry [i]</p> <p>Breast Cancer Screening [j]</p> <p>Renal Pathology [k] - full participant</p> <p>Renal Pathology - per colleague</p> <p>Neuropathology [l]</p> <p>Oral Pathology [m]</p>	<p>ALLERGY [p]</p> <p>IgE (serum)</p> <p>Allergen-specific IgE</p>	<p>ANTIBIOTIC ASSAYS [s]</p> <p>Gentamicin, Tobramycin, Netilmicin</p> <p>Amikacin, Vancomycin, Chloramphenicol, Flucytosine.</p> <p>1 antibiotic</p> <p>2 or more antibiotics</p>	<p>LEVEL 1</p> <p>PT/INR</p> <p>PT Diagnostic (for anticoagulant control)</p> <p>APTT</p> <p>Thrombin Time</p> <p>Fibrinogen</p> <p>Fibrinogen Degradation Products</p> <p>Heparin Dosage</p>
<p>1 set</p> <p>2 sets</p> <p>3 sets</p> <p>4 sets</p> <p>5 sets</p> <p>10</p>	<p>255</p> <p>Regions pay</p> <p>90</p> <p>30</p> <p>free</p> <p>free</p>	<p>215</p> <p>325</p>	<p>133</p> <p>143</p>	<p>330</p>
<p>Water Al supplement:</p>	<p>CLINICAL CYTOGENETICS [n]</p> <p>Full Scheme</p> <p>Diagnostic Bloods, Amniotic Fluids, Chorion Biopsies, Solid Tissues</p> <p>Haematological Samples</p> <p>each 120</p>	<p>ALLERGY [p]</p> <p>IgE (serum)</p> <p>Allergen-specific IgE</p>	<p>ANTIBIOTIC ASSAYS [s]</p> <p>Gentamicin, Tobramycin, Netilmicin</p> <p>Amikacin, Vancomycin, Chloramphenicol, Flucytosine.</p> <p>1 antibiotic</p> <p>2 or more antibiotics</p>	<p>LEVEL 2</p> <p>Coagulation Inhibitors</p> <p>Factor VIII : C Assay</p> <p>von Willebrand Factor Antigen Assay</p> <p>von Willebrand Factor Activity Assay</p> <p>Factor IX : C Assay</p> <p>Factors II, V, VII, XI, & XII Assays</p> <p>Factor XIII Screen</p> <p>Antithrombin III Assays : Antigen & Activity</p> <p>Protein C Assays : Antigen & Activity</p> <p>Protein S Assays : Antigen & Activity</p> <p>Plasminogen</p> <p>Both Levels</p>
<p>180</p> <p>240</p> <p>290</p> <p>300</p> <p>330</p> <p>10</p>	<p>600</p> <p>each 120</p>	<p>215</p> <p>325</p>	<p>133</p> <p>143</p>	<p>273</p>
<p>OEH, Birmingham, Dr D Bullock</p> <p>tel 0222 627 2465, fax 021 414 1179</p>	<p>Women's Birmingham, Dr G Holder</p> <p>tel 021 772 1101 x276, fax 021 773 8576</p>	<p>General Leicester, Dr PN Furness</p> <p>tel 0533 594562, fax 0533 594582</p>	<p>CRL Cardiff, Dr R Field</p> <p>tel 0222 492814, fax 0222 487671</p>	<p>PO Box 94, Bristol, Mrs S Corbin</p> <p>tel 0272 757575, fax 0272 757577</p>
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<p>Univ Surrey, Guildford, Dr A Taylor</p> <p>tel 0483 509217, fax 0483 503517</p>	<p>OEH, Birmingham, Mr F Mackenzie</p> <p>tel 021 627 2465, fax 021 414 1179</p>	<p>Oral Med, Glasgow, Prof DG Macdonald</p> <p>tel 041 332 7020 x234, fax 041 353 1593</p>	<p>HTD London, Dr PL Chiodini</p> <p>tel 071 387 4411 x265, fax 071 383 0041</p>	<p>NGH Sheffield, Dr J T Reilly</p> <p>tel 0742 434343 x4615, fax 0742 610856</p>
<p>RI Edinburgh, Dr J Seth</p> <p>tel 031 229 2477 x2820, fax 031 519 5422</p>	<p>UCLMS, London, Dr K Miller</p> <p>tel 071 380 9772, fax 071 387 3674</p>	<p>Southmead, Bristol, Dr R Howell</p> <p>tel 0272 505050 x2681, fax 0272 591792</p>	<p>Southmead, Bristol, Prof DS Reeves</p> <p>tel 0272 505050 x4187, fax 0272 593217</p>	<p>NMGH Manchester, Dr ML Lewis</p> <p>tel 061 720 2786, fax 061 720 2866</p>
<p>Tenovus, Cardiff, Dr J Middle</p> <p>tel 0222 742498, fax 0222 747618</p>	<p>Royal Marsden, London, Dr JP Sloane</p> <p>tel 081 642 6011 x4623, fax 081 770 7899</p>	<p>PO Box 894, Sheffield, Dr A Milford-Ward</p> <p>tel 0742 827514, fax 0742 619893</p>	<p>NIBSC, South Wlmsns, Dr P Phillips</p> <p>tel 0707 654753 x413, fax 0707 646730</p>	<p>R Hallamshire, Sheffield, Prof FE Pession</p> <p>tel 0742 700862, fax 0742 758989</p>

All prices are in £ Sterling for one year's participation and are applicable to UK clinical laboratories only. Some schemes apply a surcharge for non-clinical and/or non-UK participants.