

It is time to test low level laser therapy in Great Britain

T Moshkovska, J Mayberry

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Low level laser therapy (LLLT) has been used in Eastern Europe and Asia for the treatment of a wide range of conditions for many years. Its continued acceptance in these populations reflects the efficacy with which it is regarded both by clinicians and their patients. Although there have been a substantial number of reports on its clinical benefit and some practitioners have used the technique in North America and Australasia it has yet to be subjected to detailed assessment through randomised clinical trials. The purpose of this review is to stimulate interest in the technique and to encourage rigorous research into its potential value.

1995 this was opened by order of the Russian government. As a result clinicians in Russia and Ukraine now have access to a wide variety of invasive and non-invasive lasers and there are numerous specialised laser centres throughout these countries. A wide range of laser applications have been used to treat large numbers of patients and in recent times up to 1.5 million patients have been treated annually.

The reasons behind the widespread application of LLLT in Russia and Ukraine are evident. Today medicine is dominated by expensive pharmaceuticals and advanced technologies. The ever-growing emergence of resistant bacteria and patient sensitivity to drugs should encourage a search for new therapeutic modalities. Laser irradiation shows particular hope in this area with virtually no contraindications, and limited side effects. However, there are some contraindications to the use of LLLT and these include:

- malignant tumours located in an irradiated area
- epilepsy
- use over the thyroid gland
- irradiation of the abdomen during pregnancy
- light hypersensitivity
- thrombosis in a pelvic vein or a deep vein of the legs.

Today much more is known about the effects of laser light on biochemical and cellular function than was the case 20 years ago and the following benefits have been suggested:

- (1) cellular metabolic activation and increased functional activity (ATP synthesis is increased by up to 150%)¹
- (2) stimulation of repair processes as a result of increased cell proliferation^{2–4}
- (3) anti-inflammatory effects^{1, 2}
- (4) microcirculation activation and more efficient tissue metabolism^{1, 5–7}
- (5) analgesic effects as a result of increased endorphin release^{8–11}
- (6) immunostimulation with correction of cellular and humoral immunity¹
- (7) increased antioxidant activity in the blood^{9, 12, 13}
- (8) stabilising lipid peroxidation in cell membranes^{5, 6, 14}
- (9) stimulation of erythropoiesis^{1, 13, 15}
- (10) vasodilatation^{3, 6, 12}
- (11) normalisation of acid base balance in the blood^{2, 12, 16}

Low level laser therapy (LLLT) has been investigated and used clinically for over 30 years, mostly in Eastern Europe and Asia. The ability of lasers to cut, cauterise, and destroy tissue is well known throughout the medical world. However, its role at lower power is less well appreciated. The ability to non-thermally and non-destructively change cell function is known as laser biostimulation and is the basis for the current use of lasers in a number of medical fields. The worldwide interest in LLLT is illustrated by its use in more than 85 institutions in over 37 countries. Since the first study was reported in 1967, some 2500 papers have been published in a range of journals worldwide and the value of LLLT is much better reported than many believe. Its scientific background is sound enough to say that it is both safe and effective. However, positive double blind studies are unfortunately none too easy to find. Among the 100 selected for evaluation in this review, only 28 could be found on Medline. Many studies have been published in regional or national publications, which are not indexed on Medline or similar databases. The main reasons for this restricted publication include language barriers and lack of availability of professional journals because of financial constraints. Table 1 gives a summary of published studies of low intensity laser therapy for cardiovascular disease.

Most reports are in Russian and the basis for clinical research and practice was first established in Moscow in 1986. The Institute of Laser Medicine was formed through a union of 14 laser centres from different parts of Russia. LLLT emerged as a potential therapeutic modality because of the conversion of military production into areas of commercial practice including medicine. The largest complex of laser research was founded in the closed city of Kaluga and in

See end of article for authors' affiliations

Correspondence to:
Dr J Mayberry, Leicester
General Hospital,
Gwendolen Road,
Leicester LE5 4PW, UK;
jmaybe@fiscali.co.uk

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(12) reflexogenic effects on the functional activity of different organs and systems^{17 18} (fig 1)

There are indications that LLLT also has a role:

- during periods of recovery after trauma or surgery
- in treatment of hyperlipidaemia when diet and pharmacological interventions have been ineffective
- in strengthening the immune response.

In addition, Ohshiro and Calderhead¹⁹ believe low intensity laser irradiation may work through effects on the central nervous system. They have suggested this occurs through tissue photobioactivation, in which the energy levels of biological structures are changed through light quantum absorption. Human tissue absorbs light energy and this stimulates and modifies metabolic processes. It results in reorganisation of protein polymers. In particular, it changes the structural and functional properties of cell membranes as well as fermentation processes. In this way it has some similarities to the action of sunlight in plant photosynthesis.

From more than 10 years practical experience with low intensity laser irradiation in cardiology in Ukraine, it is clear that it offers new treatment possibilities. These include improved rheological characteristics of the blood and microcirculation as well as normalisation of hormonal and immune parameters.^{4 13 16 17} In particular LLLT can be part of a range of therapeutic modalities for patients with ischaemic heart disease, where it can reduce the risk of acute myocardial infarction. Over a period of 10 years one of the authors (TM) studied about 500 outpatients with this condition and 60% had laser treatment on two or more occasions. Some 70% of patients experienced a positive clinical benefit.

Methodologically there are two basic techniques—intravenous laser blood irradiation (ILBI) by HeNe laser in the red spectrum and a simultaneous percutaneous low laser irradiation by laser in the infrared spectrum on to projections of reflexogenic and acupuncture areas. From practical experience TM believe this is the best combination for treatment, but it awaits confirmation in a double blind trial.

Intravenous laser blood irradiation was developed experimentally by the Russian researchers, Meshalkin and Sergievskiy,²⁰ and introduced into clinical practice in 1981. Originally the method was applied in the treatment of cardiovascular abnormalities.

Now, the first approach that is generally used in this situation is HeNe laser (632.8 nm) via an intravenous catheter for irradiation of the blood. The usual parameters are: output at the end of the light guide inserted into a vein from 1 mW to 4 mW with an exposure 10–60 minutes. Procedures are conducted on a daily basis or every other day, for between 3 and 10 sessions. The second therapeutic approach is through skin contact using a wavelength (830 nm), and output 40 mW, frequency 5 Hz. Infrared laser irradiation of the skin is directed at the heart projection and Zaharyan's-Head's zones (fig 2). Procedures are conducted on a daily basis or on alternate days for 6 to 10 sessions. Photoactivation of the reflexogenic areas by infrared spectrum laser stimulates nervous and humoral regulatory mechanisms. This method is used in both treatment and prevention of coronary heart disease, cardiac arrhythmias,^{17 18 21} diabetes mellitus,⁵ hypertension, and occlusive vascular diseases.³

Intravenous HeNe laser blood irradiation (IV HeNe LBI) has a wide range of actions, which include biostimulation, analgesia, antiallergic effects, immunomodulation, vasodilatation, antiarrhythmic,^{4 18 22} antihypoxic, spasmolytic, and anti-inflammatory effects. In addition IV LBI procedures on

patients with ischaemic heart disease can be helpful when there is resistance to nitrates,^{2 16 17} β blocking drugs, and calcium channel blockers.^{18 22} Reported effects include reduced need for nitroglycerine tablets, decreased number of angina episodes, alleviation of pain, suppression of lipid peroxidation, increased antioxidant protection of erythrocyte membranes, reduction of fibrinogen levels, normalisation of antithrombin-III, reduced activity of the pituitary-adrenal axis, and aldosterone-renin-angiotensin system.^{23 24}

IV LBI improves the rheological properties of blood, increasing its fluidity and activating transport functions. This is accompanied by increased oxygen levels, as well as decreased carbon dioxide partial pressures. The arteriovenous difference for oxygen is increased, which confirms a reduction in tissue hypoxia with a return to normal metabolism. Probably, the basis for activation of oxygen transport by IV LBI is through an effect on haemoglobin. The augmentation of oxygen levels improves tissues metabolism. In addition, laser irradiation activates ATP synthesis and energy formation in cells.²⁴ The application of IV LBI in cardiology has shown that the procedure has analgesic effects, which increase exercise tolerance for patients and prolong periods of remission. The mechanism might be through reduced platelet aggregation and activation of fibrinolysis and so increased peripheral blood flow and tissue oxygenation. The improvement seen in the microcirculation is also attributable to vasodilatation and changes in the physicochemical properties of erythrocytes. In particular there is a rise in their negative electric charge. In addition there is unblocking of capillaries and collaterals as well as normalisation of the nervous excitability of smooth muscle in vascular walls.¹⁶

The individualisation of doses of IV LBI is an important factor in guaranteeing successful treatment. This technique has solved the problem of "secondary aggravation" of disease during laser therapy. This phenomenon depends upon the initial exposure and output power of the irradiation. The initial dose should be minimal during the first procedure and then increased gradually up to the fifth procedure. For patients under 60 years old with coronary heart disease an output power at the end of the venous light guide should be from 2 mW to 4 mW, with an initial exposure of the blood for seven to eight minutes as the standard approach. There are subsequent increases in the exposure time of up to 15 minutes during the fifth procedure. For patients over 60 years the exposure is reduced. The usual parameters of blood irradiation for this group of patients are output power at the end of the venous light guide from 1 mW to 3 mW, with an exposure from five minutes on the first procedure up to 10 minutes during the fifth procedure.

This simple method for individualisation of the course of laser therapy is based on observing the phenomenon of "scarlet blood". This is seen when placing intravenous cannulas with their light guide into a vein. The appearance of this phenomenon during the third to fifth procedures of intravenous LBI coincides with the production of nitric oxide. Nitric oxide is an endothelial relaxation factor involved in the circulation of blood, immune function, communications between nerve cells, as well as rheological characteristics of the blood and coronary microcirculation. Nitric oxide plays a key part in the maintenance of vasodilatation and decreases high blood pressure. However, surplus nitric oxide is harmful and can cause oxidative damage. It is possible to limit these harmful effects by use of antioxidants, such as a complex of two vitamins A and E, (AEVIT).¹⁷ This "arterialisation" of patients' blood means that the procedure should be suspended or carried out less frequently (every two to three days rather than daily). Sometimes symptoms of

Table 1 Summary of published studies of low intensity laser therapy for cardiovascular disease

Study	Disease	Number of patients	Outcome
Diagnostic implication of changed red cell counts in low intensity laser irradiation of blood in elderly patients with coronary heart disease. ²⁵	Coronary heart disease	41 elderly patients	Change in peripheral erythrocyte count after intravenous laser radiation correlated with effectiveness of treatment.
Laser therapy in patients with hypertension and coronary insufficiency. ²⁶	Hypertension with coronary insufficiency	82 patients Randomly divided in to two groups: 57 received infrared (0.85 nm) laser radiation on the skin + traditional therapy. 25 controls who received infrared traditional therapy.	The study shows antianginal and antihypertensive effects with improved cardiac performance and myocardial contractility. This was accompanied by positive shifts in lipid metabolism, lipid peroxidant and antioxidant activity, haemocoagulation. and microcirculation.
Intravenous use of low energy helium-neon laser irradiation in unstable angina. ⁹	Unstable angina pectoris	90 patients 25—traditional therapy 65—traditional therapy + intravenous laser therapy	Antianginal effect was shown by recorded number of anginal episodes and daily consumption of nitroglycerine tablets. The data confirm antianginal clinical effects of intravenous laser therapy.
Treatment of ischaemic heart disease with low level laser therapy. ¹⁸	Ischaemic heart disease with cardiac arrhythmias (n=7) Hypertension with cardiac arrhythmias (n=2) Hypertension (n=2)	11 patients (age 48–78) 5 patients were treated with laser monootherapy 6 patients were treated with a combination of laser therapy and antiarrhythmic drugs.	Cardiac arrhythmias disappeared after laser therapy in 3 patients without antiarrhythmic drugs. The doses of nitrates and calcium antagonists were lowered by 50% and β blockers withdrawn completely (3 patients).
Laser therapy as a method of elimination of tolerance to nitrates and increase of their action. ²⁸	Ischaemic heart disease Stable angina pectoris with hypertension	64 patients 40–69 years old (43 men and 21 women) 27 patients had a history of myocardial infarction.	Infrared laser therapy reduced tolerance to nitrates and increased their action in 80% of cases.
Lectin induced chemiluminescence of neutrophilic granulocytes in the peripheral blood of patients with myocardial ischemia before and after He-Ne laser blood irradiation. ²	Patients with stable angina pectoris Healthy donors	35 patients (32 men and 3 women) 30 people (24 men and 6 women)	Laser irradiation eliminated some less resistant neutrophils granulocytes. In the remaining cells the composition and reactivity of surface lectin receptors and their level of biologically active substances are likely to play a key part in the mechanism responsible for the therapeutic effect of He-Ne laser.
Intracardiac laser irradiation in the correction of left ventricular dysfunction in patients with progressive angina pectoris. ¹²	Progressive angina pectoris with cardiac failure	73 patients 47 patients—intracardiac He-Ne laser irradiation + traditional therapy 26 patients—traditional therapy	The beneficial effect of laser haemotherapy on intracardiac haemodynamics characteristics results from a stabilising effects on left ventricular regional contractility. It is associated with its anti-ischaemic effect.
Intravascular laser irradiation of blood in the multimodality treatment of patients with obliterating disease of the lower limb vessels. ³	Enderarteritis obliterans atherosclerosis of the lower limb vessels	80 patients Intravascular laser irradiation of the blood via a light guide in a peripheral vein.	74% positive effect due to normalisation of coagulation properties, increased fibrinolytic potential, and normalisation of the lipoprotein ratio.
A comparison of different modalities of helium-neon laser therapy in patients with stable angina pectoris. ²⁷	Stable angina pectoris.	133 patients He-Ne laser was applied (1) on the skin to the liver projection area in combination with prolonged nitrates (2) on the skin to the cardiac region and Zaharyan's-Head's zones (3) intravenous irradiation of blood.	In these patients there was a reaction of antiproteolytic enzymes to He-Ne laser therapy. The response varied with the type of laser therapy did not change the therapeutic results.
Helium-neon laser used in drug resistant cardiac arrhythmias. ²²	Chronic coronary heart disease with cardiac arrhythmias.	85 patients with frequent and persistent arrhythmias, 28 were resistant to ethacizinium and allapininum (both drugs from class I) Two groups: (1) 68 patients received intravenous He-Ne laser therapy in combination with one of the above drugs; (2) 17 patients received He-Ne laser therapy alone.	The efficacy of treatment was assessed in both groups. An anti-arrhythmic effect was more frequently seen when He-Ne laser was combined with one of the above drug than when it was given alone (67% and 36%, respectively)
Changes in the rheological activity of the blood due the He-Ne laser irradiation. ¹³	Atherosclerosis	22 patients Studies were carried out in vivo and in vitro.	No changes were seen in the rheological activity of blood in vitro, but they were seen in vivo. Blood viscosity declined with a fall in packed cell volume and reduced plasma viscosity.
Ambulatory application of combined laser therapy in patients with diabetes mellitus and dyslipidaemia. ⁵	During a two year period 205 patients with NIDDM and 54 with IDDM were observed. 89 patients (age 57–61 years old) with NIDDM constituted for this study	29 formed a control group, treated with hypoglycaemic drugs. 60 patients (with a fasting glycose of no more than 9.0 mmol/l) were treated by laser therapy with antioxidant therapy AEVIT (combination vitamins A and E) 600 mg a day alone.	Lipid profiles, glycaemic control, and enzyme activity (ALT, AST) were checked before treatment and also at 8 days, 2 weeks, 1, 4, and 9 months after treatment. Throughout the treatment plasma lipids in the control group were unchanged. However, the level of total cholesterol (TC) decreased and the level of triglycerides (TG) increased in the main group. These results were maintained up to 9 months.

Table 1 Continued

Study	Disease	Number of patients	Outcome
Evaluation of laser radiation in red and infrared diapasons in the treatment of patients with unstable angina pectoris. ¹⁵	Unstable angina pectoris	62 patients Randomly divided in to three groups: 21 used traditional therapy + intravenous laser irradiation in red diapason; 17 used traditional therapy + percutaneous laser irradiation in infrared diapason; 24 used traditional therapy + percutaneous + intravenous laser	This study claimed that combined treatment was the most effective method in unstable angina pectoris.
Low level laser therapy in patients with ischaemic heart disease and possible mechanism of hypolipidaemic action. ¹⁴	Ischaemic heart disease and angina pectoris.	38 patients received percutaneous low level irradiation by infrared laser on projections of heart and vessels on a daily basis for 10 sessions.	Lipid profiles were checked before treatment, on the fifth day of treatment, and 3 and 6 months after treatment. The level of total cholesterol was decreased by 20%–36% and remained constant during the 6 months.
Drugs and laser correction of microcirculatory disorder in myocardial ischaemia. ⁴	50 Chinchilla rabbits.	Drugs and lasers were daily used after 30 days inactivity for 7 days.	There were anti-ischaemic effects of He-Ne and nitroglycerine through increased numbers and functional activity of capillaries. Microcirculatory changes by verapamil were less significant than those causes by nitroglycerine.

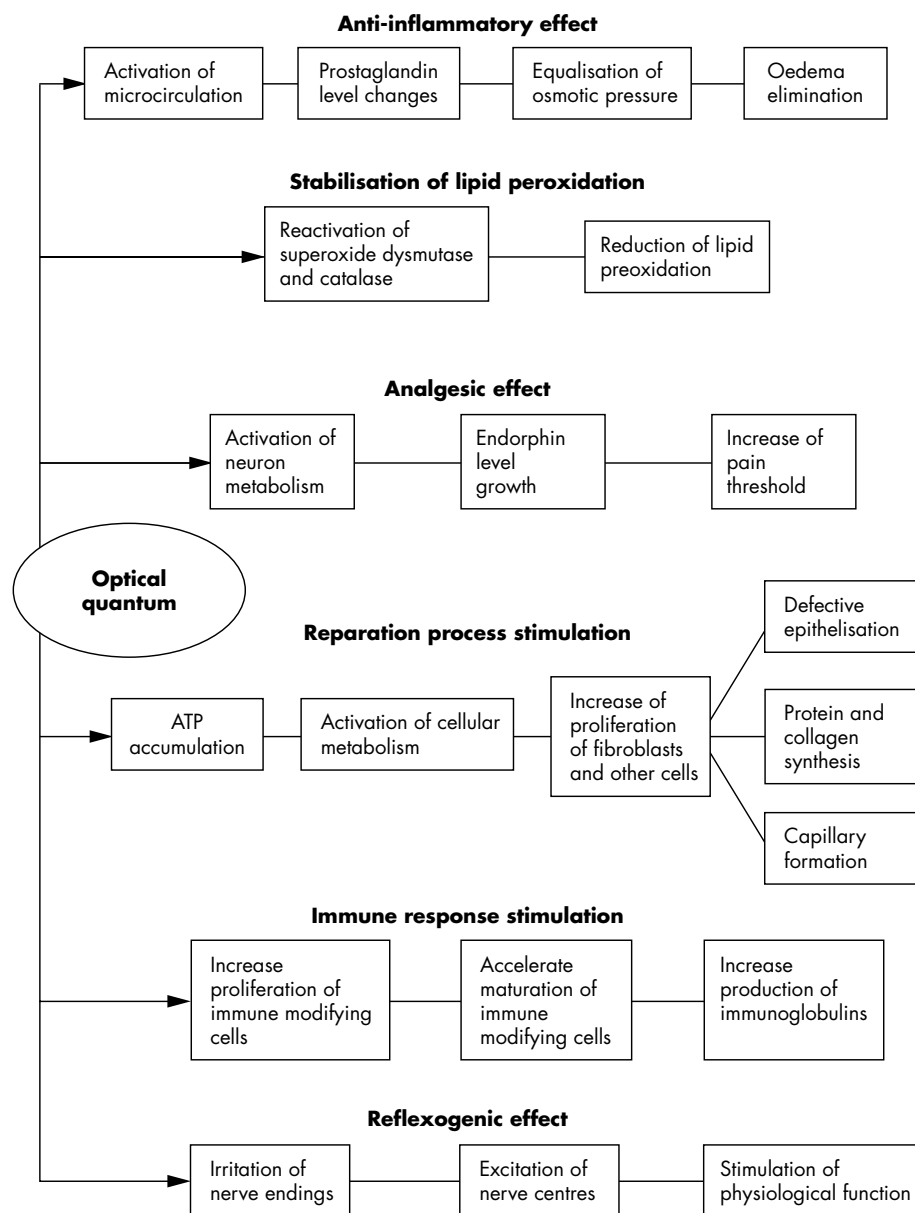


Figure 1 Mechanism of actions low level laser therapy.

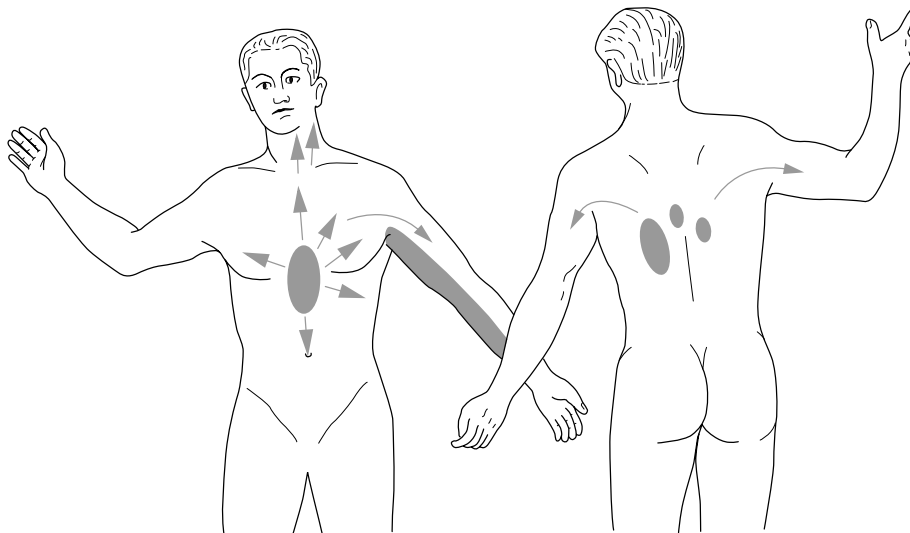


Figure 2 Reflexogenic zones (Zaharyan's-Head's areas) in angina pectoris. Reflexogenic zones or Head's zones. Associated persons: G Zaharyan (1827–1897), Sir Henry Head (1861–1940). References: Head H. On the disturbances of sensation, with special reference to the pain of visceral disease. *Brain* 1893;16:1–133; *Brain* 1894;17:339–480; *Brain* 1896;19:153–276. Description: Zones of hyperalgesia of skin, associated with visceral disease. In 1883, Russian physician G Zaharyan discovered areas "allying organ representation". Ten years later, Sir Henry Head was the first person to describe the reflex signs of disease, showing how any disturbance of internal function is quickly reflected to the external body surface, thereby giving notice of disorder, for example, attributable to referred sensation from the viscera, neck, and jaw pain can be seen in angina pectoris. In collateral irritation the organ disease causes a hyperaesthesia or pain in the skin areas whose nerves emanate from the same segment of the spinal column. Laser irradiation stimulation of such areas of "organ representation" may affect the physiological function of these organs through irritation of nerve endings. (Reproduced with permission of Meditsina, Moscow).

hypercoagulation are coincident with the appearance of "scarlet blood" and this can limit clinical efficacy.

The biological effect of laser light on various conditions is complex and more research is needed to find the optimal parameters for treatment. Scientific research and clinical experiments on LLLT will help confirm whether it has a definite role in the treatment and prophylaxis of ischaemic cardiac disease. While some may regard LLLT as a magical electrotherapeutic panacea, and others consider it useless, there is a current need for clinical investigators to research these new laser medical devices. Additional research is needed to obtain data concerning success rates in treating specific conditions. This should include length of exposure, frequency of treatments, and related therapeutic protocols. The studies must conform to rigorous standards and clearly there is a place for double blind randomised control trials. It is only with robust data from such exacting studies that LLLT will come to be accepted as an effective modality of treatment. However, the clinical experience described in this paper should be a prompt to manufacturers of LLLT equipment to fund such work.

Authors' affiliations

T Moshkovska, J Mayberry, Leicester General Hospital, Leicester, UK

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WEB TRAWL

This month's web trawl looks at two very different web sites, one each from the USA and the UK. What both do have in common, however, is that they may be regarded as national health information resources.

<http://www.seer.cancer.gov> This is the web site for SEER (surveillance, epidemiology, and end results); a programme of the National Cancer Institute in the USA. SEER has been collecting detailed statistics on cancer incidence and survival in the USA since 1973, and the result is a wealth of information available through this web site. The home page provides links to all other areas of the site. There are around 50 links listed on this page, which can be overwhelming at first view, but they are ordered by category, with subject areas including databases, statistical software, and data collection tools. A drop down menu provides access to basic statistics with regard to a large number of tumours, all listed by site or organ. For those intending to use material from the site, the basic statistics (or Fast Stats, as they are called), may be accessed immediately, but for access to the more detailed databases, an application form (downloadable from the web site) must be completed and approved. This process, according to the information on the web site, can take around 48 hours. For anyone wishing to obtain statistical data on malignancies in the USA, there are unlikely to be many other web sites providing such comprehensive data, all in the one place. Data are current up to 2002; those wishing more recent data will need to look further afield. The web site does provide a link to the National Cancer Institute's Cancer Control and Population Sciences web site, which would be a good starting point.

<http://www.nice.org.uk> This is the web site of the UK's National Institute for Health and Clinical Excellence (NICE). From the home page, the site is divided into two separate areas, clinical excellence and public health excellence; each accessed via a link. Each of these separate sites then has its own home page. The clinical excellence home page links to clinical guidelines and appraisals of technology and interventional procedures, as well as to information about how NICE actually works, and to other related organisations such as NHS Direct. The guidelines and appraisals published to date cover many areas of clinical practice. The public health excellence home page again links to guidance and evidence in public health, and also provides links to relevant news and up and coming events. Registration on the site is encouraged, and allows the user the option of receiving email alerts and newsletters, but does not give access to any additional areas on the site. Although the entire NICE web site is largely intended for a UK audience, much of the information in the areas of guidelines and technology appraisal may be of interest to health professionals (and indeed lay people) from other countries. For those living in the UK, this site provides an up to the minute source of information about what is regarded as current best treatment and practice in this country.

Robyn Webber
Web Editor