Diamorphine, with a 129-year history, is one of the longest established medications. In British medicine, diamorphine is sometimes used as a maintenance treatment for opiate addiction but is also routinely used in clinical practice to treat a number of general medical conditions. These ways of using diamorphine are very different but are often confused by observers of the British system. Although the routine clinical use of diamorphine in medicine is unique to the United Kingdom (UK), in other countries there is little awareness of this very British practice. Diamorphine is used in hospitals, primary care settings, and hospices. It may be administered by different routes, including oral, intramuscular, intravenous, subcutaneous, inhaled, epidural, and intrathecal routes. Among its most important medicinal uses is the treatment of severe and/or intractable pain. Discussion of the medical uses of diamorphine is often confused by entanglement of medical practice and illicit drug abuse problems. This article summarizes the history, regulation, and uses of diamorphine in the UK.

INTRODUCTION

There is currently a renewed debate about the role of diamorphine (heroin) as a potential treatment for opiate addiction. Large-scale clinical trials have been conducted in both Switzerland and the Netherlands (Uchtenhagen et al., 1999; van den Brink, Hendriks, Blanken, Huijsman, & van Ree, 2002). Further studies are currently being planned or implemented in Germany and the UK. The British
experience with diamorphine is unique in several respects. Firstly, diamorphine has been used in the clinical treatment of opiate addicts from the early years of the 20th century and continues to be used in this way, albeit for small numbers of patients (Strang, Ruben, Farrell, & Gossop, 1994). However, diamorphine is much more extensively used for the treatment of medical conditions in Britain.

These two uses of diamorphine are completely distinct. Unfortunately, observers of British practice often confuse them, and this leads to continuing misunderstandings about diamorphine prescribing in the UK. For example, in an overview of opiate substitution treatment in Europe, Solberg, Burkhart, & Nilson (2002, p.478) state that “heroin is prescribed by general practitioners and currently there are believed to be about 500 individuals in this kind of substitution treatment in the UK today.” This statement is misleading since it implies (incorrectly) that heroin prescribing to opiate addicts in Britain is done by general practitioners. This illustrates the confusion between the uses of diamorphine for the treatment of addiction and for the treatment of medical conditions. This paper describes the current position in the UK with regard to the lesser known, but important uses of diamorphine in British medicine.

**The Unique Place of Diamorphine in British Medicine**

Diamorphine has a curious role within British medicine. Its medical uses are, in many respects, so “ordinary” that it is not realized what a unique phenomenon this is. It is used in routine clinical practice in the UK to treat a number of general medical conditions. In most other countries, diamorphine is unavailable for medical use, and in many countries it is specifically prohibited. As a consequence, British doctors often do not realize the uniqueness of their use of diamorphine. In other countries there is little awareness of British practice nor of its potential merits.

In the United States, the use of diamorphine for any medical purpose is completely prohibited. The federal government outlawed the manufacture of diamorphine in 1924, and the Narcotic Control Act of 1956 required the surrender of the last remaining supplies. By the early 1980’s British doctors were writing just under 99% of the world’s prescriptions for medicinal diamorphine and consuming 95% of the worldwide legally produced annual quantity of about 300 kg of diamorphine (United Nations International Narcotic Control Board, 1990).

The main active ingredient of opium, morphine, was isolated in 1803. Diamorphine (heroin) is a semi-synthetic derivative of morphine with similar pharmacological properties but with greater potency. Diamorphine was originally synthesized by Charles Wright at St. Mary’s Hospital, London in 1874 but was not used as a medicine until the German pharmaceutical company Bayer marketed it in 1898. An early report in the Journal of the American Medical Association (1906) recommended diamorphine for the treatment of bronchitis, pneumonia, whooping cough, laryngitis,
and hay fever (Courtwright, 1982). Its uses rapidly extended beyond respiratory and lung diseases. The early literature described more than 30 systemic and local indications, in adults as well as children: angina pectoris, heart failure, aortic aneurysm, dysphagia, cancerous stomach, influenza, multiple sclerosis, gynecological diseases, inducing labor and narcosis. It was also prescribed for fever, high blood pressure, diabetes and hiccups, and used to treat dementia, depression, and psychosis (de Ridder, 1994).

Current Medical Uses of Diamorphine in the United Kingdom

Diamorphine may be administered by different routes, including oral, intramuscular, intravenous, subcutaneous, inhaled, epidural, and intrathecal administration. When administered by mouth, absorption within the gastrointestinal tract leads to a relatively rapid deacetylation. In this respect, orally administered diamorphine has the same effects as morphine. Diamorphine has been described as having important advantages over morphine when injections are required and especially when high doses are required (Twycross, 1977, 1982). When administering medications in palliative care through the parenteral route, diamorphine is preferred to morphine because it is more soluble and can be given in a smaller volume. It also causes less nausea and hypotension than morphine.

It is prescribed for acute pain (in myocardial infarction), chronic pain (palliative care, post operative pain), and acute pulmonary oedema and is used both in hospitals/hospices and in primary care settings. Among its most important medicinal use is the treatment of severe and/or intractable pain. Palliative care patients often have poorly controlled pain (McQuillan, Finlay, Branch, Roberts, & Spencer, 1996; Barclay, Todd, Grande, & Lipscombe, 2002). One study found “severe and mostly continuous pain” among 28% of patients in the terminal phase of cancer (Parkes, 1978).

Throughout Britain diamorphine is widely used in the treatment of the terminally ill. It was a standard component of the “Brompton Cocktail,” conceived in 1926 as an elixir for post thoracotomy analgesia by Mr. J.E.H. Roberts, a surgeon at the Brompton Hospital. Its constituents are diamorphine or morphine hydrochloride, cocaine, alcohol, syrup, and chloroform water. Since diamorphine and cocaine have a bitter taste, gin, brandy, tincture of orange, honey, and syrups are used to mask it. In one form or another, this has remained a standard treatment in many hospitals for the past 100 years.

Choice of diamorphine is primarily determined by severity of pain and not by brevity of prognosis (Twycross, 1982; McGettrick & Rodgers, 1996). Subcutaneous delivery of diamorphine, usually in combination with another drug (such as midazolam or levomepromazine), has been a common practice within specialist palliative care units throughout the UK (O’Doherty, Hall, Schofield, & Zeppettella, 2001).
Diamorphine is also used in primary care. Indeed, primary care physicians provide most palliative and terminal care in the UK.

In a study of British general practitioners' prescribing habits and knowledge (Barclay et al., 2002), most general practitioners were found to be familiar with modern techniques for the management of cancer pain, with good awareness of diamorphine as the subcutaneous drug of choice, although there was less awareness of dose conversion from oral morphine to subcutaneous diamorphine.

Diamorphine is used for other purposes in British medicine. For the treatment of acute myocardial infarction, for example, the Oxford Textbook of Medicine recommends that "The most immediate practical procedure ... is to relieve the patient's pain with an adequate dose of intravenous morphine or diamorphine" (Sleight, 1996, p. 2336). Diamorphine has also been used with patients undergoing total hip replacement (Robinson, Rowbotham, & Smith, 1991; Milligan & Fogarty, 1993) and to treat phantom pain after major lower limb amputation (Jahingiri, Jayatunga, Bradley, & Dark, 1994).

Epidural diamorphine was found to be effective in a double-blind study of primigravidae (Daniel & McGrady, 1995). Diamorphine is used for analgesia after Caesarian section (Stacey, Jones, Kar, & Poon, 2001). In a double-blind study of women undergoing elective Caesarian section, diamorphine was found to be safe, and pain scores and other adverse effects were reduced in a dose-dependent manner by intrathecal diamorphine (Kelly, Carabine, & Mirakhur, 1998).

Diamorphine has also been used with newborn infants and with children. Intravenous and subcutaneous diamorphine has been used as an analgesic with children in accident and emergency units (Wilson, Kendall, & Cornelius, 1997) and to treat acute post-operative pain in children undergoing abdominal surgery (Semple, Aldridge, & Doyle, 1996). Intravenous infusion of diamorphine has been found to reduce the stress response in ventilated newborn infants (Barker, Simpson, Barrett, Shaw, & Rutter, 1995).

**CONTROL MEASURES**

In 1912 at The Hague Opium Convention, 34 countries agreed to regulate the manufacture and distribution of opiates, with the United States taking the lead. In 1924 a United States law banning licit diamorphine was passed, but this was often ignored by local authorities. In 1950 The World Health Organization held an inquiry into a global ban on the medical uses of diamorphine. As mentioned previously, the 1956 U.S. Narcotic Control Act banned diamorphine from medical practice across the United States. United States diplomats from the International Narcotics Control Board brought pressure on other countries to follow suit.
PRESCRIBING DIAMORPHINE FOR MEDICAL CONDITIONS

A series of debates took place in 1955 and 1956 in both Houses of Parliament to decide whether to ban completely the prescribing of diamorphine in the UK. At its annual Representative Meeting in 1955, the British Medical Association passed a resolution direct the Council to oppose the drive to ban diamorphine.

At present, in the UK, diamorphine is a Schedule 2 controlled drug governed by legislation under the 1971 Misuse of Drugs Act, the 2001 Misuse of Drugs Regulations, and the 1968 Medicines Act. It may be manufactured or compounded by a licensee, a practitioner, or a pharmacist. A pharmacist may supply the drug to a patient only on the authority of an appropriate prescription where special regulations apply. These concern the handwriting of the prescriber, the dose, the form, the strength of the preparation, and the total quantity in words and figures.

For any British general practitioners who require diamorphine to stock their emergency bag, the diamorphine must be in a locked bag in a locked booth of their car when doing emergency work or stored securely in their practice. They must also keep a controlled drugs record of the date on which they received them, details of the pharmacy from whom received, and the amount and form in which received. Similar details must be recorded when supplying diamorphine. The Home Office inspectorate can request access to the controlled drugs register and examine arrangements for safe custody.

In hospitals, controlled drugs are supplied in response to a requisition from a ward, operating theatre, or other department in a hospital. On the ward, controlled drugs are the responsibility of the senior nurse who is the key holder for the controlled drugs cabinet. Administration of the drug cannot be delegated to any other person.

TREATMENT OF ADDICTION

Both nationally and internationally diamorphine is sometimes known for one of its least common and most controversial uses. In 1926, the Rolleston Committee stated that diamorphine could be prescribed to opiate addicts under certain conditions. Prior to 1965 any doctor could prescribe diamorphine for addiction in the United Kingdom, and the Brain Report (1965) led to the prescribing of diamorphine under special license by clinics. However, except for a short period after the establishment of the drug dependence clinic system (1968-1974), prescribing diamorphine to opiate addicted patients has not been widely practiced in the UK. By 1992, less than 1% of British opiate addicts were receiving prescribed heroin compared to about 98% who were receiving prescribed methadone. Department of Health guidelines (1999) devoted only a single brief paragraph to this issue and stated that as a treatment for opiate addiction, “There is very little clinical indication for prescribed [heroin]” (Department of Health, 1999, p. 57). Current British policy permits the drug to be prescribed only by physicians who have applied for and been granted a special

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Government license. At present, there are about 90 doctors who hold such a license. All are specialists in addiction treatment.

OPTIONS AND OBSTACLES TO FUTURE USE

Outside medicine, and outside the UK, diamorphine is most often thought of as the archetypical illegal drug of addiction. It has been suggested that "there is an undesirable entanglement of medical practice and law enforcement problems arising from the mistaken notion that legal strictures can be devised which apply equally well to the legal and the extralegal use of narcotics" (Lasagna, 1965, p. 58).

In the United States, in particular, it has also been suggested that the present American prohibition of medical diamorphine is immovable and that it would be "almost impossible ... to reintroduce the drug into medical usage" (Lasagna, 1965, p. 59). An attempt was made to reintroduce diamorphine into U.S. medicine in the Compassionate Pain Relief Act. This was defeated in 1985. Current high-profile developments (European trials on prescribing heroin to opiate addicts, recent UK guidelines on prescribing heroin in drug treatment, the NHS review of the legal and regulatory frameworks concerning the prescribing of control drugs by medical practitioners in England due in July 2003, and the role of diamorphine in the Shipman case [http://www.the-shipman-inquiry.org.uk/home.asp]) have again brought this medication under scrutiny. This may involve renewed interest in the introduction of restrictions or prohibitions of its availability and uses in medicine.

In the UK, diamorphine is widely regarded as a useful and effective component of the pharmacopoeia and is the preferred opiate for certain uses, such as subcutaneous infusion (McQuillan et al., 1996, Barclay et al., 2002). The continued medical use of diamorphine in the UK represents an endangered practice. In an area characterized by so much unsubstantiated opinion and incoherent thinking, if diamorphine is to have a future in medicine, this will depend largely upon the accumulation of improved evidence about its applications and effectiveness.

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