

Frank Clifford Rose

The History of the Migraine Trust

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F.C. Rose (✉)

Founding Director,
Academic Unit of Neuroscience,
Charing Cross & Westminster
(now Imperial College) Medical School
e-mail: fcliffordrose@tiscali.co.uk

Late Physician in Charge,
Department of Neurology,
Charing Cross Hospital, London, UK

Abstract The history of a medical charity founded for the purpose of initiating research into the commonest of all human afflictions - headache. Of the 100 causes, migraine is one of the commonest, and in spite of the lack of interest of the medical profession, this review shows how the pace of research rapidly increased as evidenced by the biennial International Symposia of the Migraine Trust

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Introduction

Although migraine has been known since the time of the Ancient Greeks (the term being derived from *hemi-crania* – the Greek for one-sided headache), our knowledge of its causes and treatment is much more recent. The main cause for its long neglect was the failure to consider it a serious disorder, because “everyone has headaches”. Even neurologists, specialists in disorders of the nervous system, gave it scant attention because of their need to deal with more serious, even fatal, conditions; this was in spite of the fact that a quarter of all patients attending neurological out-patient departments are there because of headache. The neglect by the medical profession was such that as a student, both undergraduate and postgradu-

ate, including neurological training, I did not receive *one* single lecture on headache.

Patients were naturally dissatisfied, so it was not surprising when one such sufferer, Peter Wilson, whose migraine started at the age of 12 and continued to his seventh decade, contacted others with the same complaint. In March 1958, encouraged by a pharmacist, George Ball, Peter advertised a meeting for those with migraine in a local newspaper, the *Bournemouth Evening Echo*. The meeting was held in the flat of one of the ten people attending; each contributed £10 so that a group was started with Peter Wilson, a local government officer, as its Honorary Secretary¹. With an announcement of its formation in a national daily paper – the *Daily Telegraph* – another 200 people became involved, including a Nobel Prize winner, well known writers, scientists and several

doctors. By the end of the following year, there were over 1000 members. In 1964 this group of patients formed the British Migraine Association; its purpose was “to encourage the creation of headache clinics and to raise money for headache research” [1]².

Although the British Migraine Association was essentially a patients’ organisation, set up as a charitable trust, the need for more medical input was required and Dr Macdonald Critchley was asked to help form the Migraine Trust, and be the founding Chairman. One of its most important functions was to organise meetings where clinical scientists could regularly review what was known about this complex disorder, stimulate research and report their results.

In the mid-1960s, the British Migraine Association, led by Peter Wilson, approached the Wellcome Foundation for support. Doctor Richard Smith was then working there on pain research and, in association with the College of General Practitioners (before it became Royal), organised a meeting for GPs on migraine, chaired by Macdonald Critchley. Discussions between Critchley and Smith reached the conclusion that “an organisation of sufficient weight” was needed to “gain the attention and support of the medico-scientific establishment” [2]. Smith approached Lord Brain, the neurologist who was then President of the Royal College of Physicians who agreed to lead the effort to create a Migraine Trust. The first Trustees besides Lord Brain were Lord and Lady Snow, Sir Cyril Musgrove (a city financier) and Doctor Macdonald Critchley, with Richard Smith as Secretary. Lady Snow (the novelist Pamela Hansford Johnson) acted as liaison between the Trust and the British Migraine Association. Lord Brain asked HRH Princess Margaret to become the Patron of the Trust, which she graciously accepted.

A fundraising dinner was held at Apothecaries Hall for the first symposium on *Background to Migraine*. Lord Brain passed away at this time and Lord Snow succeeded him as Chairman. At that meeting Sir George Godber, when Chief Medical Officer of the National Health Service, had been criticised because of the absence of special provision for migraine. He asked Critchley for help and this is how the first two hospital migraine clinics began. “For that” Sir George added, “I have always been profoundly grateful to him.”

Background to migraine

The first Migraine Symposium was held in November 1965 at the National Hospital and its proceedings published under the title of *Background to Migraine* [3]. It was at this meeting that the first Sandoz Foundation

Lecture was given by Macdonald Critchley on “Migraine: from Cappadocia to Queen Square” (Table 1). In his introductory speech, the then Minister of Health, the Right Honourable Kenneth Robinson, quoted Ralph Waldo Emerson, “at every stage we lose a foe; at fifty we lose our sick headaches”, which indicated the truth that most forms of headache lessen with age. He then wondered “what the Cappadocians were doing at this gathering”, presumably because he did not know that Aretaeus of Cappadocia was the first to characterise migraine [4].

The interest engendered by this meeting led to a further symposium in the following year with another publication [5]. On this occasion the second Sandoz Foundation Lecture was given by Sir Derrick Dunlop (Scotland) on *The therapeutics of migraine*, which featured ergotamine as the medication for the treatment of acute attacks and methysergide for prevention.

The third Migraine Symposium had as its Sandoz Foundation Lecturer Arnold Friedman (USA) whose title was *The (infinite) varieties of migraine* [6]. These proceedings included three chapters on dietary migraine and tyramine, which proved to be a false trail, but another topic, which proved highly rewarding, was by Professor James Lance of Sydney on serotonin, as it eventually resulted in the triptans being the best treatment for acute attacks.

The fourth Migraine Symposium Sandoz lecture was given by Professor John Cumings on *Migraine – a biochemical disorder?* This volume [7] was aimed at general

Table 1 Sandoz Foundation Lectures

1966	Macdonald Critchley Migraine: from Cappadocia to Queen Square
1967	Sir Derrick Dunlop The therapeutics of migraine
1969	Arnold P. Friedman The (infinite) variety of migraine
1970	John N. Cumings Migraine, a biochemical disorder
1976	John Marshall Cerebral blood flow in migraine
1978	James W. Lance Migraine: an attempted synthesis
1980	Donald J. Dalessio Recent experimental studies on headache
1982	Edwin Bickerstaff Complicated migraine
1984	Maurice H. Lessof Migraine: how much is due to allergy?
1986	Michael Moskowitz Sensory connections to cephalic blood vessels and their possible importance to vascular headaches

practitioners and had a chapter by Dr Marcia Wilkinson on *Migraine as seen in the London City Clinic*. All these four books of the proceedings were entitled *Background to Migraine*, and published by Heinemann, with which Dr Raymond Greene had a close connection³. The fifth (1972) and sixth (1974) biennial migraine symposia had only abstracts and were not published.

Headache clinics

In the UK, headache clinics had been started by Dr Macdonald Critchley at both the London hospitals where he worked, namely King's College Hospital and the National Hospital, Queen Square.

It was in the late 1960s that I was approached by a pharmaceutical company, Sandoz, to undertake a clinical trial on their new migraine preventative drug, known then only as CB105. Having been appointed in 1965 as Consultant Neurologist to the Charing Cross Group of Hospitals, I began a weekly migraine clinic at one of the constituent hospitals in Hammersmith – the West London Hospital. A clinical assistant, Felicity Hartridge, funded by Sandoz, was chosen to help⁴. The trial of CB105 as a migraine prophylactic proved successful and it was marketed by the company as Sanomigran (with the generic name of pizotifen). It proved to have side effects of somnolence and weight increase, which were particularly unwelcome in migraine patients, who tended to be younger women.

Directors of the Migraine Trust

Derek Mullis, who served as Director of the Migraine Trust during its most significant period of growth, began his connection with the trust in 1965. After reading of its founding, he wrote to the then Director offering to raise money, because both his wife and daughter had migraine. Invited to become a member of the Management Committee, he soon became its Chairman, and later joined the Medical Advisory Committee as its one “non-medic” (personal communication). Appreciating that none of the doctors who had consulted his wife for migraine had actually ever seen a patient in an acute attack, he mentioned this at a Medical Advisory Committee and it transpired that 12 out of 16 present were in favour of a clinic for the treatment of acute attacks. Since Mullis had been a Lloyds Underwriter and was familiar with the City of London, he suggested the first clinic should be there because up to a million people worked in the City during the day and

those having an acute attack would be able to be treated in a darkened room, where they would lie down and be treated until recovered.

The first City migraine clinic

A public meeting was held under the chairmanship of Lord (C.P.) Snow, with Sir Barnes Wallis as the main speaker. St Bartholomew's Hospital (Barts) was willing to have the clinic under its auspices as long as there was no financial requirement; through their Special Trustees, the Migraine Trust was given a lease of “two completely broken-down shops in Little Britain”. It was opened in 1970 by the Royal Patron of the Trust, Princess Margaret, Countess of Snowden with Dr Marcia Wilkinson as its part-time Director.

The second migraine clinic

The clinic was an immediate success and had to move to larger premises at 22 Charterhouse Square, which was actually the first house *outside* the City of London. The official opening took place on 17 May 1973 in Ironmongers Hall (where Derek Mullis was a member). Sir Keith Joseph gave the note of thanks; Sir Ronald Bodley-Scott, the Royal Physician, was then Chairman of the Trustees.

Well known personalities became associated with the Trust because they suffered from migraine, e.g., Sir Cyril Kleinwort, who became the Honorary Treasurer and gave the Trust £10 000 each year until he died; other sufferers were the Marquis of Linlithgow, who became a Trustee, as did Judge Argyle (who later preceded me as Chairman). Lord (C.P.) Snow, whose wife had migraine, was succeeded by Sir Thomas Holmes Sellors, a famous thoracic surgeon but without a specific interest in migraine.

In 1972, Mullis as Director and Critchley as Chairman invited me to form another clinic for patients with acute migraine attacks in the West London region. They offered a house similar to the one in Charterhouse Square near Charing Cross Hospital, but I pointed out that, as the New Charing Cross Hospital was being opened, there was ample accommodation available in the hospital. The Hammersmith Area Health Authority accepted “responsibility for the increased number of patients with migraine who would be attending”. The only cost to the Migraine Trust was in providing a Research Registrar. The Lease of 22 Charterhouse Square was for six years and in 1979 (with His Honour Judge Argyle, QC, as Chairman of

Trustees) it was realised that an unacceptable proportion of the Trust's income was "being spent not on research but on patient care which should be the responsibility of the National Health Service". The Trust ceased funding the clinic in the City (which has since been supported by the British Migraine Association and other private funding), and the name of the Princess Margaret Migraine Clinic was transferred to the one at the new Charing Cross Hospital.

In the 1980s research workers at the Princess Margaret Migraine Clinic were awarded the Harold Wolff Award of the American Association for the Study of Headache (AASH) on two occasions for the best scientific presentation of that year. In 1984 the Harold Wolff Award was given at the 26th Annual Meeting of the AASH, held in San Francisco; the paper was on "Metabolic abnormalities in cluster headaches". As Founding Director of the Princess Margaret Migraine Clinic, I was given the Distinguished Clinician Award of AASH in 1986 at its 28th Annual Meeting, held in Chicago.

I became a trustee of the Migraine Trust in the early 1980s and succeeded to the Chairmanship, in which office I remained for 10 years. As Chairman I helped organise the biennial Migraine Trust International Symposia and edited their proceedings⁵.

The Migraine Trust International Symposium (MTIS)

The first designated Migraine Trust International Symposium was held in September 1976 and its proceedings were entitled *Current Concepts in Migraine* [8].

The second MTIS in 1978 was not published, but the third, held in 1980, was published the following year [9]. The first section, consisting of three chapters, was on clinical aspects and included the effect of weather (Per-Olaf Lundberg, Sweden) and cyclical migraine (Seymour Diamond, USA). The Sandoz lecturer was Professor Burnstock, who hypothesised that the underlying mechanisms for migraine were in the nervous control of blood vessels. Edda Hanington postulated a platelet disorder as a cause of migraine. There was a whole section of six chapters on platelet function but the research eventually turned out to be unrewarding. Another new section was on neurotransmitters (chemical messengers), which are still being actively and rewardingly investigated.

The fourth MTIS [10], held in 1982, included a new special lecture named for Professor J.N. Cumings, a past Chairman of the Migraine Trust, and was given by Professor Murray Harper (Scotland) on the blood-brain barrier (Table 2). This named lecture was in addition to the Sandoz Foundation Lecture which, on this occasion, was given by Edwin Bickerstaff on "Complicated

Table 2 Cumings Memorial Lectures

1976	Merton Sandler Monoamines and migraine – fact or fiction?
1978	John R. Vane Prostacyclin and vascular tone
1982	A. Murray Harper Possible role of monoamines, the blood–brain barrier and ATP in the pathogenesis of migraine
1984	Jes Olesen Vascular aspects of migraine pathophysiology
1986	Aristides Leão On the inferred relationship of migraine and spreading depression

migraine" dealing with the permanent complications produced by migraine. A reflection of the current research interest was that Neurochemical Aspects included a dozen chapters. The Symposium was held at Charing Cross Hospital and the number of migraine specialists attending had grown to 250 from 30 different countries. Derek Mullis had by then retired as Director of the Migraine Trust and was followed by Commander Oliver Wright.

The fifth MTIS was held in 1984, again at Charing Cross Hospital. In his foreword to the proceedings [11], Macdonald Critchley quoted Doctor Samuel Johnson "to a man whose pleasure is intellectual, London is the place, when a man is tired of London, he is tired of life, for there is in London, all that life can afford... the full tide of existence is at Charing Cross". At this gathering there were 300 specialists, again from 30 countries. The Cumings Memorial Lecture was given by Professor Jes Olesen (Denmark), on *Vascular aspects of migraine pathophysiology*. Because of the current interest there was an additional section of five chapters on non-drug therapy.

Immediately following the fifth MTIS a series of lectures were held on *The management of migraine* [12]. Intended for general physicians and family practitioners, it presented the considerable increase in knowledge of the many different causes of headaches. Supported by the British Migraine Association and Sandoz Pharmaceuticals, it was intended to help those doctors in primary care who treated one of the most common complaints of mankind.

The biennial International Symposia of the Migraine Trust were not sufficient to satisfy the need for researchers to report their findings. For this reason, the World Federation of Neurology (WFN), at its quadrennial congress held in Kyoto, Japan in 1981, sponsored a symposium under the auspices of the WFN Research Group in Headache and Migraine. The proceedings [13] included seven chapters of research findings emanating from the Princess Margaret Migraine Clinic and funded by the Migraine Trust.

The sixth MTIS held in 1986 had broken new ground, as it had to be expanded from two to three days and the number of participants had increased to over 500, partly due to satellite meetings of the International Headache Society and the WFN Research Group on Headache and Migraine. The last section of the volume [14] consisted of 8 chapters on chronic headache. The Cumings Memorial Lecture was given by Professor Leão (Brazil), the Brazilian neuroscientist who theorised spreading depression was the cause of the migrainous aura. The other named lecture was by Professor Moskowitz (USA) on the trigemino-vascular cause of migraine, where the sensory nerves of the face also supplied blood vessels to the head.

The seventh MTIS was in September 1988 in London and, although it lasted over three days, only a minority of the submitted papers could be given as platform presentations, so that the proceedings ran to over 50 chapters [15]. This book recorded the tremendous increase over the previous two years of knowledge regarding headache and migraine, particularly in neuro-imaging and fresh understanding of chemical messengers (neurotransmitters). Divided into six sections, the first again dealt with clinical aspects, such as the cause of pain in the head and the mechanisms involved in migraine. One of the most important chapters was the International Headache Society's Classification of Headache, which listed over 100 causes of headache on a firmer basis by indicating the precise criteria for diagnosis. This classification, produced by a committee of 12, proved very useful by giving a standardised basis for clinical trials (where one specific type of headache could be used to compare different treatments). It also proved useful in studying the genetic approach to migraine⁶. The second, third and fourth sections dealt, respectively, as was usual, with biochemical, vascular and physiological (functional) aspects, but the fifth covered cluster headache, a condition quite distinct from migraine, because it affects mainly the male sex and begins at a later age than migraine. The attacks last less than a few hours but can be repeated daily for several weeks – hence the term “cluster” headache. The pain is extremely severe and, as the treatment is different from migraine, patients should be seen by headache specialists. The final sixth section on treatment concerned diet, hormones, feverfew, depression and the dangers of too many painkillers.

The eighth MTIS, held in September 1990, was on the occasion of the Silver Jubilee of the Trust. It was the largest meeting of headache researchers ever held, with over 1000 participants. The proceedings [16] consisted of 78 chapters divided into 10 sections. The section on cluster headaches now consisted of 12 chapters with an analysis of different groups, e.g., in different countries and in children (epidemiology). The treatment sessions were divided into prevention (prophylaxis), consisting of 12

chapters, and therapy of the acute attacks (8 chapters) as well as dietary aspects (5 chapters).

In 1992 the ninth MTIS was held at Kensington Town Hall, London and the resulting publication [17], in addition to the usual sections, had expanded on epidemiology (different population groups) and genetics (with four chapters). The Migraine Trust lecture was given on *Recent advances in cluster headache research* by Dr Lee Kudrow (USA). With the introduction of the triptans in 1991, there was increased support from the pharmaceutical industry.

As 1995 was the 30th anniversary of the foundation of the Migraine Trust, a special symposium was held at Leeds Castle, where 24 of the most active international researchers in migraine were invited; the proceedings were published under the rubric of *Towards Migraine 2000* [18]⁷. This four-day conference, in what has been called the most beautiful castle in the United Kingdom, was rewarding in that discussions on controversial topics between the experts continued even during refreshment breaks. It is to reflect these divergent opinions that some of the discussions were included in the publication. It was a great pleasure and honour to have the Patron of the Migraine Trust, Her Royal Highness Princess Margaret as Guest of Honour at the Symposium Dinner.

In considering book chapters based on work at the Princess Margaret Migraine Clinic, Charing Cross Hospital, worthy of mention are three contributions in the volume on headache of the huge multivolume reference encyclopaedia called *Handbook of Clinical Neurology* [19]. These three chapters were on classification (Rose), drug therapy (Peatfield) and trigeminal neuralgia (Illingworth).

The need for the Migraine Trust to inform patients and relatives in simple everyday terms about causes and treatments was soon apparent. This was evidenced by the number of calls to its Helpline and the number of questioning letters received. Lay persons had a differing emphasis, e.g., how to manage migraine without taking drugs. After careful consideration articles on complementary techniques, e.g., acupuncture, were included in the Migraine Trust Newsletter. These articles were criticised by two members of the Medical Advisory Committee on the grounds that they had not been scientifically proven to be efficacious by controlled clinical trials. (Indeed, one member of that committee – a Nobel Prize winner – resigned on this issue.)

It was the need to inform patients that induced the Oxford University Press to publish a book for sufferers. The Migraine Trust's Research Registrar, Doctor Marek Gawel, and I were asked to undertake this task [20]; it is available both in hardback and softback covers. A second edition, much revised, was brought out by another publisher nearly a quarter of a century later [21], which attempted to include the striking advances in layman's

terms. The only changes in chapter headings was an additional chapter on *Post-traumatic headaches* (headaches after a head injury) and instead of a chapter entitled “The future”, some realisation had occurred and the chapter was now “Headache clinics and the future”.

Another registrar attending the Princess Margaret Migraine Clinic (Dr Paul Davies) was instrumental in a book for lay persons entitled *Answers to Migraine* [22]. This was published between editions of *Migraine, The Facts*.

The relationship between clinical trials, researchers and the pharmaceutical companies supporting these endeavours has been much discussed. Obviously the Migraine Trust, in organising symposia, had to draw a clear line between the reported results and the support they obtained in the publications with which the Trust was associated.

An example of this was a Symposium held in 1981 (between the two Migraine Trust International Symposia of 1980 and 1982) at the University of Sussex. At that time the question of lack of oxygen to the brain as a cause of migraine was being investigated. The meeting was under the auspices of Janssen Research Foundation (funded by the Janssen Pharmaceutical Company of Belgium) and the Migraine Trust and their new product of flunarizine was postulated as a preventive remedy for migraine; following several scientific sections of this particular mechanism, I reported on a trial done at the Princess Margaret Migraine Clinic using flunarizine as a preventive of migraine attacks, and my conclusion was that “further studies are required to confirm the drug’s efficiency”. Although flunarizine was much used on the Continent in migraine prevention, it was not often prescribed for this purpose in the UK [10, 23].

Conclusion

The frequency of publications and the numbers of papers offered at each Migraine Trust International Symposium is indicative of the rapid progress made in headache science in those years.

Notes

1. Although he was later offered the post of the first Director of the Migraine Trust, he declined because it would have meant a move to London. Peter Wilson’s dedicated work was recognised officially in 1967 by the award of Member of the British Empire (MBE).
2. The membership now numbers several thousands. In 1997 its name was changed to the Migraine Action Association.
3. He was the brother of the author Graham, a migraine sufferer, and a Trustee.
4. The daughter of Professor Hamilton Hartridge, the famous physiologist, she was a graduate of King’s College Hospital and recommended by Macdonald Critchley.
5. In the 1970s Macdonald Critchley asked me to join the Research Group on Headache and Migraine of the World Federation of Neurology, later to be its Secretary and finally to succeed Macdonald Critchley as its Chairman. The Research Group was limited to 30 international experts and met at the quadrennial meetings of the World Congress of Neurology.
6. Being one of the 12 doctors responsible for The International Headache Society Classification of Headache and Migraine, I was made a life member of the International Headache Society (IHS).
7. This brought the number of books on migraine and headache with my name on the spine to 16, a measure of how often it was necessary to record the rapidly developing research in the disorder.

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