

Aristotle, godfather of evidence-based medicine

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Introduction

Aristotle, one of the greatest minds that ever existed, is indeed the godfather of evidence-based medicine. His teachings of logic and philosophy have been a driving force continuously guiding medicine away from superstition and towards the scientific method. Today, the revival of evidence-based medicine is only a reaffirmation of his early teachings dating from the fourth century BC.

Medicine in ancient Egypt

In ancient Egypt, Imhotep was the god of medicine (Fig. 1). He lived during the third dynasty of ancient Egyptian history between 2650 and 2600 BC, and was the vizier (prime-minister) to the King and priest of the sun god Ra at Heliopolis. Imhotep was the architect who built the oldest still standing stone monument on earth: the stepped pyramid of King Djoser at Saqqara. But he was also a physician and was so clever in treating patients that the Egyptians made him their god of medicine (Shehata, 2004; Mikić, 2008).

Since the early work of Imhotep, ancient Egyptian medicine evolved along the years. Various treatments and therapeutic procedures were developed and recorded in the ancient Egyptian textbooks, written in the form of papyri and many of these medical papyri have survived. The famous ones are the Edwin Smith papyrus, the Ebers papyrus, the Kahun gynaecological papyrus and the London and Leiden papyrus.

But medicine in ancient Egypt was tainted with religion (Risse, 1986). For example, the Ebers papyrus, the largest (110 pages and 20 meters long) and one of the oldest preserved medical documents dating from 1552 BC, describes many diseases concerning the heart and vessels (Fig. 2). It also contains chapters on contraception, diagnosis of pregnancy

and other gynecological matters, intestinal disease and parasites, eye and skin problems, dentistry and the surgical treatment of abscesses and tumors, bone-setting and burns. Mental disorders such as depression and dementia are also covered. However, for most of these diseases, in addition to prescriptions, the papyrus describes some 700 magical formulas and remedies and contains many incantations meant to turn away disease-causing demons (Joachim, 1890; Ebbell, 1937; Cunha, 1949).

Medicine in ancient Greece

In Greek mythology, Asclepius (Asklepios) was the god of medicine (Fig. 3). He was the son of Apollo and Coronis, and the father of Hygea, goddess of health and Panacea, goddess of cure from all ailments. Asclepius had followers for hundreds of years all across Greece and Asia Minor and numerous temples were built in his honor to which the sick would travel for purification rituals and sacrifice. These temples were called Asclepia (single: Asclepion) and the most important were those built in Athens, Larissa, Cnide and in the island of Cos. In the Asclepion, the sick's dreams were interpreted by the priest on site who would also prescribe some treatment. The priests were therefore performing the dual function of priest and healer.

The most famous Asclepion was the one built in Cos, where a famous physician named Hippocrates was in charge. Hippocrates (*ca.* 460 BC-*ca.* 370 BC) grew to become the greatest physician of the classical world and is considered "the father of Western medicine" (Fig. 4). He taught and practiced medicine throughout his life and is credited for founding the Hippocratic School of medicine. He or his followers compiled a great work known as the Hippocratic Corpus (Latin: *Corpus Hippocraticum*), a collection of around seventy early medical works



Fig. 1. — Statuette of Imhotep in the Louvre

from ancient Greece (Chadwick and Mann, 1950; Yapijakis, 2009).

Although Hippocrates work was based on observation of clinical signs and rational conclusions, many of his theories were not based on logic, particularly his theory on “humorism”, which was an extension of the Pythagorean theory on nature. Hippocrates believed that illness was the result of an imbalance in the body of the four humours: blood, black bile, yellow bile and phlegm (*dyscrasia*, meaning “bad mixture”). The person would then become sick and remain that way until the balance was somehow restored. Hippocratic therapy was directed towards restoring this balance. For instance, using citrus was thought to be beneficial when phlegm was over abundant (Garrison, 1966; Doufas and Saidman, 2010).

Aristotle

Aristotle (384 BC-322 BC) was a Greek philosopher and a student of Plato (Fig. 5). He was born in Stageira, Chalcidice, in 384 BC, near modern-day Thessaloniki in the northern Greek area of Macedonia. His father Nicomachus was the personal physician to King Amyntas of Macedonia (McLeisch, 1999).



Fig. 2. — Ebers Papyrus: treatment of cancer

At about the age of eighteen, Aristotle traveled to Athens where he continued his education at Plato’s Academy. He remained at the academy for nearly twenty years until the death of Plato in 347 BC. He then traveled to the court of his friend King Hermias of Atarneus in Asia Minor. When Hermias died in 343 BC, Aristotle was invited by Philip II of Macedon to return to Macedonia and become the tutor to his son Alexander the Great and some of his colleagues including Ptolemy I, the future king of Egypt (Dunn, 2006).

In 335 BC, Aristotle returned to Athens, where he established his own school known as the Lyceum and taught there for the next twelve years. It is during this period in Athens from 335 to 323 BC, that Aristotle is believed to have composed many of his works (Russell, 1972). Much of Aristotle’s writings were lost and the works that have survived are in treatise form and are generally thought to be lecture aids for his students. His most important treatises include *Physics*, *Metaphysics*, *Nicomachean Ethics*, *Politics*, *De Anima (On the Soul)* and *Poetics*.

Aristotle studied almost every subject possible at the time and made significant contributions to most of them. He studied anatomy, astronomy, embryology, geography, geology, meteorology, physics and zoology. He also wrote on aesthetics, ethics, government, metaphysics, politics, economics, psychology, rhetoric and theology and studied education, foreign customs, literature and poetry. His combined works



Fig. 3. — Asclepius, god of medicine in ancient Greece

constitute a virtual encyclopedia of Greek knowledge, but his main contribution to the human mind is, no doubt, the introduction of the concept of “logic”, where all natural phenomena and laws were to be based on common sense (if $A = B$ and if $B = C$, then $A = C$). The adoption of this principle in all areas of knowledge gave a strong boost to the human mind and continues to do so. Twenty-three hundred years after his death, Aristotle remains one of the most influential people who ever lived and leaves every scientist and philosopher in debt to his essential contribution to the scientific method (Durant, 1926; Dunn, 2006).

Alexandria

In 331, Alexander the great conquered Egypt and built the city of Alexandria at the site of the village of Rakotis (Ra-kedet in ancient Egyptian dialect, meaning “Ra builds”) (Sallam, 2001). After the death of Alexander, Egypt came under the rule of one of his generals, Ptolemy I (Soter), whose

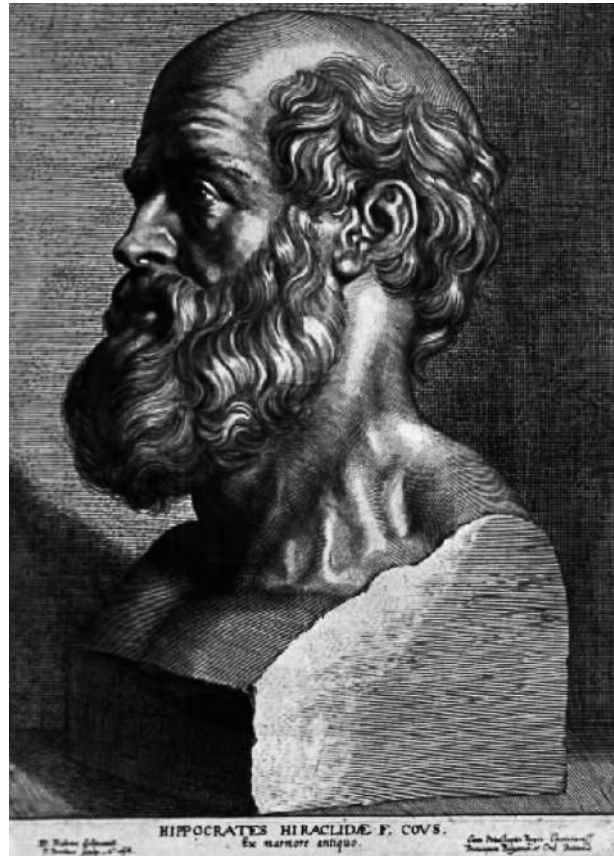


Fig. 4. — Hippocrates, father of Western medicine

descendants, the Ptolemies, ruled Egypt until 32 BC, when Cleopatra VII joined by Mark Anthony, lost the war against Octavios and Egypt became a Roman dependency.

Under the Ptolemies, Alexandria grew in size and importance and became one of the largest and most influential cities of antiquities, second in size only to Rome. At the urging of Demetrius of Phalerum, Ptolemy I established the famous Library of Alexandria and a Museum. Both the Library and the Museum formed the rock stones of the first University in history, where knowledge from the whole universe was kept. At its acme, the Library of Alexandria held about 500.000 to 700.000 books in the form of scrolls (Fig. 6).

From its beginnings, the school of Alexandria was based on the ideas of Aristotle carried over by the founders of Alexandria (Alexander) and its Library (Ptolemy I), both students of the great philosopher. The school of Alexandria (the Hellenistic or new Hellenic school) was therefore the first school of knowledge in history to be solely based on “logic” (i.e. philosophy). Every scientist in Alexandria was a philosopher, meaning that his conclusions were reached on the basis of logic and common sense (i.e. philosophy) rather than superstition or ideas that cannot be explained logically. This concept was later



Fig. 5. — Aristotle

revived during the Middle Ages, where a student would become a “doctor in philosophy” if he reaches his conclusions on the basis of logic or a “doctor in theology” if he builds his theory on metaphysical givens which cannot be scientifically proven.

Famous scientists/philosophers of the ancient Alexandria University included Euclid father of geometry, Heron inventor of the first steam engine, Archimedes the greatest mathematician of antiquity, Erasthenes the astronomer who calculated the perimeter of the earth to the nearest 100 kilometers and Ptolemy father of geography credited with the drawing of the first map of the world (Pollard and Reid, 2007).

The old Alexandria school of medicine

With the establishment of the Library of Alexandria, Ptolemy I (Soter) and Ptolemy II (Philadelphus) invited numerous physicians from Greece and from all corners of the classical world (the eastern half of the Mediterranean Sea) to Alexandria where they studied, practiced and taught medicine. These great physicians brought with them the medical knowledge of the Greek world and supplemented it with many ancient Egyptian medical practices (Ghaliounghui, 1973; Nunn, 1996), but the real contribution of the old Alexandria school of



Fig. 6. — The Ancient Library of Alexandria

medicine was to re-evaluate (critically appraise) the old medical knowledge, keeping only what conformed to the ideas of Aristotle and common sense and purify it from non-logical theories and practices (Saunders, 1963; Kudlien, 1964; Longrigg, 1992). The most famous physicians of the old Alexandria Medical School were Herophilus of Chalcedon, Erasistratus of Chios and Soranus of Ephesus (Vidal, 1985; Acar *et al.*, 2005).

Herophilus was born at Chalcedon in Bithynia and was a grandson of Aristotle. He was a pupil of Praxagoras and Chrysippus, who were among the most renowned philosophers, scientists and physicians of their period. Herophilus was a great anatomist and surgeon, considered to have been the first to dissect the human body systematically and is largely considered as the father of anatomy (Dobson, 1925; Wiltse and Pait, 1998; Strkalj and Chorn, 2008). He discovered at least seven of the cranial nerves and paid particular attention to the fourth ventricle, lying between the cerebellum and the brain stem, which he correctly identified as the main controlling center of the brain (Martín-Araguz *et al.*, 2002). He was the first to describe accurately the confluence of the brain venous sinuses at the occiput, called *torcula Herophili* after his name (Acar *et al.*, 2005). He wrote extensively on all branches of medicine, including ophthalmology, cardiology and obstetrics. He described the thoracic duct, although he did not know its purpose. He wrote the most accurate descriptions of the male and female genitalia up to his time (Sallam, 2001).

Herophilus' observations of the pulse are also outstanding. He observed the pulse and grasped its significance as a gauge for health and disease. He studied the pulse during systole and diastole and noted its rate, strength and regularity. From these measurements, he was able to make medical deductions. One of his classifications “the goat-leap pulse”

still survives. Thus Herophilus, who gave a rational explanation of the pulse, may also be called the father of cardiology. Herophilus was the first to time the pulse with a portable klepsydra (water clock), calibrated for different ages of his patients. He is probably the first physician to bring measurements into clinical investigations (Potter, 1976; Sallam, 2001).

Erasistratus was born on the island of Ceos (Chios) and served at the court of Nicator Seleucus I, first king of Syria (c. 306 to 280 BC). He later went to Alexandria where he worked for many years. His name was linked to that of Herophilus as a co-developer of the school of anatomy in Alexandria (Sjöstrand, 2001). Erasistratus rejected the ancient Hippocratic humoral pathology of the four humours. He agreed with Herophilus that the origin of the nervous system was in the brain and that sensory and motor nerves were separate entities (Tomey *et al.*, 2007). He correctly regarded the brain as the center of psychic functions. He described the liver, bile duct, spleen, kidneys and intestines, and named the trachea. From his study of the liver, he connected hardness of the liver with ascites. From post-mortem examinations, he learned the pathology of pleurisy. Erasistratus used the term “pathology” in reference to many varieties of fever, paralysis, abdominal disease, ascites and gout. He may therefore be considered the father of pathology (Christie, 1987; Wills, 1999).

Contrary to the custom of the time, Erasistratus did not advocate the treating of disease by blood-letting and disliked purgation. In haemorrhage of the limbs, he used compression bandages. He described the tricuspid and mitral valves, and came closer than anyone before Harvey to discovering the circulation of the blood. He is also said to have invented the catheter. In later years, Erasistratus settled at Samos, where he died between 250 and 240 BC (Sallam, 2001).

Soranus was born in Ephesus (near present day Izmir in Turkey) in 98 AD and practiced in Alexandria during the second century AD. Several of his writings still survive, most notably his four-volume treatise on “*Gynaecology*”, and a Latin translation of his “*On Acute and Chronic Diseases*”. He is credited with the first description of the human uterus and with writing “*the Life of Hippocrates*”. Later in his life, Soranus traveled to Rome where he practiced for few years before dying there in 138 AD (Drabkin, 1951; De Filippis Cappai, 1991; Todman, 2008).

Many other physicians worked and studied in Alexandria, before travelling to work in other parts of the Mediterranean. The most notable of them is probably Galen who travelled to Rome, achieved great fame and became the personal physician of

Emperor Marcus Aurelius and his son Commodus (Nutton, 1993; Dunn, 2003; Tomey *et al.*, 2007).

The fall of Alexandria

The medical school of Alexandria was still active until late in the 3rd century AD. However, with the spread of Christianity, the city became the site of numerous revolts, first against the pagan Roman rulers and later between the native Egyptians following their orthodox (Coptic) Christian doctrine and their local rulers following that of the Roman Emperors. At the same time, philosophy was losing ground to the new religious “dogma” and being a philosopher became an unwelcome proposition. In 389 AD, Theophilus Patriarch of Alexandria extracted an edict from Emperor Flavius Theodosius (the Great) where all symbols of the ancient pagan world were to be destroyed. In 391 AD, the mobs attacked these symbols setting fire to most of them, including the Serapeum and the secondary library underneath it, where the great body of books had been transferred (the great fire of Alexandria, 391 AD). By the end of these calamities, much of the human knowledge accumulated throughout the previous centuries was eternally lost, to be rediscovered during the Renaissance (Pollard and Reid, 2007). In 415 AD, the last of the famous Alexandria philosophers, the great mathematician Hypatia was accused of heresy and attacked by the mobs. She was a follower of the school of the 3rd century thinker Plotinus discouraging empirical enquiry and encouraging logical and mathematical studies (Fig. 7). Following one of her public lectures, she was killed and dragged behind her chariot along the streets of Alexandria. Her tragic death marked the beginning of the so called “dark ages” (Dzielska, 1996).

Arabian medicine in the middle ages

Following the death of the Muslim prophet Mohammed in June 632 AD, a wave of expansion spread out of the Arabian Desert. In 640 AD, an Arab Muslim army conquered Egypt and by the beginning of the ninth century AD, the Arab/Muslim Empire extended from Andalusia in Spain to parts of the Far East. In Alexandria and in many parts of the old Greek world, Arab scholars discovered the ideas of Aristotle. Although various schools of philosophy were established in Baghdad, Cordoba, Cairo and Tashkent, Arab scholars considered Aristotle the greatest philosopher of all time. For them, he was the “first teacher”, while their great philosopher “Al-Faraby” was always called the “second teacher” (Fig. 8). His remaining works were translated from



Fig. 7. — Hypatia of Alexandria Hypatia as imagined in a 1908 illustration.

Greek into Arabic and widely read by Arab scholars (de Micheli-Serra, 2002).

Based on the ideas of common sense and logic (the Aristotelian principle), a great cultural wave swept the Arab/Islamic empire. In the field of medicine, physicians were always described as philosophers-physicians and medical knowledge thrived under these circumstances. Many of the physicians in the Arab/Muslim Empire were not Muslims. Ibn Maseweh (Joannes Damascenus, died 875 AD), Yacub ben Ishak el-Kindi (Alkindus, 813-873 AD) and Honein ben Ishak (Joannitius, 809-873 AD) were Christians. Ishak ben Soleiman el-Israili (Isaac Judaeus, 830-932 AD) was an Egyptian Jew. Other famous physicians of the time were Abu Bakr er-Razi (Rhazes, 850-923 AD) who practiced in Rayy and Baghdad, Abul Kasim el-Zahrawi (Abulcassis 912-1013 AD), who practiced in Cordoba and Al-Hosein Ibn Sina (Avicenna, 980-1037 AD) who practiced in Bukhara (in present day Uzbekistan) and Rayy (near modern Tehran). Similarly, Abd el-Malik Ibn Zohr (Avenzoar, 1113-1162 AD) practiced in Seville, Abul-Welid Ibn Roshd (Averroës, 1126-1198 AD) practiced in Cordoba and Mousa ibn Meimoun (Maimonides, 1135-1204 AD), the famous physician

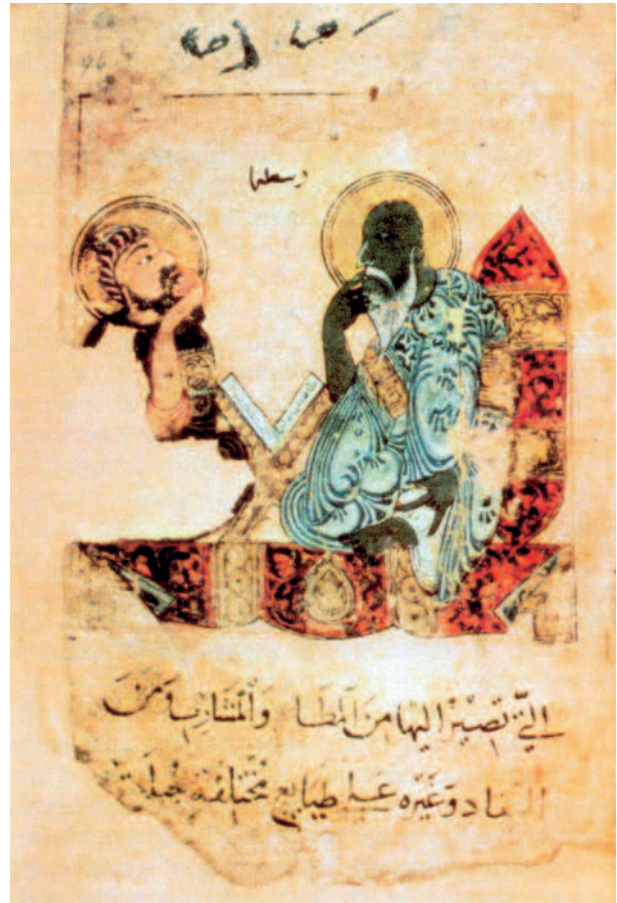


Fig. 8. — Islamic portrayal of Aristotle

and Jewish philosopher born in Cordoba, practiced and died in Cairo (Lindroth, 1999; Mestiri, 200; Martín-Araguz *et al.*, 2002; Courtemanche, 2002; Tan, 2002; Franzin-Garrec, 2003; Urquhart, 2006; Modanlu, 2008; West, 2008; Aciduman *et al.*, 2009).

By the end of the 12th century, history repeated itself and dogma started to prevail again over common sense. The Muslim scholar Al-Ghazali (1058-1111 AD) attacked the great philosopher/physician Averroes (Ibn Roshd) in his book “Incoherence of the philosophers” (*Tahafut al-falasifa*) to which the latter answered by his book “the incoherence of the incoherence” (*Tahafut al-tahafut*). Unfortunately, dogma conquered and the books of Averroes were burned in a public square (Fig. 9). Some of his books, however, survived, notably his important treatises on the surviving works of Aristotle which found their way to the Spanish intelligentsia (Kyle and Shampo, 1976; Tamani, 1994; Front, 2001; Belen and Bolay, 2009).

Medicine in Europe during the Renaissance

Meanwhile in Europe, some of this work was preserved and/or translated from Greek or Arabic to



Fig. 9. — Statue of Averroes in Cordoba

Latin by various Christian monks and physicians, most notably St Isidore of Seville (560-636), St Benedict of Nursia (480-547), Cassiodorus (490-573), Bertharius of Monte Cassino (810-883), Walafrid Strabo of Reichenau (808-849), St Hildegard (1099-1179) and Marbodius of Angers, Bishop of Rennes (1035-1123) (Iorio and Avagliano, 2002; Rengachary *et al.*, 2009).

With time, the Aristotalian principles were reaffirmed and rational medicine started to be firmly established in the new European medical schools. The most famous of these were the medical school of Salerno (*Scuola Medica Salernitana* founded in the 9th century), the University of Bologna (founded in 1088), Oxford University (founded c. 1096), the University of Paris (founded c. 1165), Cambridge University (founded in 1209), the University of Montpellier (founded in 1220), the University of Padua (founded in 1222) and the University of Naples (founded in 1224) (Andrioli and Trincia, 2004).

During the Renaissance, more rational work was discovered and described according to the principles of Aristotle and universities started to differentiate into “religious” and “free”. The most notable physicians of the time were Andreas Vesalius (1514-1564) who was born in Brussels and practiced in Bologna, Padua and Basel, Gabrielis Fallopio (1523-1562) who also practiced in Padua, Ambroise Paré of the Hotel Dieu in Paris (1510-1590) considered one of the fathers of modern surgery and Paracelsus who

practiced in Basel and later in Vienna (1493-1541) (Romero-y Huesca *et al.*, 2005).

Modern western medicine

The seventeenth century saw the expansion of modern Western medicine with the discovery of the circulation by William Harvey, the spermatozoa by Anthony van Leeuwenhoek, the capillary circulation by Marcello Malpighi, the ovarian follicles by Regnier de Graaf, the introduction of the obstetric forceps by the Chamberlen family and the obstetric crotchet by Francois Mauriceau. The Royal Society was also founded in 1660 (Dunn, 1999; Kaufman, 2005).

During the eighteenth century, more scientific advances were made by Edward Jenner who developed the first ever known vaccine, William Smellie, master of British midwifery, William Hunter, the anatomist and obstetrician, André Levret who introduced a more modern obstetric forceps, Jean Louis Baudelocque the famous gynaecologist, Bartholomew Mosse founder of the Rotunda Hospital in Dublin and Giovanni Battista Morgagni, father of modern anatomical pathology (Dunn, 1996; Dunn, 2004; Saliou and Girard, 2005).

During the nineteenth and twentieth centuries, western medicine was permanently established as the leading school of medicine and other medical schools started to follow suite. Important discoveries were made by Robert Koch (1843-1910), Wilhem Conrad Röntgen (1845-1923), Louis Pasteur (1822-1895), Alois Alzheimer (1864-1915), Claude Bernard (1813-1878), Marie Sklodowska-Curie (1867-1934) and Pierre Curie (1859-1906), Joseph Lister (1827-1912), Alexander Fleming (1881-1955) and others.

But despite these developments and the great leaps taken by modern medicine, the practice of medicine was frequently tainted by procedures and treatments based on experience rather than evidence. In every specialty, some of these treatments and procedures continued to be practiced on the basis of tradition, despite the lack of scientific evidence.

Evidence-based medicine

In 1972, Professor Archie Leman Cochrane, a Scottish epidemiologist published his book *Effectiveness and Efficiency: Random Reflections on Health Services* (1972) where he advocated the return to the basic concepts behind evidence-based practice, first formulated by Aristotle (Fig. 10). He criticized the medical profession for much of its practices based on experience rather than evidence and awarded the gynaecologists the wooden spoon. When Cochrane

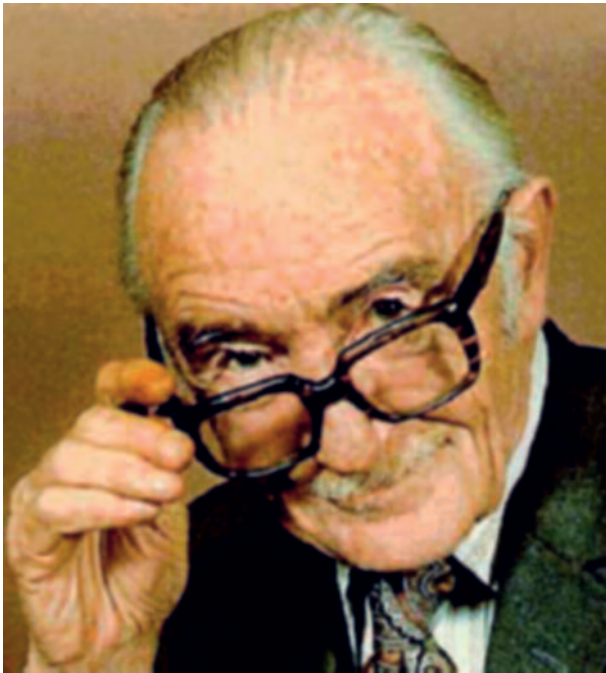


Fig. 10. — Archibald Leman Cochrane

died in 1984, his work was honored by the establishment of the Cochrane Collaboration (Sackett and Rosenberg, 1995; Culp, 2002, Winkelstein, 2009). The explicit methodologies used to determine the “best evidence” were subsequently established by the McMaster University research group (Sackett, 1998). The term “evidence based” was first used in 1990 (Eddy, 1990). The term “evidence-based medicine” first appeared in the medical literature in 1992 (Guyatt *et al.*, 1992). Today, evidence-based medicine has permeated all medical disciplines and the national and international medical bodies have embraced it as the right way of practicing medicine. In many specialties, evidence-based guidelines are continuously being formulated by these bodies and are continuously being updated as new evidence emerges (Sackett, 1998; Sackett *et al.*, 2007). It is therefore only appropriate, at this point in time, to remember that evidence-based medicine is in fact a revival of a concept formulated twenty four centuries ago by the great philosopher Aristotle, father of logic.

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