Introduction

Transplantation – that is, the transfer of tissue from one location to another – as a surgical procedure dates as far back into human history as cave paintings. As long ago as 8000 BC, domestic animals were castrated, initiating the physical juxtaposition of donor and recipient necessary for transplantation. The oldest surgery recorded in humans from the prehistoric archaeological records from the Bronze Age showed skulls from this time being subject to trephination: To relieve intracranial pressure, a circular disc of bone was removed from the calvaria and later replaced as an orthoptic autograft.

Myths and legends from Egypt, China, India and early Christendom illustrate transplantation, the oldest record being 2000 BC in Egypt. One Hindu text (700 BC) explained the procedure of nasal reconstruction in which, after a man’s nose had been cut off or destroyed, the doctor took a leaf of a plant the size of the destroyed parts, measured a piece of the cheek of the same size, and replaced the nasal defect. On this surgical wound would be placed powder of sapanwood, liquorice root and barberry covered with cotton. As soon as the skin had grown together with the nose, the connection with the cheek was cut.

From the earliest times, medical practitioners have sought divine help in their healing endeavours. In the early Christian era, there were four patron saints of medicine, all from Asia Minor and all educated in the Greek medical tradition. They were the apostle Luke, Saints Cosmas and Damian and Saint Panteleimon. Through the centuries, they have served as worthy role models for the physicians who have invoked their aid [1].

At the dawn of the Christian era, there was the popular custom of “incubation” [2]. Sick people would visit the temples of Aesculapius to pray that the gods would heal them as they slumbered. The temple attendants would apply oil and wax to the afflicted body parts and perform surgery if necessary. This was the background of the third-century “miracle of the black leg” (Fig. 1). In the third century AD, St. Cosmas, a physician, and St. Damian, a surgeon, removed the malignant and gangrenous limb of an aged sacristan of the church. While the sacristan slept, these two doctors successfully transplanted the leg of a recently deceased Ethiopian Moor to the leg stump of the dreaming patient [3]. Whilst one brother removed the diseased leg with a saw, the other went to the pagan gladiator graveyard on Vatican Hill at the Circus of Nero where St. Peter’s Cathedral now stands, exhumed the body of a recently buried Ethiopian man, procured one of his legs and returned to the church. The saints joined the Ethiopian’s leg to the dying man’s stump. The sacristan, on waking, discovered he had a new, healthy, although black, leg. The sacristan who lost his leg found this old leg later in the Moor’s grave. Although it is unlikely that the Saints Cosmas and Damian legend was derived from historical fact, it is clear that exper-
mentation with various types of transplants did persist in following centuries. There are archaeological records from Egypt, North and South America, Greece, Rome and China showing teeth transplants as early as 1000 AD.

**Fifteenth to Nineteenth Centuries**

Skin graft prognosis and techniques increased considerably during the fifteenth century. A popular hero of transplantation is Gaspare Tagliacozzi, a sixteenth-century surgeon who restored noses. He is a symbol of the glorious Renaissance after the darkness of the Middle Ages. The Italian poet Calenzio wrote that some slaves donated their own noses to their masters. In the eighteenth century, John Hunter [4], Scottish anatomist and surgeon (founder of experimental surgery) and the so-called father of British surgery, reported effective allografts of chicken testes and Achilles tendon autografts in other species. In 1804, Baronia performed free tendon allografts between sheep, and by 1880, stable corneal transplants in both humans and animals were recorded. By the nineteenth century, free grafts were documented of the following tissues: skin, tendons, nerves, cartilage and corneas.

**Twentieth Century**

Substitution of a healthy organ for a sick or damaged one has always been the dream of surgeons. Such techniques need to unite the transplant with the patient’s system of blood vessels. This obstacle was overcome by French surgeon Alexis Carrel [5] who, in 1902, introduced his vascular suture method, but the initial wave of enthusiasm ran into a basic problem: the guest organ would be rejected by the host organism. The body’s immunity defence mechanism react-
ed against such foreign cells and killed them. The efforts of Carrel and American surgeon Charles Guthrie is described in their work on the “transportation of veins and organs”, and this served as a foundation of both vascular surgery and organ transplantation [6]. In 1905 at the University of Chicago, Carrel and Guthrie performed the first cardiac transplant in animals. The early theory regarding the mechanism of rejection was malnutrition of the grafting tissue, suggested by Paul Ehrlich in 1906 [7].

In the early 1960’s cadaveric donations were thought to be impracticable and impossible and living donors were the only available source of organs for transplantation.

In 1910, Carrel noted that the physiological disturbances in transplanted organs were likely caused by biological factors. Soon after, the Viennese pathologist K. Landsteiner discovered the ABO blood grouping system that eventually led to the introduction of clinical blood transfusion. Sir Peter Medawar, in World War II, transplanted skin on badly burnt soldiers in London [8]. He understood that rejection was not due only to surgical and technical mistakes but mostly to the immune response. Without biological compatibility between the donor and the host, the transplanted organ would undergo failure. He was awarded the Nobel Prize for his pioneering work.

In 1914, the fact that lymphocytes infiltrated grafts was recognised, but it was many years before the molecular basis of T-lymphocyte activation was known as the cause of acute rejection. This knowledge of immunology led to the first successful kidney transplant between identical twins in 1954, and this initial work in the field began with the recognition that organ allografts may be transplantable. In this vein, skin grafts performed by Medawar during World War II for burn victims were successful only when performed between identical twins.

**History of Hand Transplantations**

In 1964, a hand transplant was attempted in South America with primitive immunosuppressive agents. The transplant was rejected at 2 weeks. On 23 September 1998, the first hand transplant with early success was performed on a New Zealand patient in Lyon, France. However, the hand was later amputated in the United Kingdom in February 2001 at the patient’s request. It was reported that the patient failed to follow the correct antirejection treatment and physiotherapy. In January 1999, the Louisville hand and microsurgery team in the USA carried out their first hand transplant. Their patient continues to do well, gaining strength, control and range of movement of his new left hand. In September 1999, two single hand transplants were reported from China, and since then there have been many more around the world.

**Now Back to Saints Cosmas and Damian**

Who were Cosmas and Damian, and why are they relevant to the history of hand transplantation? Cosmas and Damian are regarded as the most famous of all medical saints. They were Arabian twin brothers, the first children born in
a family of 7 boys in Cilicia, Turkey. Like their parents, they were strongly committed to the Christian faith. They were convinced that the Holy Spirit called them to study medicine. They practiced not only in the city of Aegaea, now Ayash (Ajass), on the Gulf of Iskanderun in Cilicia, Asia Minor, where they attained a great reputation, but also travelled widely, tending not only to suffering humanity they encountered along the way but also to beasts of burden. They devoted themselves to healing rich and poor alike, accepting no payment for their medical services, thus earning their title of anargyroi, the “Silverless Ones” [11]. Their example established four tenets of proper conduct for the physician: to neglect no one suffering infirmity, to apply suitable treatment, to inflict no harm and not to demand excessive fees.

Artists portray them as youthful, beardless and wearing long, fur-trimmed robes and red caps (Fig. 2). They hold medicine boxes, urine glasses, mortars, salve spatulas and other items used by contemporary physicians living in the time of these artists. Although pictures of the saint healers representing Cosmas and Damian can be found in many churches, the oldest picture is said to be in the church situated in Densus. This picture is important because one of the saints holds a small portable medical pouch in one hand that seems to be made of wood, and in the other, he holds a spoon used to administer the medicine of the time, usually pills or bolus. Many saint healers have been painted in churches but they do not have such utensils.

So popular were the brothers that in antiquity, numerous Christian doctors took the names Cosmas or Damian. During the Crusades, a group of knights formed the Cosmas and Damian Order to assist ill pilgrims and to exchange prisoners of war. Among the cities selecting the brothers as patron saints are Florence, Prague, Salamanca and Essen, as well as the country of Bohemia. They became the patron saints of physicians, surgeons, barbers,
physicists, bakers and apothecaries, and representations of them are found in the coats of arms of medical bodies to the present day. Their numerous healing successes were regarded as miracles, and their example inspired many to embrace Christianity. The emperors Diocletian and Maximian were so concerned about the influence Cosmas and Damian were having against the ideas of the Roman Empire that when the saints refused to give up their faith, they were arrested by Lisia, the governor of Aegea, and put on trial in the court of Caesar and sentenced to death by three tortures. The first torture was being cast into the sea with their hands and feet bound. A miracle occurred as they became free, enabling them to swim to shore. The second torture was burning at the stake, but a second miracle occurred as the flames failed to burn them. The third torture was by flogging but the whips would not hit their mark. After a final demand that they renounce their Christian faith was refused, Cosmas and Damian were decapitated by the sword on 27 September, 287. Their death is depicted in the famous angelic panel in the monastery of St. Mark in Florence (Fig. 3). The holy doctors were buried in a magnificent tomb in Ciro, Syria, the home of Bishop Teodoreto, their first biographer, who eulogised them in the famous Heroes and Glorious Martyrs [12].

After the deaths of Cosmas and Damian, there was a continuous procession of pilgrims and sick people to visit their grave to petition them to intercede with God to heal their afflictions [13]. When Emperor Justinian (527–565) was healed of his grave and debilitating disease, he had an exquisite basilica erected at the grave site in Constantinople, and he fortified the entire city [14]. Pope Felix IV (526–530) established a church dedicated to Cosmas and Damian in the Roman Forum built by Vespasius in Constantinople [15]. It was

**Fig. 3.** The martyrdom of the sainted physicians Cosmas and Damian, as envisioned by Fra Angelico in a painting from the predella of the San Marco altarpiece (c. 1438-1440). The Louvre, Paris
here that Galen himself taught and wrote his commentaries on the Hippocratic text in 169 AD. The aps of the new basilica was decorated with mosaics that are now considered to be one of the most unique and best-preserved examples of Byzantine art. The inscription reads: “To the medical martyrs the hope for the salvation of the people”. An eighth-century fresco in Santa Maria Antiqua in Rome also highlights Saints Cosmas and Damian. Hans Suss von Kulmbach, a late Middle Ages artist (1480–1522), depicts them as the patrons of doctors and pharmacists on two altar wings in Nuremberg, Germany. Fra Angelico (c. 1401–1455) painted their crucifixion as well as the famous leg transplant scene (Fig. 4). They also are shown as helpers during the plague in a painting by Titian in Santa Maria della Salute, Venice (Fig. 5). In Essen, woodcarvings of Saints Cosmas and Damian show them holding salve boxes and swords.

Cosmas and Damian are the patrons of the city of Gaeta in Italy, and it is believed, through their intercession, the city’s population was spared during the eighteenth-century plague. Cosmas and Damian were also very important to the Medici family – they became the family protectors. They were more than personal symbols of the Medici because they fulfilled the purpose that all saints do for Catholics, serving as spiritual mediators or, in effect, representatives of the family in heaven. The Medici were concerned with exposing their souls to as many prayers as possible, and they had built the Medici chapel of Cosmas and Damian in San Lorenzo, Florence.

A close connection between religion and medicine existed amongst primitive peoples in early civilisations. With the spread of Christianity, medicine became the concern of the priestly cast, and one of the first principles of Christianity was the healing of the sick [1]. Investigation into natural causes of the diseased was discouraged. Treatment at the time consisted of being quiet and restful in a peaceful atmosphere, with intercession and prayer and the cult of healing saints. Churches and shrines dedicated to certain saints and martyrs became places of pilgrimage. A patron saint was regarded as having the power to relieve afflictions of a particular organ or part of the body. St. Agatha was concerned with diseases of the breast, Saints Sebastian and Roch were the saints of the

Fig. 4. Saints Cosmas and Damian, seen caring for an amputee in this late sixteenth-century painting by Ambrosius Francken the Elder, had numerous miraculous cures attributed to them and later became patron saints of the healing professions. Koninklijk Museum voor Schoen Kunsten, Antwerp
plague, St. Blaze the patron saint of the throat, St. Apollonia the patron saint of toothache and Saints Cosmas and Damian the patron saints of barbers, surgeons and apothecaries. Later, the practice of surgery was forbidden to priests and therefore passed almost entirely into the hands of barbers and other uneducated men although there were always a few surgeons of high rank who attended to royalty and the nobility.

Cosmas and Damian, apart from being represented on the coats of arms of medical bodies, have hospitals, monasteries, schools and chapels dedicated to them around the world. The Society of Saints Cosmas & Damian is an Italian/American organisation formed in 1926 during a period of heavy immigration to America by many Europeans. A large group came from the beautiful coastal city of Gaeta in Italy and settled in Cambridge and Somerville in Massachusetts in the USA. These immigrants had a sense of community belonging, and a small group of women, encouraging this, met periodically to pray to these patron saints of their beloved city of Gaeta. Soon the group grew bigger and involved men, and it became a yearly festival to honour these saints in 1926. A chapel to house the life-size statues of the two saints, which had been brought from Gaeta, was built in 1940 in East Cambridge, and it underwent major renovations in 1995. The feast day of Cosmas and Damian is celebrated on 27 September.

**Conclusions**

The possibility of successful organ replacement has challenged men’s minds through the ages: Greek Chimera, the Minotaur, the wings of Daedalus and Icarus, the dragon, the gryphon, the sphinx and the siren. The dream of the Ancients from time immemorial has been the junction of portions of different individuals, not only to counteract disease but also to combine...
the potentials of different species. This desire inspired the birth of many mythical creatures, which were purported to have capabilities normally beyond the power of a single species. The modern world has inherited these dreams in the form of the sphinx, the mermaid, and the chimerical forms of many heraldic beasts [16]. The Hindu pantheon has become the object of surgical reinterpretation; the chimeric state of certain Asian gods, such as Brahma, is endowed with many arms as well as heads or faces.

It is unlikely that the legend of Cosmas and Damian derives from historical fact, but experimentation with the various types of transplants did persist in the following centuries. There is no way that the transplanted black leg could have survived when reattached to the aged sacristan. Cosmas and Damian would not have had the prerequisite vascular suture technique or immunosuppressive agents, but this legend is incorporated into transplantation medicine, if not as an actual precedent, at least as proof that the idea has existed for a long time. Transplantation existed first as a legend, but now surgery is about to make the dream come true with the advent of chemotherapy immunosuppression mercaptopurine (6-MP) in 1960, azathioprine by Joseph Murray in 1963 and cyclosporine A in 1976 [9].

Reference to Saints Cosmas and Damian even has a twentieth-century application. When a newspaper reporter asked if the Massachusetts General Hospital claimed priority for the restoration of a young boy's severed arm, the hospital spokesman referred the reporter to the Syrian surgical team of Saints Cosmas and Damian and the legend of the transplanted leg.

The dream of humankind is now being fulfilled [17]. Depicting themselves as the legitimate heirs of Saints Cosmas and Damian, fifteen centuries later surgeons of today can pursue the historiographical tradition of representing themselves as the new divine healers. Saints Cosmas and Damian are thus enrolled as allies.

References

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