# I Early Transplantation

**O** EARLY HUMANS, as to all their descendants, the possibility of restoration of lost or mutilated parts of the body was a lively issue. To make good such losses incurred by war, disease or punishment, ancient humans had recourse to local help and healers. But they also looked for supernatural help, because legends told them that such powers could be used to make the injured part whole again. And there may have been an additional imperative to ancient humans to be restored to normal. If after death the body went in a mutilated, deficient state to the afterworld, subsequent resurrection was deemed to be impossible.<sup>1</sup> This belief persists in some cultures to this day.<sup>2</sup>

#### Ancient Legends of Replacement

Stories of successful magical replacement of lost tissues are found in the themes of folklore from all parts of the ancient world. The tales of restoration of lost limbs or eyes, and even replacement of decapitated heads, are hardly less popular in ancient lore than the raising of the dead or magical cures for paralysis or blindness. These transplant claims are found in the legends of all nations, from Iceland to Africa.<sup>3</sup>

The tales fall into a number of patterns. An arm, hand or leg, or eyes have been lost. The sufferer is in some way worthy of cure, and a priest or shaman successfully restores the necessary part, but, in other stories, less noble forces are at work. In one variant, villagers capture malevolent marauders and cut off their heads, but new heads grow again immediately, and the raiders continue to attack. In other accounts, an attacker's freshly removed head is replaced immediately, but at an angle, resulting in a permanently twisted neck. In other versions, the head is replaced back-tofront, adding to the terror of the appearance of the restored bandits.

Irish and North American Indian transplant stories tell of a juggler given the power to remove his own eyes a specified number of times, and, having exceeded his quota and thus lost his own, he uses animal eyes to replace the lost globes. In a splendid Irish legend about Nuada, an important ruler who loses a hand in battle, there are many familiar themes: According to Celtic custom, no maimed person could rule, and Nuada was removed from power. But who should turn up on his doorstep but Miach, a celebrated physician. After impressing the half-blind doorkeeper by replacing his bad eye with a good one from a cat, they easily gained access to Nuada himself....

Miach had Nuada's own long-since buried hand dug up and placed on the stump. Over it, Miach chanted one of the best known of old Gaelic charms, enjoining each sinew, each nerve, each vein, and each bone to unite, and in three days the hand and arm were as if they had never been parted....

Ever afterwards the poor doorkeeper's cat's eye stayed awake all night looking for mice.<sup>4</sup>

Traditional tales from China even relate to heart transplantation. In one, Judge Lu assists an illiterate man by giving him a new heart "picked in the nether world from among thousands of human hearts." In another, the Chinese doctor Pien Ch'iao exchanges the hearts of two men to "match their energies better" and uses "potent herbs" to ensure success after the operations.<sup>5</sup> Less dramatically, Hua T'o, the talented "surgeon of the Three Kingdoms," is able to remove, wash, and replace defective intestines.<sup>6</sup> Greek legends recount that the Graiai were sea goddesses who lacked teeth and eyes but successfully passed one of each between them for use. On the utopian island described by Iambulus around 100 BCE were tortoises whose blood had a glue powerful enough to reattach severed body parts. In Apuleius's circa AD 160 Latin retelling of the Greek tale *The Golden Ass*, the hero's nose and ears are removed by witches and then replaced with wax.

These early stories feature the first ethical dilemmas of transplantation. In one, a goddess switches the heads of a married man and his brother. Which part, the tale asked, was now the real husband—the body or the head? Less ethically complex was Zeus's action in stitching the doomed, premature baby Dionysus onto his thigh until the child grew bigger and was ready to be born. A later tale, surviving to medieval times and collected by the brothers Grimm, told of a transplant that transferred the donor's personality: a hand transplant from a thief makes the recipient turn to stealing.

#### **Chimeric Monsters**

Another class of legend testified to the possibility of fusing tissues from different species to produce hybrid beings.<sup>7</sup> Ancient humans harbored a lively belief in the centaur (half man, half horse) and in other fusions that resulted in dragons, griffins, mermaids, Pegasus the winged horse, the Minotaur, and the Sphinx.<sup>8</sup> Hittite temple carvings depict some fierce composites with the head of a man, body of a lion, and wings of an eagle. The young Hindu god Ganesha, son of Shiva and Parvati, gained a new



The hybrid "mantichora" shown in Edward Topsell's *Historie of Fourefooted Beastes* (London, 1607), 344. Image courtesy of Glasgow University Libraries Special Collections.

animal head after decapitation by his angry father. Repenting of his act, the father told his servants to obtain the head of the first living being they could find, which was an elephant.<sup>9</sup> In ancient Greece, the fire-breathing Chimera (part lion, part goat, and part serpent) was the alarming creature of *The Iliad* that terrorized ancient Lycia in Turkey before the heroic Bellerophon destroyed it. The unpleasant lamia was a female who was part snake, and the harpies were ugly, winged birdwomen who stole food and abducted humans, while the manticore had a man's head, the body of a lion, and a scorpion's tail. The myths about these creatures suggest that most were aggressive and unpleasant, but others were more kindly, notably Chiron, the wisest of the centaurs, who was teacher and mentor to the young Aesculapius, Greco-Roman god of medicine.



Christ replacing the lost ear of the servant of the high priest, cut off by Simon Peter. From *The Arrest of Christ*, by the school of Dirc Bouts. Image courtesy of Rheininsche Bild-Archiv.

These tales merged slowly into the earliest science-fiction writings, and, in the fourteenth century, Sir John Mandeville's *Travels* (which leaned heavily on the works of Pliny the Elder) told his credulous readers about men with the heads of dogs, men with horse hooves, and lions with eagle heads.

## The Power of the Saints

Although such fantastical tales were common across many different lands and cultures, the Christian involvement in tissue replacement in the Western world is perhaps best known.<sup>10</sup> The New Testament is replete with healing incidents because Christ had exhorted his disciples to go forth "two by two, preach, cast out devils and heal the sick." Christ himself, as an act of forgiveness, miraculously replaced the high priest's servant's ear, cut off by Peter during Christ's arrest.<sup>11</sup> Tradition holds that Saint Peter, who witnessed this reattachment,

later accomplished a similar restoration of the breasts torn from Saint Agatha during her torture. Thereafter, a number of miracles of hand replacement were taken as credible then, but subject now to skeptical analysis. For example, Saint Mark, late in the first century, was said to have replaced a severed, mutilated hand. A legend from the fifth century holds that Pope Leo punished himself by cutting off his own hand and that Mary, Mother of Christ, appeared to him in a dream and reattached it. When Leo, emperor of Constantinople, falsely accused Saint John of Damascus (AD 645–750) of treason, he then ordered John's right hand to be amputated. This was reported as done, and John carried his severed hand to his oratory and slept, but after sleeping awoke to find the hand replaced and healed. Some cynics immediately accused him of fraud and claimed that the hand had never been lost and that by bribery he had averted the mutilation. John was ordered to show his right hand for assessment at the court, and the surface of the hand showed a convincing scar.<sup>12</sup>

## Later Saints' Miracles

Although the cult of cures surrounding Christian saints was to continue, in the next few centuries the pattern of such miraculous intervention changed. Instead of obtaining healing through personal encounters with

itinerant holy men, believers began to seek "posthumous" healing from long-dead saints. Religious authorities encouraged the public to visit saints' places of birth or burial to seek a cure. The Church began to invest in shrines to the saints in many churches and cathedrals throughout Europe. If a reputation was gained for healing, it brought pilgrims, penitents, and income to the institution.<sup>13</sup>

Individual saints even became credited with very specific healing powers long after their own deaths. According to the belief, around the year 1150 the spiritual intervention of the twin saints Cosmas and Damian resulted in a successful leg transplant.<sup>14</sup> Little is actually known of the lives of Cosmas and Damian except that they were martyred in Syria during the Diocletian persecution in the second half of the third century. The shrine where the miracle took place was in Rome, far from their homeland (which may have been Arabia), many centuries after their deaths. A written account of the miracle appeared about one hundred years after its supposed occurrence, and thereafter the event gained fame and evoked many paintings and other representations of the event: few other single miracles have such a rich iconography.<sup>15</sup>

The cult of Cosmas and Damian increased from the sixth century onward, and they were elevated as particular patrons of medical practice. Numerous shrines to them were built, and artists generally depict them as physician and surgeon. In Rome alone, three churches were dedicated to them, in that part of the Forum traditionally associated with medicine, and the miraculous leg transplant probably occurred at a church erected by Saint Felix, pope from AD 526 to 530, one filled with brilliant mosaics of the two saints. According to the legend, the worthy sacristan of that church had a cancerous growth of the leg. As it was customary for those seeking healing during pilgrimage to use votive "incubation," that is, to sleep in the sanctuary, the sacristan did so. During the night, the saints appeared to the sacristan in a dream and replaced the diseased limb, using the leg of a recently buried black Ethiopian gladiator who had died the preceding day and been buried two miles away. The cancerous leg was thoughtfully retained by the saints to bury



Cosmas and Damian, the twin Christian saints with a reputation for healing, died as martyrs about AD 303, and people visited shrines to these saints hoping to be cured. As in this wood engraving, Cosmas and Damian are often shown as physicians or apothecaries. Some artists depicted them as surgeons. Image courtesy of Wikimedia Commons.

with the donor's remains, thus allowing for the resurrection of a body that was whole.<sup>16</sup>

The story is given with fanciful detail in *The Golden Legend*, Caxton's English translation of an earlier compilation of such miracles. The two saints conferred, and

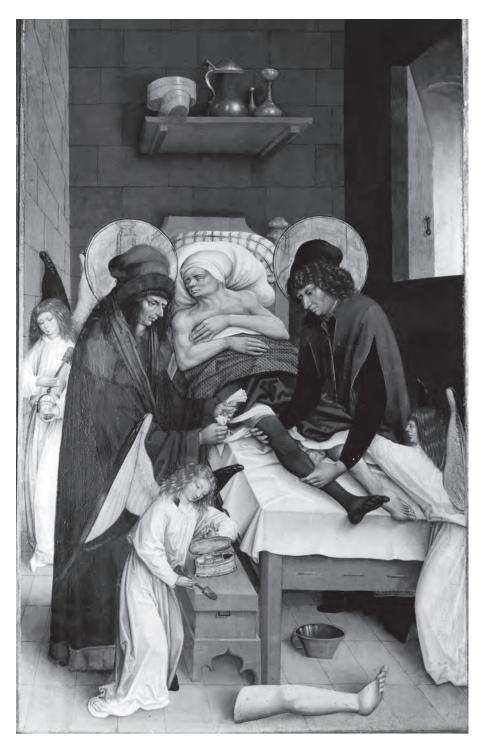
thenne the other sayd to him, "There is an ethyopyen that this day is buryed in the chirchyerd of saynt peter ad vincula whiche is yet fresshe, late vs bere this thyder and take we out of that moryans flesshe and fyll this place with all." And soo they fette the thye of this dede man, and cutte of the thye of the seke man and soo chaunged that one for the other. And when the seke man awoke and felt no payne, he put forthe his honde and felte his legge withoute hurte, and thenne tooke a candel and sawe wel that it was not his thye, but that hit was another. And when he was well come to hym self, he sprange oute of his bedde for ioye and recounted to al the people how hit was happed to hym, and that whiche he had sene in his slepe, and hou he was heled. And they sente hastely vnto the tombe of the deede man, and fonde the thye of hym cutte of and that other thye in the tombe in stede of his.<sup>17</sup>

Other Christian saints performed similar but less celebrated miracles. In the thirteenth century, Saint Anthony of Padua (1195–1231) was credited with reattaching a severed leg. In Irish hagiography there are also a number of examples of lost tissue replaced after the intervention of the saints. In one well-known account, Saint Ciaran restored the decapitated head of an Irish chief, but with less than perfect alignment, since the head remained twisted thereafter.<sup>18</sup> English pilgrimage sites also reported miraculous tissue restoration. At Worcester in 1200, Saint Wulfstan was said to have cured a man whose eyes and testicles had been removed as punishment. At Canterbury, site of Thomas Becket's martyrdom, a sleeping penitent's liver was taken out, cleansed, and replaced. Becket is also credited with restoring the losses of a cleric castrated by a jealous husband. This event gave the wits of the day their chance for satire:

Sublustri rutilans allusit abyssus abysso, Cura, teste nova, testiculisque novis.<sup>19</sup>

The thrust of the text is that the chaste cleric, though restored, should have no use for new testicles.

In general, these reported miracles and the earlier legends had moral content and served to instruct: the lessons were that divine healing in general, and organ replacement in particular, was possible, but only under some conditions. It was helpful that the penitent's illness or injury was unsought and unfair, but above all, the sufferer had to be worthy and deserving of such intervention.<sup>20</sup> These arguments about who was worthy of such miraculous healing were to reappear when organ transplantation began to be an accepted medical procedure.



Leonberg's depiction (circa 1500) of the miraculous replacement of a diseased leg by the posthumous intervention of the saints Cosmas and Damian at a shrine to their honor in Rome. Image courtesy of Württembergisches Landesmuseum, Stuttgart.

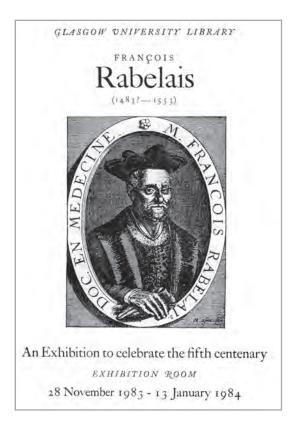
#### Decline of Magic

By medieval times, belief in magical cures was in decline, affected by the secular learning and rise of humanism; after all, the texts from ancient Greece carried no accounts of miraculous healing. Fewer individual priests claimed personal powers of healing, and routine visits to shrines began to decline. Stories of the replacement of body parts diminished in frequency, and only modest claims for magical regeneration, rather than transplantation, remained.<sup>21</sup> Supernatural grafting could now be ridiculed, and François Rabelais (1483?–1553), the Renaissance polymath and priest-turned-doctor, could now invoke only secular surgical methods in his satirical description of the successful replacement of a severed head in *Pantagruel* (1534):

Having gone out to search the field for Episthemon, they found him stark dead with his head between his arms all bloody. But Panurge said, "my dear Bullies all, weep not one drop more, for he being yet all hot, I will make him as sound as ever he was." In saying this, he took the detached head, and held it warm fore-against his cod-piece that the air might not enter into it, and the other two carried the body. "Leave off crying," quoth Panurge, "and help me." Then he cleansed the neck very thoroughly with white wine, afterwards he anointed it with I know not what ointment, and set it on very just, vein against vein, sinew against sinew, and spondyle against spondyle, that he might not be wry necked: this done, he gave it round about some fifteen or sixteen stitches with the needle: suddenly Episthemon began to breathe, then opened his eyes, yawned, sneezed, and afterwards let out a great fart.<sup>22</sup>

His use of the antiseptic white wine is laudable, as is his support for speed. Two aspects of Rabelais's surgical mindset are interesting. First, he assumes that reunion of bulky tissues, when placed together, will occur by end-to-end union, notably of the divided blood vessels. Second, he believes that such detached grafts should be kept warm before attachment. These assumptions were durable and were widely affirmed later. The first lasted until the mid-1800s, and the second, namely, the view that for organ grafting "warm is good," lasted until the mid-1900s.

Despite the decline of belief in magical cures, credence in transcendental healing had not entirely disappeared. In late medieval times, a lively belief in the devil intensified, and it was understood that the evil powers of black magic could be called up by some for the infliction, or cure, of disease.<sup>23</sup> Humble citizens thought to be using such aid could attract accusations of witchcraft, and the activities of learned men were also watched. Transplantation of tissues had until then been associated with *acceptable* supernatural powers, but now those medieval surgeons who cautiously attempted even skin grafting had to watch out for their reputations. Gaspare Tagliacozzi, the first known Western surgeon to use con-



François Rabelais, doctor, scholar, and author, used the myths of head replacement in his epic tale *Pantagruel* (1534). Image courtesy of Glasgow University Library, Special Collections.

ventional methods of plastic surgery, suffered posthumously as a result of gossip from his rivals, who claimed that he had used evil influences.

## The Remaining Legacy

One aspect of the age of miracles and magic cast a long shadow over tissue transplantation that extended almost to the twentieth century. The tales of successful human grafting and the belief in hybrid animals meant that the public remained deeply conditioned to believe that transplantation of tissue from animals to humans or from one person to another could succeed. Even though the notion of miraculous grafting was increasingly discredited, the possibility of successful grafting using ordinary surgical methods remained. It was not until the twentieth century that the ancient "default" belief that humans could readily accept foreign grafts was reversed, and then only with difficulty. A paradigm shift to the notion that rejection was the rule following all living grafts—both homo-

grafts (from other people) and xenografts (from animals)—was remarkably slow to emerge and difficult to establish.

However, there had also been some early, secular, nonmagical surgical tissue replacements, using skin flaps moved from one part of the body to another (autografts). Skilled operators did these procedures far from Europe, and their methods did not reach Europe until the Renaissance.

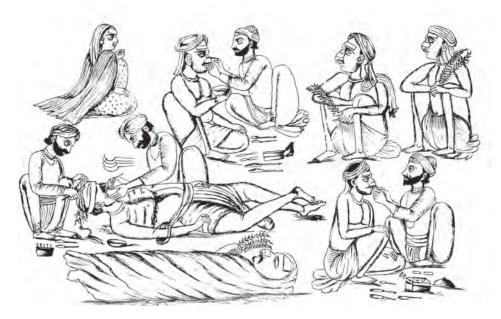
#### Early Plastic Surgery in India

One of the world's oldest medical texts describes plastic surgery. The Hindu Sanskrit text *Suśruta Samhita*, of about the sixth century BCE, describes restoration of damaged ears or noses by methods similar to modern reconstructive surgery.

The tradition is that Suśruta was a surgeon, teaching at Benares in India.<sup>24</sup> His approach to tissue replacement in the face was to create a local skin flap, rotate it to cover the defect, and fix it in place. The operation may have been of some antiquity, and when it was discovered still in use in India in the nineteenth century, it initiated the rapid emergence of plastic surgery in Europe.<sup>25</sup>

The ancient Indian operations were used for those disfigured not only by disease but also by violence or warfare, notably when sword wounds damaged or excised soft tissue from the head and face. In addition, some sufferers had received mutilation in civil feuds or as revenge, or as judicial punishments for serious crimes. Ruthless rulers would deal with threats to their power by mutilating the faces of their opponents, notably by removal of the nose.<sup>26</sup> Such injuries humiliated the victim, equating them with criminals, and would also leave them defective and handicapped in the afterlife.<sup>27</sup> The practice may have been widespread; facial mutilation was common in Chile up to the time of the Spanish colonial period and has persisted to this day in Afghanistan.<sup>28</sup> In Peru, pre-Inca Chimú pottery images placed in the graves of distinguished persons showed evidence of such facial injuries.<sup>29</sup> A Roman fort in Scotland was found to have a collection of human hand and foot bones, doubtless removed from local insurgents to discourage their fellows.

In Asian cultures, a less dramatic deformity of the ear was not caused by punishment but by the use of beautifying heavy earrings or fenestrating ornaments, which intentionally stretched the lobe but could split the thin ring of skin. *Suśruta* gives an elaborate typology of such defects.<sup>30</sup> If local repair of the ear deformity was not possible, the surgeon attempted complete replacement of the ear lobe. The operative detail in *Suśruta* is scanty, but the approach was clear: "A surgeon well-versed in the knowledge of surgery should slice off a patch of living flesh [skin] from the



The ancient Indian plastic surgical procedures were illustrated in use late in the nineteenth century in B. H. Baden-Powell's *Handbook of the Manufactures and Arts of the Punjab* (Lahore, 1872).

cheek of a person devoid of ear-lobes in a manner so as to have one of the ends attached to its former seat. The part, where the artificial ear-lobe is to be made, should be slightly scarified and the living flesh, full of blood and sliced off as previously directed, should be adhesioned to it."<sup>31</sup>

The principle involved in the surgery is clear, and the operative detail is convincing. A "rotation" flap was used, namely, one with its base remaining attached in its original position and, hence, still supplied by the original blood vessels. After moving the free end and fixing it, sometime later the base and the original blood supply could be safely severed.

The *Suśruta* is best known for its description of the method of restoring damaged noses. The following passage describes the operation, which was again a rotation flap from the cheek:

Now I shall deal with the process of affixing an artificial nose. First the leaf of a creeper, long and broad enough to fully cover the whole of the severed or clipped off part, should be gathered; and a patch of living flesh, equal in dimension to the preceding leaf, should be sliced off (from down upward) from the region of the cheek and, after scarifying it with a knife, swiftly adhered to the severed nose. Then the cool-headed physician should steadily tie it up with a bandage decent to look at and perfectly suited to the end for which it has been employed.

The physician should make sure that the adhesion of the severed parts has been fully effected and then insert two small pipes into the nostrils to facilitate respiration, and to prevent the adhesioned flesh from hanging down. After that,

the adhesioned part should be dusted with powders of Pattanga, Yashitmadhukam, and Rasanjana pulverised together, and the nose should be enveloped in cotton and several times sprinkled over with the refined oil of pure sesamum. Clarified butter should be given to the patient for drink, and he should be anointed with oil and treated with purgatives after the complete digestion of the meals he has taken, as advised in the books of medicine.<sup>32</sup>

The method emphasizes that the flap should be cut accurately and that special bandaging was important. As in other ancient surgical procedures, exotic ointments were used for local application, and postoperative medication and diet were important.

Indian surgical technique was advanced at the time. Those learning the technique practiced suturing on fruit or leather, and models stood in for humans for bandaging practice. The *Suśruta* text shows that student surgeons learned anatomy by dissecting cadavers. It seems that surgery had a high status at the time, and since it was taught together with internal medicine, it is likely that a distinguished and literate man like Suśruta might perform the surgery he describes. In the centuries that followed, however, manual work of any kind became offensive to the higher castes in India, and with their cultural distaste for touching the human body in life or death, the study of anatomy declined, as did the practice of surgery among the learned.<sup>33</sup> Later, when Western colonizers discovered that the ancient Hindu plastic surgery techniques were still in use, the operations were being performed by artisan surgeons associated with the lowly trades of potter and brick maker.

Early Indian surgeons may also have succeeded in transplanting skin without use of flaps. They could use detached skin, that is, "free" grafts, since some Indian texts mention the use of skin taken from the buttock to replace defects elsewhere. This skin is too thick to use unchanged elsewhere on the body, so donor skin was prepared in a special way. A suitable area of the buttock was flayed by a whip, causing swelling and bruising, and the skin was then removed and used. Since skin prepared in this way was fissured and split by the trauma, this perhaps created, in later terminology, a partial-thickness skin graft. This thin layer might heal in and survive, unlike the thick, normal buttock skin.

## Later Accounts of Plastic Surgery

These ancient methods used by indigenous healers probably continued unchanged in India for centuries and certainly persisted there until the end of the nineteenth century. It would be surprising if the methods were not in use widely in the Middle East in ancient times, but the many Arabic medical texts are silent on this topic up to medieval times. The techniques are hardly mentioned in the surgical texts of the great Greek medical writers,

beginning with the contributors to the Hippocratic collection, written about the fifth century BCE. There is no evidence that such surgery was carried out in ancient Egypt, but later, Alexandrian writers did briefly describe plastic surgical methods.<sup>34</sup> This knowledge must have passed to the Romans, since the surgical techniques appear in the works of the medical authorities Celsus (25 BCE-AD 50) and Galen (AD 129-216).35 Both writers describe briefly, but vaguely, methods for replacement of lost tissue, and it may be that these methods were merely copied from text to text. Learned medical writers often included operations that were thought to be possible or were in use by the humbler "artisan" surgeons, rather than in use by the learned author.<sup>36</sup> The Byzantine encyclopedists, notably Oribasius, used the same material that had appeared in Galen's work, and it also appears in the works of Paulus Aegineta of Rome, written prior to the Muslim invasion of AD 640. Later Arab surgical works, notably that of Rhazes (circa AD 924), continued to give short references to techniques for addressing deformities. By the tenth century, the caliphate of Córdoba was the most culturally advanced area in Europe, and, under the rule of Al-Hakam II, Muslim scholarship, manuscript collection, and translation flourished. It is significant that plastic surgery is absent from the influential Chirurgia section of the thirty-volume medical treatise by Al-Hakam II's court surgeon and physician, Abulcasis (Abū 'l-Qāsim Khalaf ibn 'Abbās al-Zahrāwī, AD 936–1013). It seems that the techniques had not reemerged in the western Mediterranean at that time nor were they featured in the older Muslim texts held in Córdoba.<sup>37</sup> Possible explanations for this absence are that the need for plastic surgery was small or that, in the Western world, attempts at plastic surgical repair were now deplored as vanity and thus cosmesis was left to beauticians.<sup>38</sup> Abulcasis had another constraint on his practice. Distinguished surgeons at the time avoided "capital" operations, which included procedures like cutting to remove bladder stones or for relief of strangulated hernias, because they could have a fatal outcome. There were others in the "medical marketplace" who might offer such surgery-notably the humble local artisan or itinerant surgeons, who, being illiterate, left no writings.<sup>39</sup> They had empirical skills guarded by semisecret trade practices.<sup>40</sup>

## The Revival of Plastic Surgery

The Renaissance, starting in Europe in the fourteenth century, led to a hunt for the ancient texts containing the knowledge and wisdom of Greece and Rome. The visual arts were also liberated and reborn. In medicine, the classical manuscript texts were sought and studied anew, and, in Italy, migrant Greek scholars assisted with translation of the works of Galen and Hippocrates. With the introduction of movable type printing in Germany

in 1438, wider dissemination of knowledge occurred by books rather than via copied manuscripts. In Italy, soon to be a major printing and publishing center, the new humanism first assimilated and built on the classical medical knowledge and finally began to challenge the revived Galenic wisdom. The surgeon-anatomists were particularly innovative, and, in the north of Italy, the universities at Bologna and Padua both taught surgery; the medical teachers had salaries exceeded only by those of the professors of law. The celebrated Italian surgeons with this new elevated status moved their craft forward and, in doing so, accepted a scholarly obligation to share their knowledge through publication of elegantly illustrated texts.

However, the ancient Indian use of methods of skin grafting by flaps reemerged first in southern Italian practice, not in northern academic circles.<sup>41</sup> The ancient Eastern learning entered Italy via Mediterranean trade routes, and the passage of the Crusaders and streams of pilgrims visiting the Holy Land further disseminated knowledge. Sicily was a central point in these movements of people and information, and it grew to be the major power in the Mediterranean under the rule of Roger II (1096-1154). Economic confidence and a cosmopolitan attitude also aided scholarship, and Roger added distinguished scholars to his court. The need for medical men in the armies of the Crusades grew and encouraged medical teaching in Sicily, which notably flourished under the patronage of Frederick II (1215-1250). The medical school at Salerno-the Schola Medica Salernitana—had a laudable emphasis on empirical clinical study by apprenticeship, rather than a traditional focus on theory and disputation. It may have been medical practitioners or travelers returning from the East or perhaps Sicilian naval campaigns that brought news of old, forgotten surgical skills, including the Indian methods of facial plastic surgery, back to the island. Whatever their route, these techniques probably first appeared in Europe in Sicily in the fourteenth century, and it was the local, craft-trained practitioners who used them.

#### The Sicilian Surgeons

The first Sicilian surgeons known to offer nose reconstruction (rhinoplasty) were the Brancas, a father and son in Catánia on the east coast of Sicily, opposite Reggio de Calabria in mainland southern Italy. While Branca the elder used the original Indian method of rhinoplasty—using an adjacent flap of skin swung over from the cheek or forehead—the son significantly improved on the older Indian strategy, starting to use more distant flaps of skin, notably from the arm.

The methods were a trade secret, but news spread and interest in the Sicilian activities grew among the elite northern Italian surgeons.<sup>42</sup> A con-

temporary account by one such surgeon describes his visit with the Brancas and erroneously credits them with developing the rhinoplasty technique that they had actually inherited from abroad. The northerner's account gives a version of the operation, though a flawed one; perhaps the Brancas did not let him see too much:

Branca, the elder, was the inventor of an admirable and almost incredible thing. He conceived how he might repair and replace noses that had been mutilated and cut off, and developed his ideas into a marvelous art. And the son Antonius added not a little to his father's wonderful discovery. For he conceived how mutilated lips and ears might be restored, as well as noses. Moreover, whereas his father had taken the flesh for the repair from the mutilated man's face, Antonius took it from the muscles of his arm, so that no distortion of the face should be caused. On that arm, cut open, and into the wound itself, he bound the stump of the nose so tightly that the patient might not move his head at all, and after fifteen days, or sometimes twenty, little by little with a sharp knife he cut away the flap, which had become attached to the nose; finally he severed it entirely from the arm, and shaped it into a nose with so much ingenuity that it was scarcely possible with the eye to detect the flap that had been added.<sup>43</sup>

This otherwise clear account had a major error in describing the use of the muscle of the upper arm, rather than skin flaps. This important and improbable misunderstanding was to be a persisting source of confusion for two centuries thereafter.

These face or forearm flap operations, performed by humble Sicilian surgeons, were known in Italy for some decades before some of the distinguished university-based surgeons of the northern Italian towns ever mentioned them. The professor of surgery at Padua, Alessandro Benedetti (c. 1445–1525), knew of the work of the Brancas and gave a brief account of it in his text *Anatomice, sive historia corporis humani* (1514). In that book he included some advice regarding care of the new nose after its creation, notably that it should not be roughly handled.<sup>44</sup> This practical detail suggests that he was studying patients who had returned from Sicily after surgery and reported to him. Benedetti was, however, cautious about carrying out novel or heroic operations, sharing the attitude among the elite surgeons at the time that one should seek to avoid professional disaster.<sup>45</sup> It was only Gaspare Tagliacozzi who was prepared to try.

## Tagliacozzi's De curtorum chirurgia

Tagliacozzi (1545–1599) had studied under eminent teachers in Bologna, notably Girolamo Cardano and Ulisse Aldrovandi. He then set up in that town as a surgeon and teacher of anatomy, soon achieving a reputation for wound management, and he succeeded Giulo Aranzio in the university's chair of anatomy. In 1597, at the age of fifty-two, Tagliacozzi published his first and only book. This famous, beautifully illustrated text, De curtorum chirurgia per insitionem (On the surgery of mutilation by grafting), contained a detailed description, based on Tagliacozzi's years of treating many patients, of the theory and practice of plastic surgery.<sup>46</sup> Tagliacozzi graciously made it clear in his text that his inspiration came from southern town surgeons in Calabria who followed in the Branca tradition.<sup>47</sup> But as one of the new academic surgeons, he had to distance himself from the artisan surgeons' approach and claim that his own methods were superior, since they were based on a university training that gave him a sophisticated understanding of the physiology of healing. He gives verbose descriptions of the erroneous biological science of the day and how it applied to surgery, but his faulty theory did not hinder him in copying the Brancas' empirically successful surgery. In some matters, Tagliacozzi may have improved upon the operative technique, notably in measuring and marking the bed and graft, and his text shows minute attention to the details of pre- and postoperative management, together with some timeless, wry asides. When operating, for instance, "the attendants must observe diligently every nod of the surgeon, for many things happen during an operation which need to be indicated by a nod, and not by speech. One must

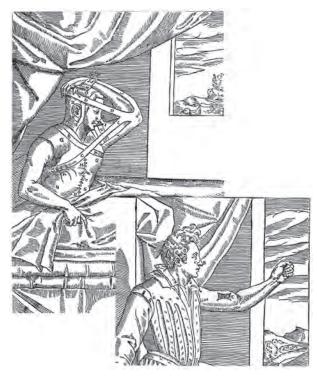


Gaspare Tagliacozzi, surgeon of Bologna, gained a lasting reputation because of his celebrated text on plastic surgery and his manuscript text, shown in the background. He was appointed professor of anatomy in the University (Studium) of Bologna in 1570. Image courtesy of Wikimedia Commons.

be sparing of words." The best operative environment for carrying out surgery, he wrote, was "two nimble assistants, good light, and all others to leave the room."<sup>48</sup>

Tagliacozzi's patients, as revealed by his text, were wealthy. They came to him due to their loss of a nose, ear, or lip, usually from warfare, violence, or dueling. Increasingly, however, a new reason for patients to seek his help was syphilis, which had spread rapidly from Naples through Europe in 1495. In its tertiary stage, syphilis could erode the inner nose. Tagliacozzi did treat such patients but only after attempts to control the disease with mercury.

Tagliacozzi followed the younger Branca's technique by raising a flap of skin from the upper arm and applying it to the freshened bed of the deficient nose. The numerous illustrations in his book show his attention to detail and that Tagliacozzi had brought to perfection the design of bandaging necessary to hold the donor arm and skin flap firmly in position against the face for



A wood engraving from Tagliacozzi's *De curtorum chirurgia per insitionem* showing the use of a flap of upper arm skin to replace tissue lost from the nose. The important system of support for the arm is shown. This illustration has been used in the seal of the American Association of Plastic Surgeons. Image courtesy of Wikimedia Commons.

some time. He also provided elegant shields to protect the new nose after the surgery.

In his analysis of the mechanism of attaching the skin flap to the nose bed, Tagliacozzi's mindset was markedly conditioned by horticultural practice. The urban Italian savants often owned country villas and had estates to supervise, and there they might use the services of tree grafters.<sup>49</sup> Tagliacozzi freely used their word *scion* to describe his grafts, and the term *insitionem*, used in the title of his book and throughout its text, was a word then used for grafting in agriculture. Tagliacozzi at one point uses the phrase "as in human surgery, as in the orchard," and he transferred two specific technical insights directly from the orchard to his surgical technique. The first was that the grafting of the upper part (scion) of one type of tree or shrub into the root system of another (one more vigorous or disease resistant) required prolonged close contact and fixation. A second strategy from horticulture was the grafting variant of "layering,"

which meant lowering and burying living limbs of trees or plants into adjacent soil, waiting until a new root system penetrated the soil, and then dividing the original connection to leave a new, freestanding tree.

Although Tagliacozzi's greatest contribution was in autografting (i.e., transferring tissue from one part of the body to another), his name was drawn into a heated debate in the next century on homografting, that is, grafting from one human to another (known as allografting in the later nomenclature). He was incorrectly thought to support the use of human donors to supply a new nose.

Tagliacozzi's text contains nothing to suggest use of another person as a donor, though it is less clear whether or not he was hostile to this idea. In chapter 12 of his book, he dismisses the idea of using another person as a donor, though it seems that some fearful patients had requested doing so, hoping to avoid some of the pain of the procedure. He refused, mainly because of the difficulty of binding the donor and recipient together during the many days required for the graft to heal in. His view was that

no one in his right mind would argue that for some slight gain of beauty and saving of effort we should call the entire fate of the work into danger . . . which certainly happens if we try to perform this operation with the aid of another person. . . . And so no one can fail to see from the difficulty of tying together and from the necessity of inconvenience which two persons tied together encounter, how doubtful, if not entirely vain, will be the outcome of the art. . . . Hence it appears superfluous for us to reply to those who, either in the interests of the appearance of the arm or pandering to their own sensibilities, refuse this operation on their own persons.<sup>50</sup>

These technical objections to using a donor for the operation seemed uppermost in his mind. However, in the final part of the chapter where he makes these objections, there is a remarkable statement that might hint that he dismissed the idea of grafting between humans for biological reasons:

Now let it suffice that judgment in regard to the flap [from another person] is extremely difficult and almost impossible, and that the singular character of the individual entirely dissuades us from attempting this work on another person. For such is the force and the power of individuality, that if anyone should believe that he could accelerate and increase the beauty of union, nay more, achieve even the least part of the operation, we consider him plainly superstitious and badly grounded in physical sciences.<sup>51</sup>

In this passage, Tagliacozzi seems to dismiss the idea of grafting between individuals because of an incompatibility—a "singularem illum individui characterem." This concept of the "force and power" of individuality, elegantly expressed on his part, may be a philosophical stance rather than biological assertion of human individual uniqueness. But it is tan-

talizingly close to the understanding of the transplantation immunology that emerged much later, and very slowly. One additional scrap of evidence supports this conclusion. The Venetian adventurer Nicolò Manuzzi (1639– 1717) settled in India and left a travelogue manuscript, published much later, in which he records that he had seen many natives with restored noses. Manuzzi had acquired some surgical skills and was asked to repair a nose but to use a slave donor for the skin. Manuzzi replied that "it would be of no avail, for being another's flesh it would not unite."<sup>52</sup>

Tagliacozzi died in 1599. There were immediate tributes to his skill, and requiem masses were said in his honor. But shortly after, the old allegations of links between successful transplantation and magical assistance were invoked by his gossipy detractors, who put it about that his surgical skills involved recourse to unacceptable supernatural powers.<sup>53</sup> Helpful "white" magic was acceptable at the time, but the "black" magic of the witches and others was condemned. Tagliacozzi's reputation was restored after an investigation, and a few surgeons, notably his pupil Giovanni Cortesi, felt it was safe to follow his master's lead cautiously, but only for a while. There was sufficient interest in the long and detailed *De curtorum chirurgia per insitionem* for a pirated edition to appear quickly in Venice and then in Frankfurt. Nevertheless, Tagliacozzi's innovative surgery was mysteriously put aside. Remarkably, it was not revived until about 1800.

Tagliacozzi's surgery failed to be incorporated into the routine textbased surgery of the day, and aiding this neglect were some added basic misunderstandings, even about the technical surgical detail. It may be that gossip and academic myths still had greater force and authority in the medical discourse in the early days of printing than did the printed word.

The first continuing misunderstanding of the Tagliacozzi technique was that the nose was to be buried into the arm, rather than a flap raised, and that muscle was used to form the new nose, despite Tagliacozzi's clear engravings showing use of the skin. But the second and more serious misunderstanding of Tagliacozzi's method was that the donor skin for the new nose could be taken from another person. Commentators wrote that Tagliacozzi used slaves or servants as donors of skin to restore their masters' mutilated faces, whereas his text shows not only the opposite but also his hostility to such grafting. This error, with its assumption that such homografts could succeed, was to intrude into the writings on plastic surgery and transplantation for centuries.

Another dampening effect on the use of Tagliacozzi's innovative rhinoplasties was that there was a safe alternative: a false nose could be fitted. Such replacements were known to be in use from earliest times and have



Tycho Brahe, the Danish astronomer, had a nasal deformity as the result of a duel, and he favored a prosthesis, which is detectable in some portraits. Portrait by M. J. Mierevelt, image courtesy of the Royal Society, London.

been found, still in place, on Egyptian mummies.54 The surgeon Ambroise Paré described a wide range of such prosthetic devices for lost or absent human tissue, and these gold or silver devices were skillfully enameled to give a fleshlike appearance when used to replace eyes, noses, and ears. There were a number of distinguished users of such prostheses. The duke of Urbino (1422–1482) had one, and when Tycho Brahe (1546-1601), the great Danish astronomer, lost the bridge of his nose in a duel in 1566, he opted for a skin-colored metal prosthesis. This device, stolen from his coffin after death, can be seen in some portraits of him. However, having opted for the safety of a prosthesis, it gave him little comfort, and he was never reconciled to his deformity. Brahe became "unapproachable, uninhibited, unsparing and ever vengeful."55

The neglect that overtook plastic surgery in general, and Tagliacozzi's work in particular, in the 1600s is perhaps surprising. War was endemic in Europe, war wounds were common, and legal mutilation still existed. In 1637, the Puritan activist William Prynne was branded and had his ears "clipped" off as punishment for antiroyalist pamphleteering, and there were similar mutilations during the unrest in Scotland, mostly removal of hands and ears. But perhaps the switch from swords to firearms as the main weapon in warfare made damage to the nose or ear less common. Also, the virulence of syphilis may have decreased after its rampage around Europe from 1495 onward, and so there were fewer severe nasal deformities. The status of surgery relative to medicine declined, and all forms of cosmetic work may still have been shunned by established practitioners.

## The New Biology

Other medical inquiry flourished during the 1600s, however. This period witnessed the rise of investigation by experiment, and no longer was

study of the ancient texts seen as the primary means toward progress. From Francis Bacon's teachings in his influential book *Novum organum* came a new method of advancing knowledge to replace the scholasticism of the humanists and their dependence on ancient authority. Instead, data were to be sought and gathered, then observations made and conclusions inductively drawn. But there was a snag in this admirable new emphasis on personal contemporary experience: at first, every experience was given equal weight in the new mood of the times. In the little world of tissue transplantation, every new, flawed tale, from whatever source, was looked at eagerly and believed.

As direct knowledge of Tagliacozzi's original textbook waned (despite the three editions available in print), descriptions of his method were still distorted, and new stories supported the myths about his work. The most damaging claim was that human donors could be used for his nose replacement. One widely believed report claimed that Tagliacozzi had grafted the nose of a slave servant to a nobleman and, after a successful outcome, the grateful recipient granted the slave his freedom. The slave later died, and, it was said, the transplanted nose then also died and fell from the nobleman's face. This tale of the "sympathetic" loss of the grafted nose—an urban myth too good to be false—caught the imagination of writers and philosophers keen to gather all information that might help them understand the natural world. Scholars were steadily dropping belief in miraculous intervention in disease, but now there were other novel influences they could study, forces that could also act unseen. The power of magnets and gravity and the forces influencing the compass were of interest. It was not unreasonable to explain the slave nose donor story as tissue loss at a distance via an invisible force.56

The influential philosopher Tommaso Campanella (1568–1639) accepted the slave donor story and then, reasoning metaphysically, concluded that since the human soul was indivisible, the death of the donor inevitably meant death of the graft, no matter how distant from the deceased.<sup>57</sup> This unity of the soul, he went on argue, also meant that grafts could be used to send signals and thus could enable communication between donor and recipient. But the Jesuit polymath Athanasius Kircher (1602–1680), writing in 1643, sternly denounced Campanella's claim for this imaginative use of reciprocal skin grafts: "By pricks inflicted upon themselves according to numbers which had been agreed upon for the various letters of the alphabet, and reciprocally felt, they could speak to each other about anything whatsoever at any distance whatsoever." He then rebuked Campanella: "But away with such foolish absurdities and stupid imaginings of crazy men, whose part it is, lacking true science, to

seek glory, which they could not otherwise attain, from dubious and false arts with the aid of the devil." $^{58}$ 

The old allegation of satanic assistance being needed to achieve graft success is overt in Kircher's denunciation of Campanella. But the tale of the paid slave donor would not go away, and there were hopes that it involved a hitherto unknown force-at-a-distance. Jean Baptiste van Helmont (1577–1644), one of the controversial new Paracelsian physicians who rejected the ancient teachings of Galen and sought to introduce chemical therapy, robustly retold and supported the sympathetic graft loss story, using it as crucial evidence in a new, evidence-based medical world. He also tried to dismiss supernatural influences:

This one experiment [i.e., the slave donor graft] of all others, cannot but be free from all suspect of imposture, and illusion of the Devil. A certain inhabitant of Bruxels, in a combat had his nose mowed off, addressed himself to Tagliacozzius a famous Chirurgeon, living at Bononia, that he might procure a new one; and when he feared the incision of his own arm, he hired a Porter [servant] to admit it, out of whose arm, having first given the reward agreed upon, at length he dig'd a new nose. About thirteenth months after his return to his own Contrey, on a sudden the ingrafted nose grew cold, putrified, and within a few days, dropt off. To those of his friends, that were curious in the exploration of the cause of this unexpected misfortune, it was discovered, that the Porter expired, neer about the same punctilio of time, wherein the nose grew frigid and cadaverous. There are at Bruxels, yet surviving, some of good repute, that were eyewitnesses of these occurrences. Is not this Magnetism of manifest affinity with mumy, whereby the nose, enjoying, by title and right of inoculation, a community of life, on a sudden mortified on the other side of the Alpes? I pray what is there in this Superstition? What of attent and exalted Imagination?59

These hidden mechanisms, thought to perhaps be related to magnetism, found a welcome even in the influential writings of Sir Thomas Browne (1605–1682). His influential *Pseudodoxia epidemica, or, Enquiry into very many received Tenents, and commonly presumed Truths,* sought to banish "vulgar errors" and replace them with sound knowledge based on the data-collecting Baconian strategy. He concluded that the slave skin graft had been linked in some way to its donor at death and that "this Magneticall conceit how strange soever, might have some originall in reason."<sup>60</sup>

These unseen forces that were surmised seemed related to another class of influence, one advocated at the time by Sir Kenelm(e) Digby, namely the power of "sympathy." Digby, a polymath, diplomat, traveler, and early member of London's Royal Society, supported attempts to cure injury by transferring the damage away from the sufferer, back to the weapon that had caused the harm. He attempted this transfer by treating the weapon with a "weapon salve" or "powder of sympathy."<sup>61</sup> Digby's most important work dealing with sympathetic medicine was his A

Late Discourse Made in a Solemn Assembly of Nobles and Learned Men at Montpellier in France. In the Frankfurt edition of 1661, the work is prefaced by an engraving with some vignettes showing sympathetic power in action. One of these panels shows the rejection of the slave nose graft after the death of the donor, the first illustration, albeit a fanciful one, of homograft skin loss.<sup>62</sup> Many other scholars added new frills to the "learned myth" slave donor story in the 1600S.<sup>63</sup>

The mood finally changed, and attitudes outside of learned circles became more skeptical. The savants' flirtation with these sympathetic powers attracted the ridicule of writers. When Samuel Butler published his mock-heroic tale Hudibras in 1663, a satire on the puritanical revolutionary regime that had recently been overthrown, Butler did not spare the fanciful ideas of sympathetic medicine.64 He used the slave donor story in a modified way, incorporating the idea that the skin was taken in the ancient Indian way, from the flayed buttocks. Word of this technique must have already reached British popular culture from India by an unknown route.

So learned Taliacotius, from The Brawny Part of Porter's Bum, Cut supplemental Noses, which Wou'd last as long as Parent Breech; But when the Date of Nock was out, Off dropt the sympathetic Snout.

But the wits missed the point. They assumed that such an operation had occurred, and this assumption helped fix the myth that the innocent Tagliacozzi had indeed used such donors.<sup>65</sup>



Vignette from the frontispiece to the 1661 Frankfurt edition of Sir Kenelm Digby's A Late Discourse Made in a Solemn Assembly of Nobles and Learned Men at Montpellier in France allegedly showing "sympathetic" loss of a living, unrelated donor skin graft to the nose, after the death of the donor. Image courtesy of James Tait Goodrich.

## **Surgical Opinion**

Although the European literati of the day can be excused for accepting the claim that Tagliacozzi used human donors, the practical surgeons should have been better informed. One serious student of Tagliacozzi was the Scottish-educated London surgeon Alexander Read, who translated part of Tagliacozzi's *Curtorem* and used it in his own text, *Chirurgorum comes* (1687). Even though he had read the original *Curtorem* text, however, Read thought that Tagliacozzi might have used human donors. Read, also influenced by botanical analogies, reasonably asked "what should hinder a piece of one man's body from being ingrafted into anothers, seeing both are of the same kind, and nothing near as different as one kind of tree is from another ...?"<sup>66</sup>

The standard English surgical text of the late 1600s was *Mellificium chirurgiae*—*The Marrow of Surgery*, by James Cooke (1614–1688) of Warwick. Cooke, after describing the Tagliacozzi operation briefly, repeats all the old misconceptions about it, namely that muscle was used, that the graft could be taken from a donor, and that the graft may be lost when the donor dies:

The operation being so difficult and painful, besides the necessary preparation for the Work, the Symptoms that fall out, the danger that follows the least neglect, 'tis almost altogether unattempted, yet to satisfy the curious, take somewhat of it here, and then if any have lost a part and like the Operation let them take their Penance. The Nose lost, may be restored both the former ways. To restore it from the Body, it may either be from their own Body, or the Body of others. If the last, let them be sure they can, that such be longer-liv'd than themselves, lest they lose what they have got before they die. To perform this work, remove the Callous Edges of what's remaining of the Nose; after make Incision into the Biceps Muscle of the Arm.<sup>67</sup>

#### London's Royal Society

The upheaval of the English Revolution and the Civil War of the mid-1600s reinvigorated many of London's ancient institutions, and new radical groupings emerged. One venture was the College for the Promoting of Physico-Mathematical-Experimental Learning, known from 1662 onward as the Royal Society of London, one of the world's first learned academies. The new society was a cooperative venture organized by a group of men interested in advancing natural sciences, and this cooperation was a change from the secrecy exhibited by some savants, notably the still-active alchemists. The society was also largely free of the outside influence of any institution or patron. Some of the European courts had a court "scientist," but his role might be to entertain rather than enlighten; one such appointee, Francesco Redi (1626–1697), the distinguished Tuscan physi-

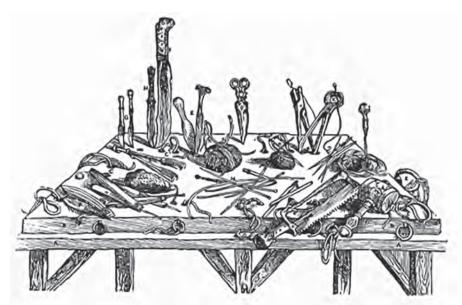
cian, had to put on entertainments for his idle, gossipy Medici courtiers. On one occasion, Redi convinced them that he could replace the head of a praying mantis after its decapitation. His trick was possible because the detached heads adhered strongly to the trunk via the viscous fluid exuded, and privately Redi scorned the court, who "only saw but did not observe."<sup>68</sup>

The members of the new Royal Society acted as peer witnesses of the results of each other's projects, and, in the Baconian spirit of the times, they appointed a "corresponding secretary" to gather reliable, relevant news from abroad. A deliberate attempt was made to banish abstruse discourse and instead substitute functional, plain language. They also resolved not to engage in personal disputes. The Royal Society looked to Bacon's writings not only for his new observational method but also for an appropriate administrative structure for research.<sup>69</sup> The new Baconian research method involved not only observing nature but also testing and taking nature apart, by experiment. "Eyes not ears" were important, and, as the society said, "The want of this exactness has very much diminished the credit of former *naturalists*." Later, the society's motto "*Nullius in verba*"—"nothing upon another's word"—suggested a growing skepticism toward unchecked claims brought to them.

Kenelm Digby's sensible botanical text of 1660 was the Royal Society's first publication, and, shortly afterward, the group turned its novel investigative arrangements toward a study of tissue transplantation. The Royal Society had a remarkable format for its twice weekly meetings. Ideas for investigation were proposed and discussed, with presentations of evidence from all available publications, personal experience, and information from scholars located elsewhere. Having reached a preliminary consensus on the matter at hand, an experimental protocol was then agreed upon, and the project was handed over to a salaried experimenter.

In 1663, the Royal Society turned its attention to skin grafting, one of the procedures they considered would be of likely use. Perhaps one of the members was aware of the dispute surrounding Tagliacozzi's work, and since Butler's poem *Hudibras* had been published earlier that year, this poem may have brought the disputed matter of tissue transplants to their attention. The society organized an experimental attempt at skin grafting (using dogs as subjects) that turned into a muddle and, in the end, a story of high farce. Nevertheless, the independent outlook of the investigators, as well as their attempt to investigate this procedure by experiment, marks a crucial break with the past. It was also noteworthy as the earliest recorded animal experiment in tissue transplantation, and criticism of the society's use of vivisection promptly appeared.

Transplantation was still a sensitive subject for other reasons. Dur-



The arrangements for the Royal Society's experimental dog surgery would resemble those in Andreas Vesalius, *De humani corporis fabrica* (1543).

ing this period, a celebrated Amsterdam surgical text by Jobi Janszoon van Meek'ren described the case of a Russian nobleman who had a severe skull injury that was repaired by the use of a rabbit bone graft. The Church threatened to excommunicate the patient because of this implant, so he asked the surgeon to remove the graft.<sup>70</sup> Meek'ren's account came second- or thirdhand from contacts in Russia, so it may have been another unreliable transplant myth.

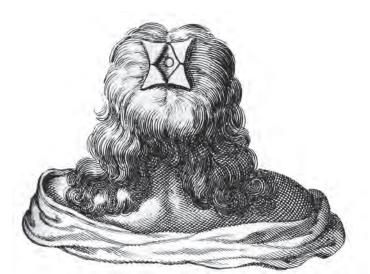
The impetus for the Royal Society's landmark skin grafting experiment was a proposal by John Wilkins (1614–1672), a founding member and the society's first secretary. According to the society's minutes, on September 16, 1663,

Dr Wilkins proposed the experiment of making a piece of the skin of a dog to grow upon another. Some things were objected against the probability of success thereof, viz., how veins, arteries, and fibres could disseminate themselves and grow into this strange piece of flesh patched on: it being necessary even to the restoring of a separated part to the same animal that there may be left some vessels, and that they join another, and it being hardly conceivable, how the healing can be effected, where the orifices of said vessels do not meet. Others alleged experience and several examples of separated parts healed together again.<sup>71</sup>

This preliminary discussion on the proposed experiment was a familiar clash between theory and empiricism. The theorists could not con-

ceive that new blood vessels could penetrate into the graft, and thus they assumed that successful transfers could succeed only if the arteries and veins of the donor skin made Episthemon-like union directly with the vessels of the recipient. The chances of this happening were slim, as they reasonably pointed out, if only because these vessels were not lined up. The new empirically minded members of the group alleged that grafting had been accomplished in the past, and that was enough for them: experience was as important as theory.

The empiricists carried the day, and all present at the meeting favored a trial, rather than a debate. As a start, they sensibly proposed that instead of grafting from one dog to another (an allograft/homograft), a simpler autograft transplant should be attempted first: "It was ordered hereupon that the experiment should be first with a piece of skin cut from the body of a dog, and sewed again upon the same dog: and Dr Croune and Mr Hooke were appointed curators thereof, and the operator ordered to provide a dog against the next meeting." The members then added some extras to the transplant agenda: "Mr Hooke was also desired to try the growing of hair, and of a cock's-spur upon the head of a cock."<sup>72</sup> Thus, the Royal Society was also preparing to investigate other known types of tissue transplantation, including hair transplants and a spur-to-comb transfer in the chicken, an experiment usually credited to John Hunter's



A representation of the Russian bone graft from a rabbit donor to a human patient. From Jobi Janszoon van Meek'ren, *Heel-en Genees-Konstige Aanmerkkingen* (Amsterdam, 1668). Image courtesy of Glasgow University Library, Special Collections.

studies in the next century.<sup>73</sup> On another occasion, human tooth transplantation was discussed briefly at the society, and they carried out some animal blood transfusions.

The dog skin transplant project was handed over to Robert Hooke (1635–1703), the Royal Society's salaried "curator," a talented, disabled man of humble origins who had the responsibility for conducting all of the society's experiments.<sup>74</sup> His talents and patience were regularly stretched by the enthusiasm of the members. Hooke's achievements were considerable, and he can be accorded the honor of being the first experimental tissue transplanter.

A month after Dr. Wilkins proposed the skin grafting experiment on the dog, the society's minutes for October 14 record a delay: "Dr Croune and Mr Hooke having not yet met to cut a piece of dog's skin and sew it on again in order to see whether it will grow; and Dr Charleton, affirming that he had tried this experiment formerly, he was desired to meet on the Friday following with the other two curators at Gresham College, and there to make the experiment together. Dr Hoare promised to bring in an account of a cock's spurs growing on a cock's head."<sup>75</sup>

James Hoare (died 1679) was one of the less active members and missed a place in the history of transplantation by failing to give his promised paper on the transplantation of the cock spur to its comb. Walter Charleton (1619–1707) was an Oxford-educated physician, and, as the translator of van Helmont's text on sympathy and the "magnetick" cure of wounds, he had a direct interest in the matter of the dog experiment. These extracts from the society's minutes show that he claimed previous experience of skin transplantation. However, it is unlikely that a cultured physician of the time would do such manual work, and his role was probably to encourage Hooke to make haste with the experiment.

By October 21, 1663, the experiment had been carried out, but Hooke had encountered a technical problem, one familiar in later attempts. Hooke reported "that as soon as the skin was cut off, it shrunk into half its dimensions, so they could not stretch it out so far as to cover the whole flesh with it, as it had done before... The whole process was ordered to be given, in writing, by Mr Hooke." Hooke was also appointed curator for the ingrafting of feathers upon a cock's comb. There was no update on the dog skin graft project at the society's meeting on November 25, but the members did agree to a further delay until "a warmer season."<sup>76</sup>

Springtime was generally agreed to be a propitious time for surgery. On May 4, 1664, the members gave instructions for a further attempt, and on May 25, Charleton and the dilatory Hooke at last did the surgery. One week later came the sad report that he had met with another prob-

lem that became all too familiar to later surgeons: "The dog, a piece of whose skin had been cut off and sewed on again, had got it off: [Hooke] was desired to repeat the experiment at the next meeting, and think upon a way of securing the patch." Even if Hooke had managed to secure the graft, still a further and final misfortune ended the experiment in the next month. The minutes of June 22 explained: "The dog that had a piece of his skin cut off at the former meeting, being inquired after, and the operator [Hooke] answering, that he had run away."<sup>77</sup> There is more than a hint that the put-upon Mr. Hooke, now that the dog was gone, was no longer interested in the project.

A plague epidemic soon afflicted London, and the frightened physicians fled to the safety of the country. In March 1666, it was judged safe to return to the capital, and when the society meetings resumed, they turned instead to another related matter: attempts at blood transfusion. The society may have been energized by the news from Paris in June of that year that the French had carried out a human blood transfusion. Members King and Lower, piqued at the French initiative, and concerned about their priority, then reported a similar human transfusion in November 1667. They ruefully recorded the timeless surgical innovator's lament, claiming that their hesitation and failure to be first was because there were no suitable patients. Also, ethical constraints had arisen: "We have been ready for this experiment this six Months, and wait for nothing but good opportunities, and the removal of some considerations of a moral nature."78 The blood transfusion they finally performed was into a "feeble-minded cleric" who agreed to be transfused, on two occasions, for twenty shillings. There were no serious reactions.

The Royal Society made no further attempts at skin grafting, studying the cock's comb, or studying tooth transplantation. The distinguished and productive group at the society had failed in their worthy plans for experimental transplantation, defeated in the end by bad luck and technical failures. There may have been sensitivity about further animal experiments, since the society received criticism when Hooke used dogs to demonstrate in public the success of open-chest resuscitation using bellows.<sup>79</sup> Hooke wrote to Robert Boyle, the distinguished Oxford investigator, in 1664 that he had looked for an "anesthetic" to assist the experiment: "I shall hardly be induced to make any further trials of this kind, because of the torture of the creature: but certainly the enquiry would be very noble, if we could find a way so as to stupefy the creature, as that it might not be sensible, which I fear there is hardly any opiate will perform."<sup>80</sup>

Even the plans for further human blood transfusion were put aside. In 1668, a second transfusion experiment in Paris had killed the patient,

and the incident produced, in France, the first interdicts on human experimentation. In spite of this precedent, shortly afterward the Royal Society applied to Bedlam, the large mental asylum in London, to use a patient for another transfusion, but the physician in charge declined to cooperate "on a scruple."<sup>81</sup> This, plus the earlier "considerations of a moral nature," were early stirrings of ethical concerns about human experimentation.

Whatever the reason, at the end of the 1600s, the Royal Society turned away from all forms of experimental biology, and, with the medical men among them leaving to form a separate College of Physicians, which did not favor experimental work, the remaining *virtuosi* focused their considerable talents on studies of the physical sciences.

#### **Satire Continues**

The matter being undecided, the London satirists were free to continue to ridicule transplantation, and Tagliacozzi was mentioned once again, this time in William Congreve's popular comedy *Love for Love* (1695). In it, the proposal was to transplant new, sturdy legs to a decrepit old man: "Alas, poor Man; his Eyes are sunk and his Hands shrivelled; his legs dwindl'd and his back bow'd. Pray, pray, for a Metamorphosis. Change thy Shape, and shake off Age; get thee Medea's Kettle and be boil'd a-new, come forth with labr'ing Callous Hands, a Chine of Steel, and Atlas Shoulders. Let Taliacotius trim the Calves of twenty Chairmen [sedan chair carriers] and make thee Pedestals to stand upon, and look Matrimony in the face."<sup>82</sup>

Worse still, *The Tatler* of December 7, 1710, at the start of an enlightened century, carried a ponderous essay, "Noses," by Addison in which Butler's lampoon of Tagliacozzi in *Hudibras* was repeated and the Italian surgeon ridiculed. The surgical textbooks of the new century, notably Lorenz Heister's hugely successful *Chirurgie* of 1718, dismissed the Tagliacozzi operation and suggested that an artificial nose would suffice for those disfigured in the way described.

Although the outcome of the transplantation studies in the otherwise progressive 1600s had perhaps been unimpressive, the Royal Society's approach signaled a major shift in attitudes to the study of the natural world. No longer were matters to be decided by study of classical texts or by anecdote. Instead, experimental biology was emerging, and in the following century, two investigators with the new outlook, Abraham Trembley and John Hunter, used their talents to look at tissue transplantation.