FRANCIS GLISSON AND HIS CAPSULE

The Thomas Vicary Lecture delivered at the Royal College of Surgeons of England

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by

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EVERY MEDICAL STUDENT knows about Glisson's capsule, but how much do we know about Glisson himself? The great Dutch physician, Boerhaave, described him as " omnium anatomicorum exactissimus ", but he was also a physiologist, a physician and a philosopher, and he has even been described as an orthopaedic surgeon. He was born about 35 years after Thomas Vicary died and was some 20 years junior to William Harvey, whose views on the circulation of the blood he was amongst the first to accept. He occupied the Regius Chair of Physic at Cambridge for 41 years, and he was President of the Royal College of Physicians at a time when they, like the Company of Barbers at present, were without a hall of their own in which to meet because of the ravages of fire, in their case the Great Fire of London of 1666.

Previous knowledge of the liver

Glisson's work on the liver was published in his *Anatomia Hepatis*, the first edition appearing in 1654, but it is necessary to go back and see how far knowledge of the function and structure of the liver had progressed before his time. For the earliest attempts to ascribe any functions to the liver it is necessary to go back to the cradle of civilization, Mesopotamia, where the Babylonians and Assyrians believed that blood was the sign of life, and the liver being an organ full of blood was the seat of the soul (1). At least as far back as 2000 B.C. the liver was used as a means of divination; the god to whom an animal was sacrificed became associated with the soul of the animal and thus with its liver, so that by means of a study of the liver the wishes of the god could be ascertained. Before embarking on a project such as a battle campaign, animals, usually sheep, would be sacrificed and any unusual signs on the liver would be interpreted as favourable or to the contrary. Thus a key was required to provide a means of interpreting these signs, and such a key, in the form of a clay model of a sheep's liver, is to be seen in the British Museum, the model being covered by cuneiform inscriptions naming the different parts and describing the interpretations which should be placed on any abnormalities (Fig. 1). Thus the size of the gall-bladder, the lengths of the cystic and hepatic ducts, the shape of the porta hepatis and every other anatomical detail came to have a special significance. Sometimes these descriptions were written on tablets, and one such tablet, dating from the 7th century B.C.,

deals with the " processus pyramidalis ", which we now call the caudate lobe. This method of divination spread to other parts of the ancient world, and was further developed by the Etruscans in the days of the Roman Empire.

It was in this atmosphere of mysticism that the early Greeks began to make a more scientific study of anatomy and medicine. In the writings of Hippocrates (2) we learn that " in most cases dropsy starts from the flanks and the loins, but sometimes from the liver ", " inflammation of the liver causes hiccough " and " in cases of jaundice it is a bad sign when

Fig. 1. Clay model of a sheep's liver, used for divination by the Babylonians in the 17th century B.C.

the liver becomes hard ". Aristotle (3) wrote: " The human liver is round, like that of an ox. This is the case also in animals offered for sacrifice, as in the district of Chalcis in Euboea, where the sheep have no gall, and in Naxos it is so large in nearly all the animals, that strangers who come to sacrifice are surprised, and think that it is ominous, and not at all natural. The liver is united to the great vein, but has no part in common with the aorta, for a vein branches off from the great vein, through the liver, at the place where the gates of the liver, as they are called, are situated. The spleen also is only connected with the great vein, for a vein extends from this to the spleen." His anatomy is more difficult to follow when he continues, " there are two branches of the vein, one of which terminates upon the diaphragm and what is called the praecordia,

the other returns through the armpit to the right arm and unites with the other veins near the interior of the elbow. For this reason physicians treat certain diseases of the liver by venesection of this vein."

Celsus (4) wrote: " The liver having its origin from the diaphragm itself on the right side under the praecordia is internally concave, externally convex; which being prominent slightly rests on the stomach and is divided into four lobes. The gall-bladder adheres to it inferiorly." It seems to have been Rufus of Ephesus (5) who started the idea which persisted down to the time of Vesalius that the liver was a five-lobed structure; he took this from the anatomy of the dog, but Galen, who said that the number of lobes differed according to the species of animal, thought that the liver of man had four lobes. Thus these ideas continued down to the 16th century.

Charles Estienne of Paris (6), whose father had printed some of the Galenic texts, and who himself wrote a great deal on anatomy as well as on other subjects, still maintained the idea of the five-lobed liver, but about the same time, just before the revolution in anatomy caused by the publication of Vesalius' *Fabrica*, Nicolo Massa of Venice wrote in 1536 that the liver was superficially divided into only two lobes, but he added: " The vena porta divides in the substance of the liver into five veins which traverse the five lobes and then ramify in many branches in the convexity, whence emerges the vena cava. But you will note that these minute branches are united with the branches of the vena cava. This you will see better if you macerate the liver for some days and then boil it so thoroughly that the flesh can be separated easily from the vessels. You will then perceive the substance of the veins to be interwoven, as it were into a sort of network." It is clear that he adhered to the Galenic views of the function of the liver, in which blood was manufactured out of the chyle brought to it by the portal vein and here endowed with natural spirit, but he was looking for the means by which the blood got into the venous system. Even Vesalius had not realized the error about the lobes of the liver, for the first of his six anatomical tables, which were published in 1538, deals with the portal system, and shows a five-lobed liver (6). This table is headed, " The liver, workshop of sanguinification, receives chyle from the stomach and intestines through the Vena Porta which is called Stelechiaia by the Greeks and Varidhascoer by the Arabs, and expels the succus melancholicus into the spleen ". He thus accepts completely the Galenic view of the physiology of the circulation with its ebbing and flowing in the veins. However, when we come to the *Fabrica*, published in 1543, the anatomy is much better described; not only is the shape of the liver reasonably accurate, but the cystic duct, common bile duct, and hepatic vessels and nerves are shown. It seems unlikely that he made any study of the internal structure of the liver for he still persists in saying that the portal vein divides into five branches, and this view

remained for a further hundred years, until Johannes Vesling of Padua published his *Syntagma Anatomicum* (7) with a correct representation of the portal vein dividing into its two main branches.

It was believed in Galenic physiology that the gall bladder was the site of formation of one of the four humours, the choler or yellow bile, and it had to await the histological studies of Malpighi, who first described the liver lobule, to show that bile was produced by the cells of these lobules, and this was in 1666, twelve years after the publication of Glisson's book.

Harvey (8) adhered to the opinion that blood was manufactured in the liver though he maintained the view of Aristotle that the heart was also necessary for this purpose. He wrote: " The action of the liver is concoction and sanguinification but only as the instrument of the heart and secondarily.... The liver serves as a warm fomentation and accordingly is abundant in blood and innate heat." And again: " Hence it appears that both the liver and the heart are necessary, the latter because it is the source of heat, the former for the sake of concocting the food, wherefore no sanguineous animal can lack these two organs." He of course destroyed the idea that blood ebbed and flowed in the veins, and applied this to the portal system (9). " Even as the umbilical veins ", he writes, " absorb the nutritive juices from the fluids of the egg and transport them for the nutrition and growth of the chick in the embryo state, so do the mesenteric veins suck up the chyle from the intestines and transfer it to the liver: and why should we not maintain that they perform the same offices in the adult? For all the mooted difficulties vanish when we cease to suppose two contrary motions in the same vessels, but admit but one and the same continuous motion in the mesenteric vessels from the intestines to the liver." He pointed out that the blood in the mesenteric veins was similar to blood in other veins, and not a mixture of chyle and blood, but he thought that in the embryo there was no use for the liver and this was why the ductus venosus caused blood to by-pass this organ.

The lacteals had been described by Aselli of Padua in 1622, but he thought that they carried chyle to the liver, and it was Pecquet of Paris who discovered the receptaculum chyli and the thoracic duct and showed that the chyle entered the blood stream by this route. Harvey mentions that he had observed the lacteals before Aselli's book was published, but he failed to appreciate their significance (9).

Thus by the time that Francis Glisson began his studies of the liver, rather more than ten years after the publication of Harvey's great work, much was known and described about its gross anatomy, but without a microscope its detailed structure was unknown, and views on its function were relatively primitive, as could only be the case in the absence of any knowledge of organic chemistry.

Glisson's life and work

Most of the accounts of the life of Francis Glisson state that he was born in the village of Rampisham in Dorset in 1597. I believe that both the place and date are wrong. Before giving my reasons it is necessary to look at his ancestry, and we are fortunately able to do this because parts of the family pedigree are recorded in the Visitations of Dorset (10) and of Somerset (11), both of which were made in 1623. From these we learn that his great-grandfather was Thomas Glisson of Suffolk, whose son Walter came to Bristol and married a Joane Cooke of that city (Fig. 2). He was a Notary Public (12), but he must also have engaged in trade, for in 1568 he purchased for the sum of £68 an orchard, garden and lodge in Earl's Mead and a pasture; in addition he purchased a storehouse upon the " Key " and other storehouses next to the Marsh Gate. In 1569 he was a churchwarden of St. Lawrence's parish, and in 1595 he was one of the feoffees of St. John's. His second son, William, was the father of Francis. He is described in the Burgess Books of the City as a " tayler " and was made a freeman of the city in 1593. In his will, which is in the Bristol Probate Registry, dated 17th January 1604, Walter Glisson bequeathed to his son William his " white ale cup of silver not gilded which I use daily to drink in, and also my signet of gold with the red cornelian stone which I commonly wear ". In a former will he had bequeathed to William the " garden, ground, houses and tenement adjoining in manner aforesaid being all situated in the parish of little St. Augustine's ", but in this will he revoked that legacy and left his Bristol property to his elder son Israel. When we look at the parish registers of this Dorset village, which are preserved in the county Record Office at Dorchester, they show that the first of William's family to be baptized there was Hester, and this was on 19th March 1604/5. William Glisson had a large family, nine sons and four daughters by his wife Mary, daughter of John Hancock of Kingsweston, Somerset, and one daughter by his second wife, Margaret Bampfield, who was descended from the Bampfields of Poltimore in Devon.

Of this large family Francis was the second son. The most likely explanation of the fact that no births of the family are recorded at Rampisham before 1604/5 is that the family only moved there shortly before, and it was possibly on account of the move that William's father altered his will. A search has been made of the available parish registers of several Bristol parishes, but so far no record of the births of the first six members of the family has been traced.

As regarding the date of Francis Glisson's birth we find it stated in the Visitation of Dorset that his elder brother, also named William, is described as " *filius et haeres, aet.* 26, 1623 " so that he was probably born in 1597, and as Francis was not a twin he could hardly have been born in the same year. When Francis went up to Caius College (13) he

FAMILY OF GLISSON

Arms.—Sable, on a bend argent, three mullets, pierced, gules. (A crescent within an annulet for difference.)

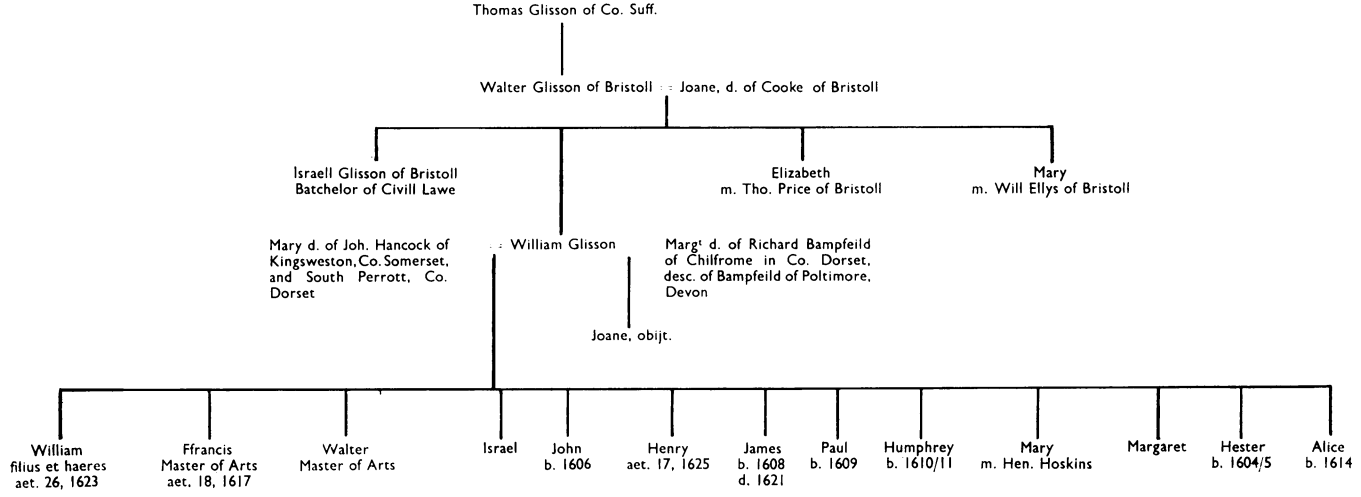


Fig. 2. Pedigree of the Glisson Family.

enrolled in June 1617 and gave his age as 18, which would have put his birth at the earliest at June 1598. So I think that we must come to the conclusion that he was born in 1598 or 1599, and probably in Bristol. Incidentally his grandfather, in his will to which I have already referred, left to each of his grandchildren, including Francis, " twenty shillings apeace, the which I will shall be payd over by my executor to my said son William to the said children's use to be employed by him to their most profit and commoditie until they shall severally be of age to receive the same with the increase thereof ".

Certainly Francis spent much of his childhood at Rampisham. The village cannot have changed greatly since that time; the church has been rebuilt, but the original tower remains. In the churchyard, adjoining an early 16th century cross, is a curious dole table, which Glisson must have seen used for the first time, for it was erected in 1605. Some of the present thatched cottages may have been there then, but we do not know which was the property that his father owned or where the large family was brought up.

When Francis went up to Cambridge in 1617 his previous education was given as seven years at the school at Rampisham under Mr. Allot (13). I suspect that he spoke the Dorset dialect, for when his younger brother Henry went to Caius in 1625, and Francis acted as his surety, the name of the master has become Hallett. Francis was admitted to the scholars' table on 28th June 1617, and was a scholar from Michaelmas that year to Michaelmas 1624 He obtained his B.A. in 1620/1 and M.A. in 1624. On this degree he was incorporated at Oxford on 25th October 1627. He became a junior fellow of his college at Michaelmas 1624, and a senior fellow from Michaelmas 1629 to Michaelmas 1634. In 1625–6 he was Greek lecturer, and became Dean of the college in 1629. It thus seems that his education up to this time was classical, and he did not turn to medicine until he was nearly 30 years old. There is no evidence that he went abroad for his medical education, and Michael Foster (14) thought that he carried out his studies in London. He obtained his M.D. of Cambridge in 1634 and was admitted a Candidate of the College of Physicians on 15th September of that year and elected a Fellow on 30th September of the following year (15). At that time the number of Fellows was limited to 30, and Candidates to six, so this was rapid promotion, but, as four completed years of practice was a condition of admission as a Fellow, this suggests that Glisson had been practising since 1631, and possibly in London for it was most unusual to elect Fellows who were not in practice in London. In 1636 he was appointed to the Regius Chair of Physic at Cambridge in succession to Dr. Ralph Winterton, who had died at the age of 36. Glisson continued to hold this office until his own death in 1677, longer than any Regius Professor before or since. The Chair had been founded by Henry VIII in 1540, the first medical

professorship in Britain, but the duties were not onerous, and Glisson resided in London during most of his occupancy. There is no evidence that he ever gave any courses of lectures at the University.

We know nothing further of Glisson's work until 1639, when he was appointed reader in Anatomy at the College of Physicians. The following year he was chosen Goulstonian lecturer, and he wrote (16): " I was appointed by the physicians of the Coll. of London to read a publick anatomical lecture in the theatre belonging to the Coll. to be performed in the year 1641, thus was allowed about a twelvemonth time for my preparation, so I applied myself to the study of the liver " (Fig. 3).

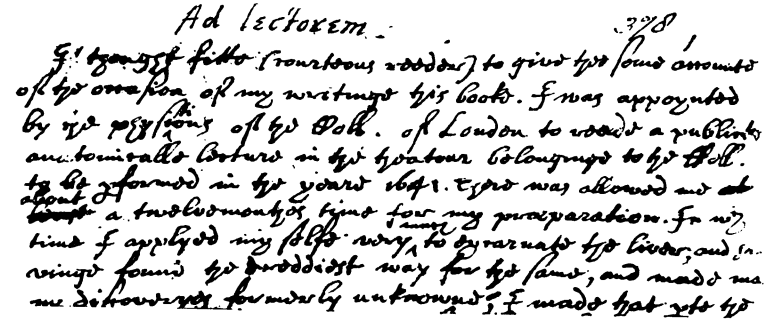


Fig. 3. Glisson's note concerning how he started the study of the liver (see text).

This brings us to another controversial point. All accounts of his life state that he lived in Colchester from 1640 until after the siege of that town in 1648, and that in August of that year he was sent on two occasions by the Mayor and Aldermen to treat with Lord Fairfax, in order to get better terms on the surrender of the town, but he failed to get any concessions. The evidence for this is to be found in the *History and Antiquities of Colchester* by Philip Morant, published in 1748 (17), who wrote: " The learned physician, Dr. Glisson, was also an inhabitant of the parish ", St. Mary's at the Walls, " for several years. But he removed afterwards to London where he died in 1677." Now I think that Morant had confused Francis Glisson with his younger brother Henry, who is known from contemporary evidence to have practised in Colchester. Henry entered Caius College (18) in 1625, obtained his M.A. in 1632 and M.D. in 1639, and was admitted an Honorary Fellow of the College of Physicians in 1664, when this category was first introduced, each Honorary Fellow paying £20 but not having any part in the jurisdictions or elections of the College (19). In this way the College raised well over a thousand pounds, but most of it was stolen during the time of the plague. The first list of these Honorary Fellows (20) is with the Glisson papers in the British Museum and contains 65 names, but

five or six seem to have been admitted without payment of the fee. Also in the British Museum is a letter from Henry written from Colchester on 27th April 1647 to his brother Francis at his lodgings in Fleet Street near the Three Kings (21). It is unlikely that Francis would join his brother in practice in Colchester for eight years, and we have plenty of evidence that he was much in London during that time, so I think that we may consider that he spent these years in Colchester as being incorrect. He has been described as a pronounced Presbyterian (22), but this is also, I think, due to confusion with his brother. The only other piece of information about the years before 1640 is that he got married, for in the British Museum is a letter dated 1638 from Thomas Morgan to his daughter, Maria, wife of F. Glisson at Caius College, Cambridge (23), but nowhere else is there any reference to her, so I think we may guess that she died soon afterwards and that there were no children.

I have mentioned that we have evidence that he was much in London during the time of the Civil War, for in 1645 he was one of the group " of divers worthy persons inquisitive into natural philosophy and other parts of human learning ", as John Wallis (24) described them, who met regularly and formed the nucleus out of which the Royal Society developed. The majority of this group were doctors. They comprised Dr. Jonathan Goddard, who later became Professor of Physic at Gresham College, Dr. George Ent, who succeeded Glisson as President of the College of Physicians, Dr. Charles Scarborough, later anatomical reader at the Surgeons' Hall, and Dr. Christopher Merrett, who, after a long dispute with the College of Physicians, was expelled from the Fellowship. In addition there was Dr. John Wilkins, who was interested in many mechanical things including means of flying to the moon, but he was a cleric, a great pluralist, who eventually became Bishop of Chester and Rector of Wigan. Finally there was John Wallis, a former pupil of Glisson's at Cambridge and a mathematician, who occupied the Savilian Chair of Geometry at Oxford for over 50 years. This group met weekly, sometimes at Dr. Goddard's house and sometimes at the Mitre in Wood Street, but after a few years of the turmoil of the civil war, Wilkins, Wallis and Goddard went to Oxford, where they continued their weekly discussions with Robert Boyle, Christopher Wren and others, and founded the Philosophical Society there which continued until 1690.

In addition there was another group of doctors which communicated with each other written observations on diseases, as Glisson mentions in the preface to his book on Rickets. The group included Jonathan Goddard, but also George Bate, Nathan Pagett, Assuerus Regimorter, Thomas Sheaf, Edmund Trench and Robert Wright, all then or soon afterwards Fellows of the College of Physicians. In both of these groups Glisson was the senior man, and it was probably on his initiative that they became so active. The second group delegated Glisson, Bate and

Regimorter to write a treatise on Rickets, which was then thought to be a new disease in England, but when Glisson had written his part, which concerned the causes of the disease, the whole of the rest of the work was entrusted to him, so it was published in his name. He recounts all this in the preface, but he insisted that the other two names should appear on the title page.

Glisson's association with the College of Physicians became closer as the years went by. In 1655 he was named an Elect, of whom there were eight, and whose duty it was to choose the President, the Consiliarii and the Censors of the College, the President being chosen from their number. The next year he became a Censor. At that time the College was at Amen Corner, but in September 1666 it was completely destroyed by the Fire, with the loss of nearly all its property including Harvey's library which he had recently presented to them. Shortly before this the plague had ravished the City and many of the population fled. The College of Physicians nominated eight physicians to attend plague patients and of these the Lord Mayor selected two, Dr. Hodges, a Candidate, and Dr. Witherley, an Honorary Fellow (25). In the event, 24 physicians, five surgeons and seven apothecaries remained at their duties, though five physicians and three surgeons died (26). Glisson was one of the physicians who remained, and he attributed his escape from infection to the fact that when visiting patients he thrust up his nostrils bits of sponge dipped in vinegar (27).

He was elected President of the College in 1667, and set to work to raise funds for rebuilding, heading the list of subscribers, dated 28th April 1669, with a donation of £100 (28). He was re-elected President in 1668 and 1669, but after that he seems to have taken a much less active part in the College, though he was a Consiliarius from 1666 until the time of his death.

Glisson was not present at the meeting at Gresham College on 28th November 1660 at which it was decided to form the society which became the Royal Society, but he was named among the 41 persons " judged willing and fit to joyne them in their design ", and he became one of the original fellows (29). This caused some annoyance to Dr. Hamey, his colleague in office at the College of Physicians, who thought that he was betraying the College by supporting the Royal Society (30). Among his contemporaries was Thomas Wharton, who was a great friend and described Glisson as " our illustrious colleague ".

Glisson's third book, *Tractatus de Natura Substantiae*, is dedicated to Anthony Ashley, Earl of Shaftesbury. In the dedicatory epistle he mentions that he has been for several years physician to that nobleman and his family, and acknowledges the obligations that he was under to him for his patronage and assistance in several difficulties, but he gives no

hint as to what those difficulties were. Lord Shaftesbury lived at Exeter House in London from 1650 onwards, and became Chancellor of the Exchequer after the Restoration and Lord Chancellor in 1672. In 1666 he went to Sunninghill to take the waters, taking as his medical attendant John Locke, who was then studying medicine at Christ Church, Oxford.

The Glisson papers in the British Museum are written in a handwriting which is often difficult to decipher. His medical notes are mostly in Latin, though he often changed into English even in the middle of a page. One group of these papers deals with his salary as Regius Professor. This had been fixed by Henry VIII at forty pounds a year to be paid quarterly, but payment seems to have ceased in 1639. Glisson made a number of petitions to " The Honourable the Committee appointed for the King's revenue " in which he recounts the terms of his appointment to the Professorship, and in one of them he ends, " And whereas your petitioner for 5 years and a half ending at our lady day last past hath received no part of the said fee; whereby there remaineth in arrears and unpaid to your petitioner at our Lady last the sum of £220 to the great damage and discouragement of your said petitioner " (31) (Fig. 4). At midsummer 1643, £150 was owing, but some time afterwards he received a payment of £80; thereafter the debt mounted and further petitions followed, for £280 at Michaelmas 1648 and for £320 at Michaelmas 1649. He eventually received payment in full, for at a meeting of the Council at Whitehall on 7th April 1654 it was " ordered by his highness the Lord Protector and the Council that the Receiver General of the public revenue pay to Doctor Glisson all such moneys as are due and in arrears for his fee for his said professors place any former order of restraint to the contrary notwithstanding " (32) (Fig. 5).

By 1675, he evidently felt that he could no longer carry on his duties as Regius Professor, although they were very light, so he by deed did " institute and appoint Robert Brady, Doctor of Physic and Master of Gonville and Caius College in the said University to be my Deputy to perform all disputations, exercises and duties to me the said Francis Glisson appertaining to be done as Reader or Professor aforesaid " (33). Dr. Brady two years later was appointed to the Regius Chair after Glisson's death.

The only known contemporary portrait is the one which hangs in the Royal College of Physicians and is attributed to William Faithorne; a copy is in the Bodleian Library at Oxford. It must have been painted before 1672 for engravings from it are to be found in Glisson's last two books. The family shield was sable on a bend argent three mullets pierced gules; a crescent within an annulet for difference.

Francis Glisson lived in the City all the time after he left Cambridge. In 1647 he was " At the sign of the Three Kings in Fleet Street " or " above a cutler's shop next to the Three Kings " and in 1665 he was at his lodgings

in Fleet Street. In 1671 he was at his house in Bow Street, but he held a lease in Fleet Street near Shoe Lane in the parish of St. Bride's which was renewed on 22nd May 1666, and he was residing there at the time of his death. He died on 14th October 1677 and was buried at St. Bride's, this being recorded in the church register on 22nd October.

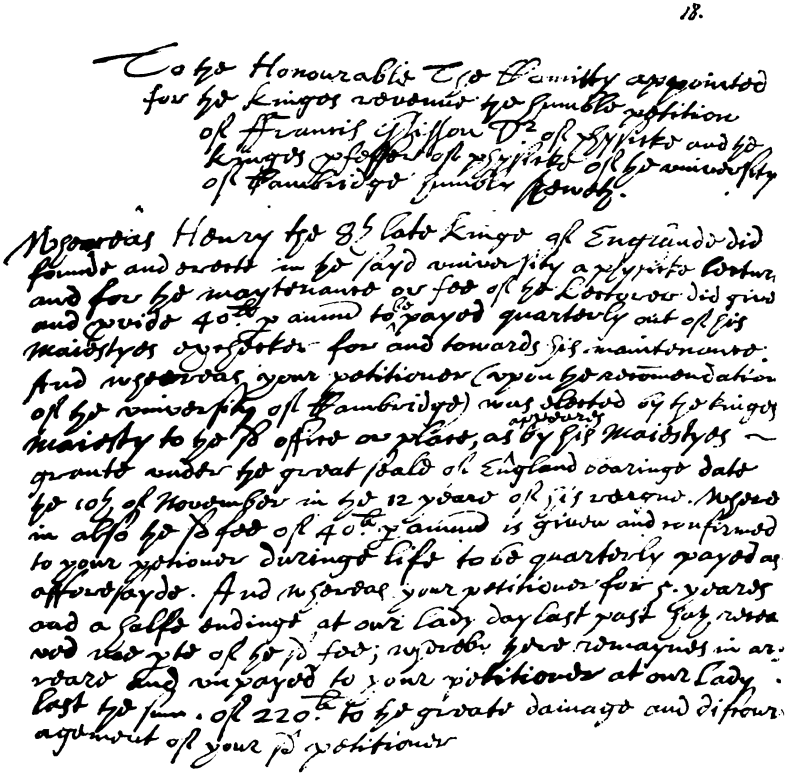
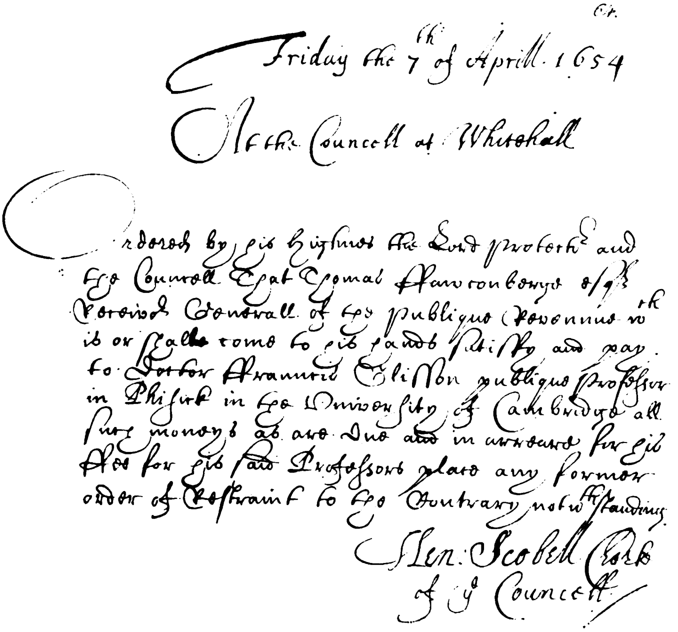


Fig. 4. Glisson's Petition to the Committee appointed for the King's Revenue for his salary as Regius Professor of Physic.

In his will, which is at Somerset House, he left most of his property to his relatives, but his colleagues at the College of Physicians, Sir George Ent, Sir Charles Scarborough, Dr. Goddard and Dr. Staines each received a piece of plate value five pounds, and to Caius College in Cambridge he left two pieces of plate, each of value six pounds thirteen shillings and four pence, " with the arms of the said college and my arms and as of my gift engraven thereon ", and to Trinity Hall one piece of the same value to be similarly engraven. In addition to three messuages in New Street, he owned property in the parishes of St. Giles in the Fields and St. Clement Danes. Part if not all of the property at Rampisham had been

sold to a Mr. Lawrence in or before 1665. He left £50 to his brother Henry plus £10 for mourning and forty shillings to Henry's wife for a ring. His brother John was residing at Marnhull in Dorset in 1647 and his three daughters received legacies; another brother, Paul, went into the church, and is probably the Paul Glisson who wrote two religious tracts about Beverley in Yorkshire. Francis seems to have helped other members of


Friday the 7th of Aprill 1654

At the Councell at Whitehall

Ordered by his Highnes the Lord Protector and the Councell ... Receiver Generall of the publique Revenue ... to pay to Doctor Francis Glisson publique Professor in Phisick in the University of Cambridge all such moneys as are due and in arreare for his Fee for his said Professors place any former order of Restraint to the Contrary notwithstanding.

Hen: Scobell Clerk of ye Councell

Fig. 5. Order in Council for the payment of Glisson's salary as Regius Professor of Physic.

the family from time to time, and judging by correspondence in the British Museum he appears to have had considerable difficulty in the recovery of a loan to a nephew.

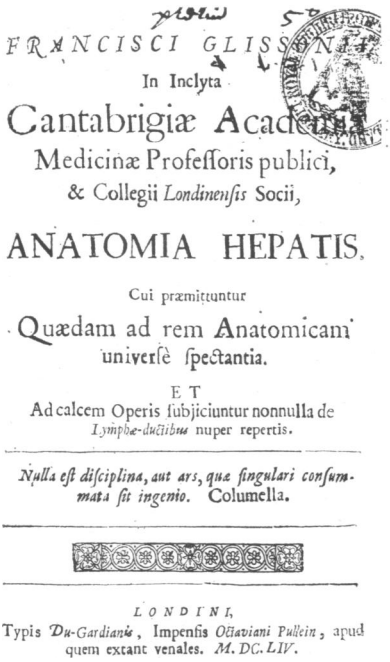
So, after this account of Glisson's life, let us look at his writings and see what he did for medicine and science.

The " Anatomia Hepatis "

The *Anatomia Hepatis* was Glisson's second publication, but he probably wrote much of it before his work on Rickets. The first edition was published in London in 1654 and is an octavo volume of 458 pages (Fig. 6*a*). The first 10 chapters deal with general anatomy, and after this they are renumbered with 45 chapters on the liver. Subsequent editions

were printed in Amsterdam in 1659 and 1665 and in the Hague with some copies dated 1681 and some 1682. No English translation has ever been published.

For those not acquainted with the anatomy of the liver, I should say that the portal vein and hepatic artery are the two vessels which carry blood to the liver, and, to quote Gray's *Anatomy*, " The portal vein and hepatic artery . . . are all enveloped in a loose areolar tissue, termed the hepato-biliary capsule (of Glisson) which accompanies these vessels in their course through the portal canals in the interior of the liver ".



FRANCISCI GLISSONII

In Inclyta

Cantabrigiæ Academia

Medicinæ Profeſſoris publici,

& Collegii *Londinenſis* Socii,

ANATOMIA HEPATIS,

Cui præmittuntur

Quædam ad rem Anatomicam univerſè ſpectantia.

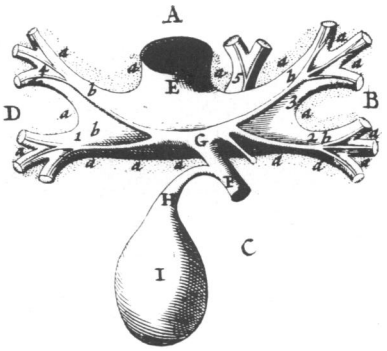
ET

Ad calcem Operis ſubjiciuntur nonnulla de *Lymphæ-ductibus* nuper repertis.

Nulla eſt diſciplina, aut ars, quæ ſingulari conſummata ſit ingenio. Columella.

LONDINI,

Typis *Du-Gardianis*, Impenſis *Octaviani Pullein*, apud quem extant venales. *M. DC. LIV.*



A. Hepatis gibbum.
B. Pars illius dextra.
C. Cavum hepatis.
D. Pars ſiniſtra.
E. Truncus Portæ ſurſum re-flexus, ut cætera vaſa facilius conſpiciantur.
1.2.3.4.5. Ejuſdem quinq; rami majores.
F. Ductus communis.
G. Porus bilarius, ipſiuſque prima diviſio.
H. Meatus cyſticus.
I. Veſicula fellis.
a.a.a.a. Capſula communis aperta.
b.b.b.b.b. Pori bilarii ſubdiviſiones.

2^do. Ad

Fig. 6 (*a*) The title page of the first edition of *Anatomia Hepatis*. (*b*) Illustration of the division of the portal vein, from Glisson's *Anatomia Hepatis*.

It must be admitted that the presence of Glisson's capsule had been noted before he described it. Johannes Walaeus or de Wale of Brussels wrote two letters to Thomas Bartholin of Copenhagen in 1640 concerning the motion of chyle and blood, and in one of these he states that the branches of the coeliac artery, of the portal vein and of the bile ducts all lie together in a common sheath (*communi tunicae*), but he does not describe this tunic in any detail. These letters were published in an edition of the works of Spigelius by J. A. van der Linden in 1645.

It is to Glisson that we owe the first thorough description, and he applied the name capsule to it. In his account of the portal vein (chapter XXV) he writes: " As soon as this vein enters the liver it assumes another membrane: unless it is better to call this additional membrane by the name of common capsule because it embraces two sorts of vessels." Chapter XXVII is headed, " On the distribution of the common capsule to the portal vein and the bile duct ". " This part ", he writes, " was completely unknown to the ancients and thus lacked a name until now. I first had occasion to identify this part (unless I am mistaken) when 12 years ago on the instructions of the College of Physicians of London it fell to me to prepare a public lecture and to that end I freed the livers of several animals of their parenchyma. . . . When first it receives the trunk of the portal vein, it is continuous with the covering of the liver (and by this means with the peritoneum). For this capsule extends into the interior of the liver, where the portal vein enters, and as soon as this vein approaches the liver, it enters the capsule, and when it reaches the interior it must be connected to the covering which here encircles the liver. As soon as the capsule embraces the portal vein and the bile duct, it at once divides following the pattern of the portal vein, and is divided with it into minute capillaries and achieves distribution throughout the whole liver." He then describes how the capsule is extended in the foetus to include the umbilical vein and the ductus venosus.

There is still an echo of the five-lobed liver in Glisson's description of the branches of the portal vein in the liver, for in one of his diagrams they are labelled 1 to 5, but he also clearly shows that in fact the portal vein divides into two main branches as soon as it enters the liver, and that the branch to what he calls the protuberance, and which we now call the caudate lobe, comes off in a rather different way, and not by division of a main trunk into two more or less equal branches, which is the way the veins normally branch in the liver (Fig. 6*b*). He says, " The portal vein enters the liver in this fashion. After it has penetrated it for about the length of half a thumb, it is carried part on the right and part on the left, and then it is fashioned as it were into a fold . . . and from there it is divided into five wide branches; of these, four are diffused far and wide through the substance of the liver, but the fifth leads straight towards the protuberance."

I myself have had on many occasions to dissect out this area in the living patient when making a portocaval venous anastomosis in order to expose the division of the portal vein into its two main branches. It is necessary to divide Glisson's capsule where it is attached to the vein. At the point of division the larger right branch is in a more direct line with the portal vein than the left branch, which usually makes an angle of about 120° with the main vein. The branch to the caudate lobe usually comes off the right branch, but sometimes it arises at the division so that the main portal vein appears to divide into three branches, each of which may have

to be ligatured separately. Normally, as Glisson states, the division is just inside the liver, but with a small fibrotic liver the quadrate and caudate lobes become withdrawn upwards so that the division of the portal vein comes to lie quite outside the liver.

Glisson studied the internal anatomy of the liver by injection methods and by making casts. His illustrations show casts of the portal vein and of the hepatic veins (Fig. 7). To make these casts, which he calls " defleshing " the liver, he describes two methods which had been used by

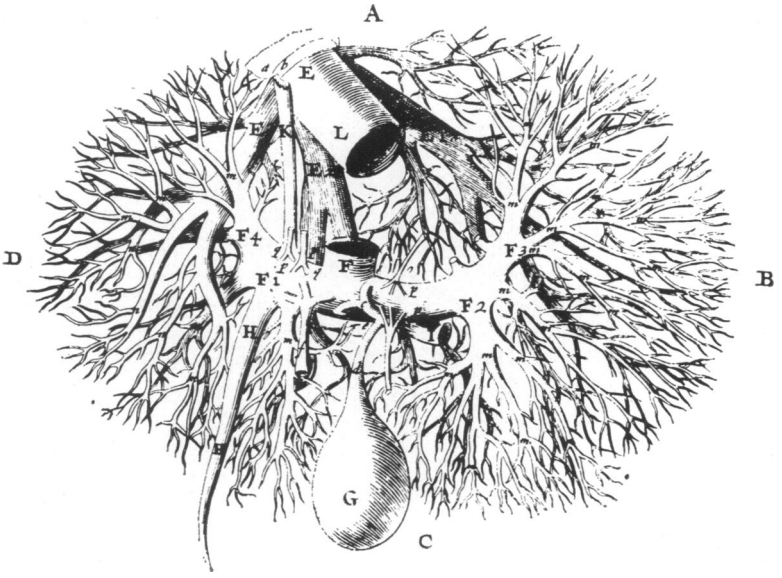


Fig. 7. One of Glisson's drawings of a cast of the intrahepatic vessels, from his *Anatomia Hepatis*.

Spigelius, who had been professor of anatomy and surgery at Padua. The first was by cooking the liver in a little water and then rubbing off the soft tissue with a small piece of wood, stone or blunt metal, but he found the method " neither tidy, convenient or effective ". The second method, which he describes as easier, is to " place the liver in a heap of ants and leave it there until it has been eaten away by them (as happens very quickly) ". But he discounts this method for many reasons—" one would have to make sure that the liver so buried was not mangled by animals and birds of prey; that the ants themselves were not too torpid in winter to take part in the feast; that the liver was not subject to being putrefied by the sun in summer which would make accuracy impossible. In winter the liver would stiffen in snow, frost and ice, and then thaw and become flabby when rain fell. In summer the outside would become

hard and dry before the ants had eaten away the inside. Perhaps ", he concludes, " one would have to avoid being bitten." Rejecting both these methods of Spigelius, he advises thoroughly cooking the liver for one hour, and then, when it is cool, dissecting off the parenchyma with small specially prepared sticks using the utmost care not to damage the vessels.

Glisson devotes a long chapter to discussing how the blood from the portal vein gets to the vena cava, for at that time there had been no microscopic study of the liver and the sinusoids had not been demonstrated. He came to the conclusion that the blood passed through capillaries, and also demonstrated that the colour of the liver is due to the contained blood. His observations are worth recording. " To confirm this theory once and for all I offer a remarkable experiment, which sheds illumination not only on the passage of the blood from the portal vein to the cava, but also on many aspects relating to the circulation of the blood. Not long ago, a private dissection of a lady was effected at the Anatomy Theatre at London, which was attended by only a few members of the College; an attempt was made to establish how easily water forcibly injected into the portal vein would pass through the liver. We filled a large ox bladder attached to a syphon (just as we usually do in giving enemata) with warm water coloured with a little milk, and we tied with a thread the end of the tube into the portal vein near its entry into the liver, so that we could make certain that none of the liquid returned. What happened? When the bladder was strongly compressed, the water instantly passed through the liver entering the cava, and from there was carried to the cavity of the right side of the heart, and approached the lungs through the arterial vein, and after passing through these it returned to the left ventricle, from there it was carried to the aorta, and finally we found clear traces of this milky fluid in the kidneys themselves. But setting aside that part of the tale which does not concern the present subject, the liquid thus injected into the liver washed out the blood gradually not only from the larger vessels, but also from the capillaries and from the parenchyma itself. For the bloody colour of the parenchyma appeared perceptibly to fade; and when all the blood was washed out the liver became yellow with a dusky white colour. And this colour (as I think most probable) is closer to the natural colour of the liver than the ruddy hue which it borrows from the blood flowing through it." In this way Glisson opposed the view of Bartholin that there were direct venous anastomoses between the branches of the portal vein and the vena cava in the liver.

I have already mentioned that the lacteals had been described by Aselli in 1622 and that Pecquet had shown in 1651 that they did not carry chyle to the liver. It is surprising, therefore, that Glisson wrote: " I first became acquainted with them through the evidence of Dr. Jolyffe, in the year 1652, at the beginning of June; at that time he was about to obtain his doctorate, and had met me at Cambridge to that end."

Evidently Dr. Jolyffe's thesis dealt with the lymphatic system, but we know nothing more of the author. When Glisson read Bartholin's book on the lymphatic veins, published in 1652, in which it was stated that some of them came from the liver, he took more interest and carried out some investigations himself, and so proved that the lymph flows in these vessels away from the liver. " But if one devotes time ", he wrote, " to the investigation into how the humour in them inclines, it will become obvious that it flows from the liver, but not towards it, and this can be clearly proved from the structure of the valves which can be found in them in large numbers; though they allow an easy passage for the liquid flowing from the liver, they are closed to it if it returns." He adds that these lymphatics leave the veins and " proceed straight to the common receptacle into which they disburden themselves ".

The full title of the book is *The Anatomy of the Liver, prefaced by some matters of general anatomical importance. And to this work is added something concerning the lymph ducts only recently discovered.* It is the one which earned for Glisson the tribute of Boerhaave, and Dr. Singer described it as " The first original work of anatomical importance printed in England ".

A brief note can be made here of Glisson's other publications. His first book was the one on *Rickets*, published in London in 1650, with further editions in 1660 and 1671. Copies were printed in Leyden in 1671 and in the Hague in 1682. An English translation by Philip Armin came out in 1651, and in some of the copies there is a note that it was " enlarged, corrected and amended " by Nicholas Culpeper, the noted herbalist, who had recently published an unauthorised translation of the pharmacopoeia of the College of Physicians. A further English edition came out in 1668.

Glisson believed that Rickets was a new disease and that it had made its first appearance earlier in the century in Dorset and Somerset. It is first met with in the Bills of Mortality for the City of London in 1634, and Glisson was forestalled by at least two medical writers about the disease. Daniel Whistler, who had taken the degree of M.D. at Leyden in 1645 gave as the title of his inaugural dissertation " Concerning the disease of English children which in the country of its origin is called ' The Rickets ' ", and gave a general account of the disease. The controversy as to whether he got his information from Glisson has been discussed in detail elsewhere (34, 35) and need not be repeated here. The other writer was Arnold Boate, who published a book in 1649 concerning *Medical Observations on Neglected Diseases*, in which he gave a short account under the name *Tabes Pectorea.* Glisson's work was much more detailed than either of these and remained the classical description for over 200 years. It is Glisson's writings on the use of splints and slings which led Little (36) to describe him as an orthopaedic surgeon, and he

tells us that Glisson's sling for the treatment of spinal deformity was in use, especially on the Continent, up till the 19th century.

Glisson's third book, published when he was about 75 years old, is a philosophical one with the title which may be translated as *A treatise concerning the natural energy of matter, or the nature of life, of which there are three primary factors, natural perceptions, natural passions and natural motives.* His philosophical views have been summarized by Dr. Pagel (37), who shows that Glisson's ideas are in the direct line of Aristotle and

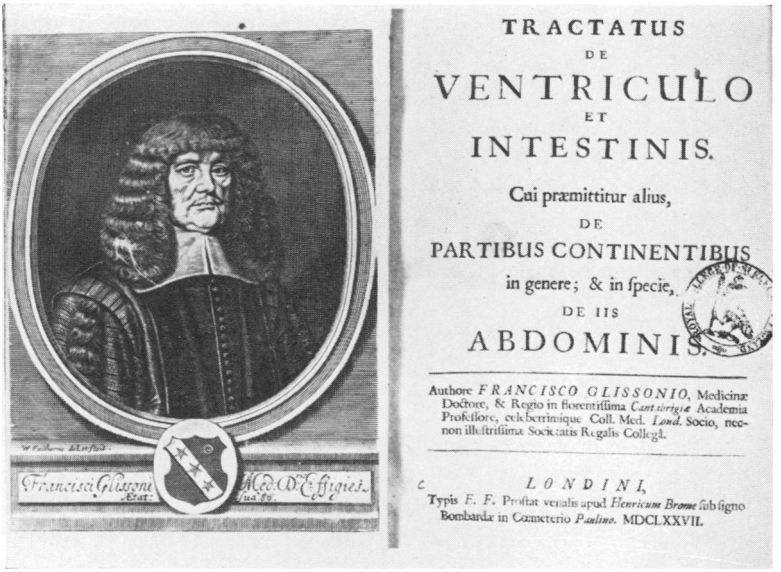


Fig. 8. Title page of Glisson's last book, with the engraving by W. Faithorne.

Harvey. Opposite the title page is an engraved portrait by W. Dolle, evidently taken from the painting to which I have already referred. The book was printed in London in 1672, and as his age is given on the engraving as 75, this probably accounts for his birth having been placed in 1597.

His last work appeared in the year of his death, though he had been working on it since 1662 (Fig. 8). It is his treatise concerning the *Stomach and the Intestines*, published in Latin in London in 1677, with another edition in Amsterdam in the same year, and one in Leyden in 1691. This also contains an engraving of the portrait, this time done by W. Faithorne, and the age is given as 80. This book is concerned with the anatomy and the physiology of the alimentary canal, and it received in the next century generous tributes from that famous Swiss physiologist,

Albrecht von Haller. In it he sets out his theory of irritability and spontaneous contraction. He opposed the still current Galenic theory that animal spirits were formed in the rete mirabile of the brain and were distributed by minute channels in the nerves to the organs and muscles. However, as Needham points out (38), Harvey had recognized the spontaneous irritability of tissues, for in his *De Generatione*, published in 1653, he had written, " Nor is it less new and unheard of, that there should be sense and motion in the foetus before the brain is made; for the foetus moves, contracts and extends himself when there is nothing yet appears for a brain, but clear water ".

There seems to be no doubt that Glisson was the first to make use of plethysmography, by which he demonstrated that the volume of a muscle does not increase during contraction. He describes his experiment thus: " Let there be provided a glass tube, in length and bore enough to hold a man's arm, and to the upper orifice of it on the outside fix another glass tube about an inch diameter in bore, shaped like a common weather glass, only with a wide mouth like a funnel, so that the lower end may be open into the greater tube, whose bottom is firmly stopped. Then having erected both tubes, let a man of strong and brawny muscles thrust his whole naked arm into the greater tube up to the very shoulder, above which the orifice of the glass must be closely luted, that no water may flow out that way. This done, let as much water be poured in as both glasses will receive, leaving only a little space at the top of the lesser empty. Finally, let the man strongly contract all the muscles of his arm by clenching his fist and relax them again by turns; and you will observe that when he contracts his muscles, the water in the lesser tube will sink somewhat lower, but rise again when he relaxes them. Whence it is evident that the muscles do not swell up, nor are inflated at the time of their contraction, but rather are lessened and contracted in all their three dimensions; otherwise the water would at that time not descend, but ascend, in the neck of the funnel " (39).

To sum up, we may regard Francis Glisson primarily as an anatomist, but he also made new observations in clinical medicine and in physiology. He has been acclaimed as an orthopaedic surgeon, and in his later years turned to philosophy. He was one of the great doctors of the 17th century who helped to advance English medicine at a time when Harvey's discovery was opening up wide fields of new ideas. He was not limited in his outlook, and he was a most accurate observer. It is perhaps unfortunate that his name has become associated with a trivial anatomical structure, which he was not in fact the first to discover, which is of no practical importance, and has now rightly been relegated to small print in the anatomy books. At least it remains to bring his name before us.

Finally, my Lord President, I must thank you for inviting me to give this, the 46th Thomas Vicary lecture. If your invitation has done nothing more, it has given me the stimulus to much interesting study.

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