

The case of the “S-shaped tubule”: how over-user-friendly nomenclature can lead to a century of embryological errors

Jamie A. Davies

Deanery of Biomedical Sciences, University of Edinburgh Medical School, Hugh Robson Building, George Square, Edinburgh EH8 9XD, UK

SUMMARY

Standardized nomenclature is important to biology. Anatomical naming usually uses standard Greek- or Latin-derived terms to describe shape, but sometimes draws comparisons with everyday objects, aiming to reduce ambiguity and increase clarity. In the case of developing kidney, it did the opposite. In 1883 and 1889, two stages of nephron development were named after typographical characters, comma and ‘S’. This caused confusion in 3 ways; (i) an ‘S’ shape can be seen in different ways at different phases of nephron development, encouraging stage misidentification; (ii) ‘S’ has a completely different shape in Roman and Fraktur (‘Germanic’) fonts, used in a still-cited paper; (iii) a printed, rather than cursive, ‘S’ implied a stand-alone object, causing authors wrongly to represent S-shaped nephrons as unconnected. This story acts as a warning against making names so easy that they give an illusion of understanding without the need to check the original source.

Key words: Nomenclature – S-shaped tubule – Font – Typography – Expectation bias – Scientific error – Kidney development

INTRODUCTION

Accurate and agreed nomenclature has long been considered essential for descriptive sciences (Bruford et al., 2022). Global organizations that coordinate specific fields often have formal committees that publish authoritative nomenclatures and ontologies (e.g. the Human Genome Nomenclature Committee, the Nomenclature Committee of International Union of Basic and Clinical Pharmacology, and the Federative International Program for Anatomical Terminology). Ideally, names will be unique, unambiguous, and easy to understand even to people who have not met a particular name before. Unambiguousness and ease of understanding appear at first sight to be well aligned ideals, but sometimes a name can be chosen so well that readers will think they understand it instantly without having to consult the original definition; this can result in persistent misunderstanding. This short report examines one anatomical/ embryological case that has been causing confusion for at least the last hundred years.

The issue centers on the description of anatomical phases of tubule development during the organogenesis of the mammalian kidney. Kid-

Corresponding author:

Jamie A. Davies. Deanery of Biomedical Sciences, University of Edinburgh Medical School, Hugh Robson Building, George Square, Edinburgh EH8 9XD, UK. Phone: +44-131-6502999. E-mail: jamie.davies@ed.ac.uk

Submitted: June 6, 2025 **Accepted:** September 12, 2025

<https://doi.org/10.52083/JTDF9120>

ney development begins when an initially unbranched tube, the ureteric bud, invades an area of specialized mesenchyme, the metanephric mesenchyme (sometimes called metanephrogenic mesenchyme; e.g. by Huber, 1905; Grobstein, 1956; Perantoni et al. 1991; Davies, 1996; Huber et al. 2000; Davies and Fisher, 2002). Under the influence of signals derived from the metanephric mesenchyme, the ureteric bud grows and branches repeatedly to make the tree-like urinary collecting duct system, the ‘trunk’ of the tree becoming the ureter. Signals from the bud to the mesenchyme causes it to produce ‘caps’ of stem cells around the tips of the ureteric bud branches. These caps maintain their own population and give rise to cells that will be ‘left behind’ by the advance of the branch tip and its cap; these differentiate to form excretory nephrons. Each nephron begins as a relatively simple cyst-like epithelium and then develops into a tube, one end of which will form the Bowman’s capsule around the glomerulus, where blood is filtered, and the other end of which will connect to the collecting duct system. Between these two ends, the tubule grows long and convoluted, and acquires regional specializations.

The process by which the intricate anatomy of the mature nephron emerges was interesting to embryologists, who divided the process into a succession of stages and named them. The challenge of the kidney is that the thousands or millions of nephrons in a kidney (depending on species) develop similarly but at different times, rather than precisely in parallel, so stages of nephron development cannot be named in a way that refers to the age of the embryo. Instead, they must be named in reference to the characteristics of the nephrons themselves, at each stage of their development. Given that the nomenclature was first established in the 19th Century, the characteristics had to be morphological as there was no possibility of defining stages by gene expression. The first stage of nephron development, a relatively uniform sphere (Fig. 1a) was named using standard morphological terms as the ‘renal vesicle’ (Émery, 1883). The next two stages were named for their similarity to typographical characters; the ‘comma-shaped body’ (Herring, 1900)

(Fig. 1b) and the ‘S-shaped body’ (Golgi, 1889) (Fig. 1c). Beyond that, the nomenclature returns to being straightforwardly anatomical without reference to typography; the ‘capillary loop stage’, followed by the ‘maturing renal corpuscle’, before converging with the anatomical terminology that is applied to the adult kidney (Little et al., 2007). Of these terms, the ‘comma-shaped body’ and ‘S-shaped body’ would seem to be the most easily understood because of their reference to the homely and familiar. Yet it is these terms, particularly the ‘S-shaped body’, that have caused trouble and continue to do so.

Fortunately for historians, and for any experimentalists interested enough to check, the embryologists who first coined the terms published very clear diagrams, drawn from sections, to illustrate them. Figure 2 shows the drawing that accompanied Golgi’s 1889 coining of the term ‘S-shaped tubule’, together with an excerpt of his original text, and an English translation. The similarity between what he drew, particularly the right hand ‘S’ of his figure, and the micrograph in Fig. 1c is obvious and it is not surprising that the nomenclature based on the letter ‘S’ caught on (the left-hand of the two nephrons Golgi drew is like an ‘S’; the other is mirror-image). It has, however, created two types of misunderstanding; one about the precise stage to which it refers, and the other about the independence of the nephron at these stages. Thankfully, the first of these misunderstandings is probably now consigned to history, but the second continues to haunt the field.

MISUNDERSTANDING 1: WHICH ‘S’?

The clear implication of the phrase ‘S-shaped body’ (or ‘S-shaped nephron’/‘S-shaped tubule’) is that if a researcher can see the shape of the letter ‘S’ in the nephron, the nephron must be at this developmental stage. The problem is that the letter S can be mapped to several stages of development, especially if care is not taken to exclude the collecting duct itself from being part of the form of the ‘S’. This was understood soon after the term ‘S-shaped body’ was coined. From at least the turn of the 20th century, researchers began to apply the term ‘S-shaped body’ to both the stage indicated by Golgi (1889), and also to earlier stag-

es at which an S-shape was discernible but less developed (Fig. 3). To complicate things further, the careful analysis by Stoerk (1904) drew attention to the fact that the letter 'S' can be seen in at least two distinct ways during nephron development; he called Golgi's the 'primary S' and then indicated the presence of a 'secondary S' that was produced by further convolution of the middle of the original 'S' (Fig. 3).

A much deeper confusion was sown by William Reinhoff, in his 1922 publication, Development and growth of the metanephros or permanent kidney in chick embryos. Reinhoff was an American, born in 1894 in Springfield, Missouri, and studying at Cornell and Johns Hopkins. He published his paper in English in the Johns Hopkins Hospital Bulletin and this, like all English-language journals, used a Roman font (that

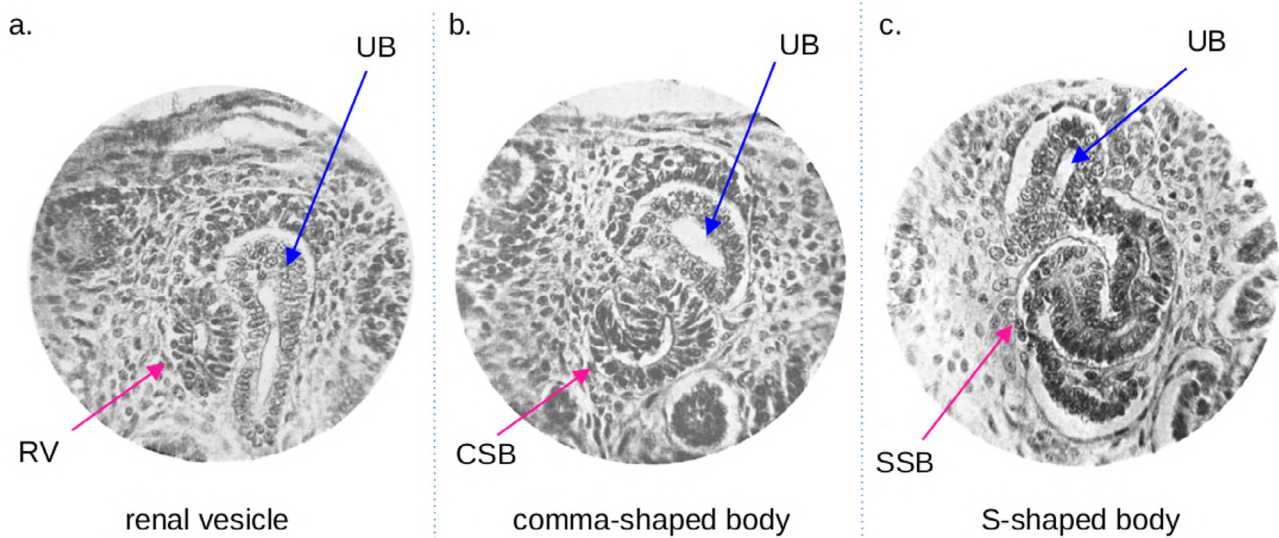
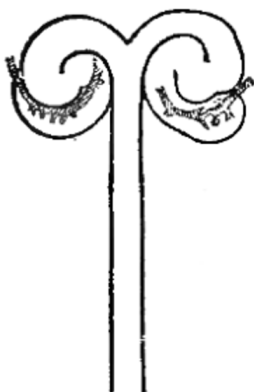


Fig. 1.- Stages of human nephron development, in a series of photo-micrographs taken from Herring (1900), who coined the term 'Comma-shaped body'. Out of copyright (Herring died in 1947).

— 339 —



« Riguardo alle particolarità di formazione, nei preparati anzidetti, dirigendo l'attenzione sull'estremità periferica dei canalicoli retti, si può rilevare la formazione di iniziali bottoni epitelari, i quali, sviluppandosi, si incurvano prima in basso e all'interno, poi in senso opposto, formando una S a curve strettamente avvicinate (v. fig. 2^a primo disegno a sinistra). In queste

With regard to the particularities of formation, in the above-mentioned preparations, directing the attention to the peripheral end of the tubules, the formation of initial epithelial 'buttons' can be detected, which, as they develop, curve first downwards and inwards, then in the opposite direction, forming an S with closely approached curves. [Google Translate]

Fig. 2.- Figure from Golgi (1889), in which he drew the form of what he referred to as an S-shaped body (coining the word for the first time). To the right of the figure is a facsimile of his original text, showing the precise Roman font used, and below that is a translation. The right-hand of the two S-shaped bodies in the diagram, both of which are shown connected to the central ureteric bud branch, can be compared directly with Herring's micrograph in Fig. 1c. The other is mirror-reversed.

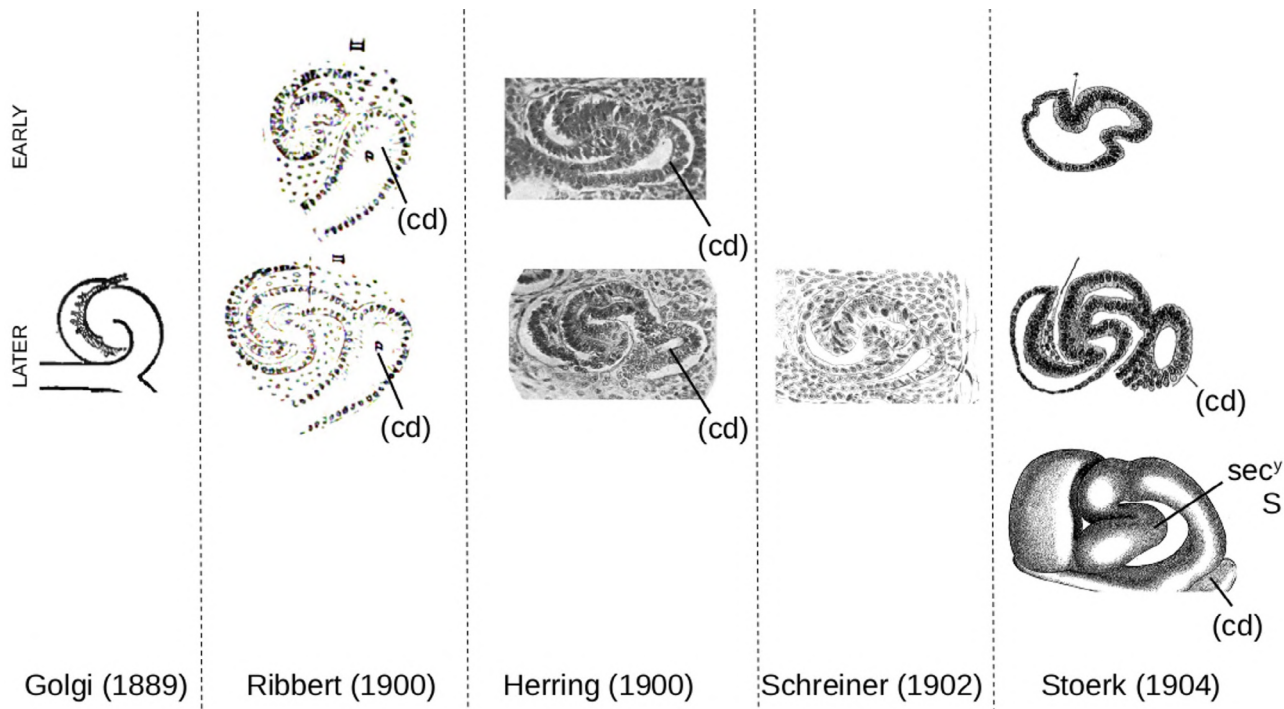


Fig. 3.- Drawings of the S-shaped tubule from various researchers near the turn of the 20th Century. Golgi (1889) coined the term 'S-shaped body' and drew a representation of what he meant. At least from the time of Ribbert's 1900 publication, some authors grouped more than one morphological stage under the term 'S-shaped body' (the upper drawings being of less mature stages), though Schreiner (1902) stuck with Golgi's specification. Stoerk (1904) drew explicit attention to the development of a 'secondary S' that formed by further morphogenesis of the maturing tubule. In this figure, original drawings have been rotated so that they align with each other as closely as possible. The label 'cd' is used to distinguish the collecting duct, and the label 'secy S' points to the secondary S of Stoerk.

is the type of font you are reading now, assuming you are reading in the English original and not a translation to a language with a different alphabet). Yet, for some reason, when he wanted to refer to the 'S-shaped tubule', he switched from a Roman font to a Fraktur font in which a capital 'S' is rendered as 'Œ'. Reinhoff made no comment about why he made this choice. Fraktur font, often called informally 'the German typeface', was still relatively common in newspapers and public documents in German-speaking countries, and was in occasional use in some Baltic states and in Norway. It was not, however, in use in the German language journals that had published studies on kidney development (e.g those that published Ribbert, 1900, Schreiner, 1902, Disse 1902, Stoerk 1904). All of these were printed using Roman fonts, like this one, in which the key letter is rendered as 'S'. At least one German author, Stoerk, writing in German, was aware that the differences between fonts could be a source of confusion and he described the tubule as having "die Form eines römischen S", meaning "the shape of a Roman S" (Stoerk, 1904). Similarly, G. Carl Huber, an

American born in India to German-Swiss parents, and writing about kidney development in English, specified Roman font for the S to which nephrons are compared (Huber, 1905). Naturally, the key paper in which Golgi defined the S-shaped tubule, being in Italian, was printed in a Roman font (Golgi, 1889). I have failed to find any relevant papers before Reinhoff that used a Fraktur font. One possibility is that he misunderstood the nature of the Roman font specified by the two German-speaking authors mentioned above, and thought that 'Roman' was the word for the 'German font' rather than the one already standard in the USA. Another possibility, that he had first read about the nephrons from hand-written letters from German authors, seems unlikely for two reasons. First, for more than a century before 1911, Germans were taught in school to write in Kurrentschrift (German cursive), a script used for hand-writing that is not the same as printed Fraktur (in Kurrentschrift, the shape of the letter does not look like any kind of nephron). Second, Reinhoff cited numerous German papers and, assuming he had read them before citing them, he would have seen

that they used a Roman S.

The problem about Reinhoff's '€' is that it matches rather well the form of what is normally called the comma-shaped body, the predecessor to the S-shaped body. This is illustrated in Fig 4a, which compares '€' to a comma-shaped body drawn by Herring (1900) and Fig 4b, which compares 'S' to an 'S'-shaped body, also drawn by Herring (1900). Reinhoff uses the phrase 'comma-shaped body' in his paper and discusses the comma-to-'€' transition extensively, so he was quite clear in his mind that the comma is a stage distinct from the later 'S'. What is more, when he drew S-shaped tubules (Fig 4e), he drew them in a standard way that matched the earlier work of others. This makes his use of '€' even more difficult to understand; perhaps he focused only on part of the nephron to see his '€' shape, as indicated speculatively in Fig 4c. This, though, seems unlikely as he stressed that the nephron grows into the collecting duct (rather than a branch of collecting duct growing into the nephron), so he must have been aware that there was no reason to exclude any parts of the nephron shown in his drawing in his attempt to map nephron shape onto a typographical character.

It is difficult to estimate how many people have read Reinhoff's '€'-containing paper, but it has been cited 86 times, according to Google Scholar, and it continues to be cited as a foundational reference well into the 2020s (e.g. Schnell et al., 2022). It is therefore not surprising that entities matching almost exactly the shape of an '€' continue to be identified as S-shaped tubules. An example is shown in Fig 4d from Chung et al. (2017); this particular image was chosen for its clarity and its ease of re-use thanks to a CC-BY-4.0 licence and I am in no way singling out its authors for criticism. Indeed, there is no criticism to be made, because since Reinhoff and possibly because of him, and because of Stoerk's 'secondary S', the range of morphologies covered by 'S-shaped tubule' has become broader and less precise than when Golgi offered his original 1889 definition.

MISUNDERSTANDING 2: A FALSE INDICATION OF INDEPENDENCE

When Golgi drew his definitive S-shaped tubule, it was connected to the collecting duct (Fig 2). All of the other drawings and micrographs reproduced in Figs 1-4 also show this connection; this

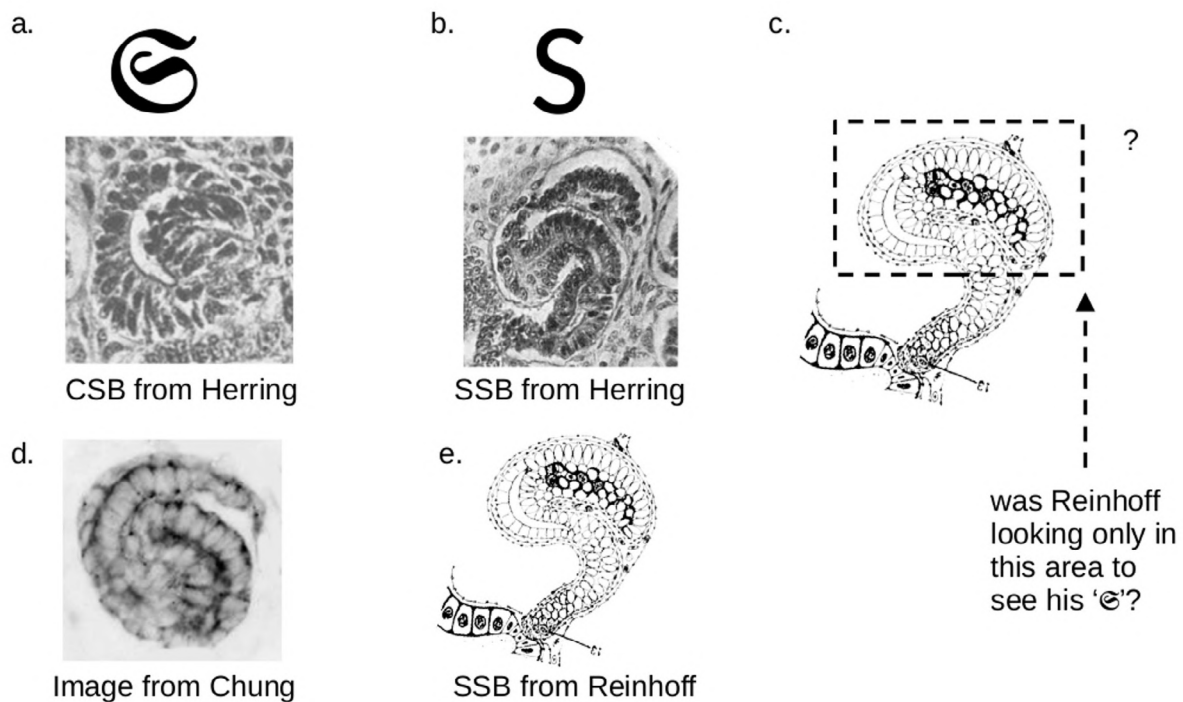


Fig. 4.- Reinhoff's drawings, and real photomicrographs that align with his Fraktur character. (a) shows two drawings taken directly from Reinhoff's paper, but rotated 90 degrees for compatibility with Fig. 3. The sketches are very similar to those of the authors whose drawings appear in Fig. 3, suggesting that Reinhoff was seeing the same thing that they thought were 'S' shaped. Strikingly, it is much easier to see how they contain the shape of the Roman S than the Fraktur character shown in (b). Panel (c) shows a photomicrograph from a much more recent paper (Chung et al., 2017; the figure comes from their Fig. 1c lower row panel 4, with other tubules blanked out, and the image inverted and rotated here to align with this Fig. 4a.). This was identified by Chung et al. as being an S-shaped tubule. Here the morphology looks very much more like the Fraktur S, and has no real character of the Roman one.

is entirely correct as the S-shaped body is always connected in this way in a real developing kidney. But the capital ‘S’ used to refer to this stage stands alone; it is not a cursive character and it carries no hint that it should be joined to anything. Perhaps for this reason, many authors, even those who have looked at real kidneys many times in their research career, have drawn the S-shaped tubule as existing completely independently of the collecting duct, with no indication of any contact or joining. Examples drawn from a variety of modern research papers, chosen here among many others simply because they have a copyright that allows free re-use of images, are reproduced in Fig 5. The misunderstanding matters because the collecting duct may well be a source of at least some signals that pattern the nephron (Lindström et al., 2015), and if researchers think about them as separate objects, rather than the continuum they really are, promising hypotheses about patterning mechanisms will be missed.

CONCLUSION

This story, in an admittedly obscure and niche corner of anatomical nomenclature, illustrates a danger of making nomenclature too user-friendly. Slightly difficult nomenclature forces a researcher entering a field to look at proper source material to understand what it meant. Apparently very obvious nomenclature that draws analogies with letter shapes (or other everyday items) can seem so straightforward that there is no need to check the original definition, and that can lead to misunderstandings. No such misunderstandings have plagued the other stages of nephron development, named in a less accessible way. Paradoxically, then, non-obvious naming may serve the end user much better than ‘user-friendly’ names that seem to save them work.

STATEMENTS AND DECLARATIONS

AI: AI tools were not used in the writing of this report. Google Translate was used to provide the translation included as part of Fig. 2.

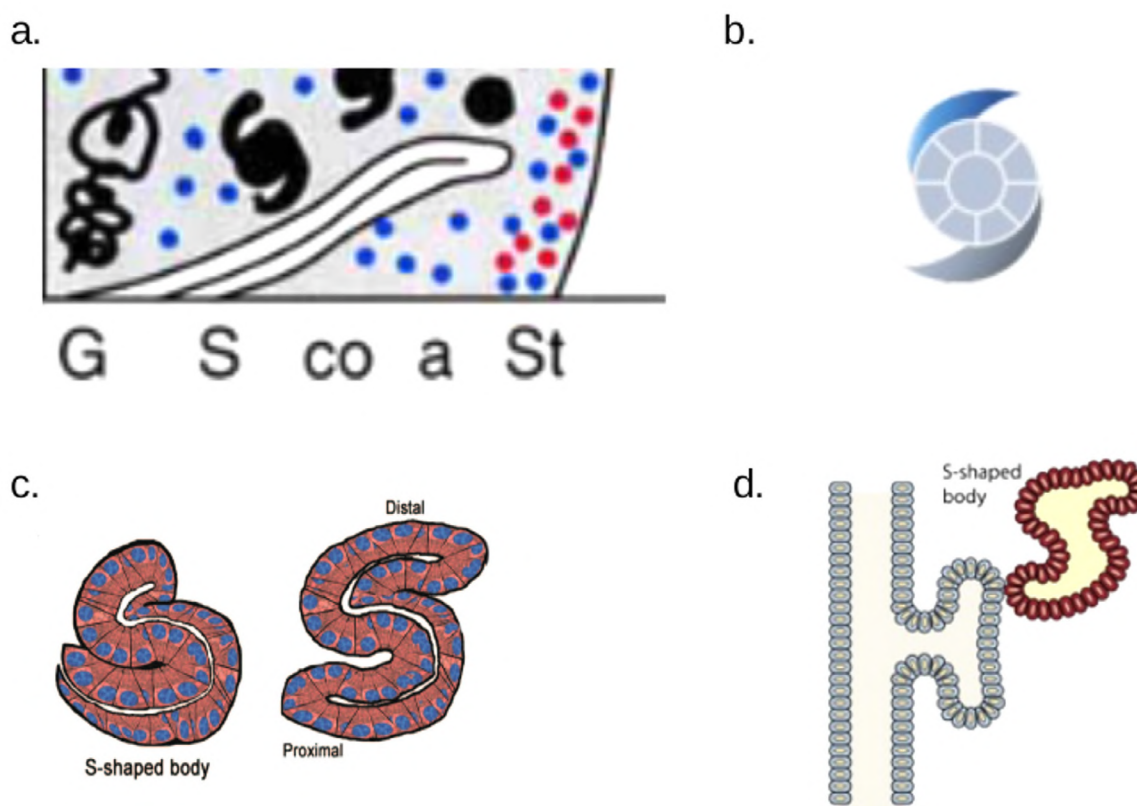


Fig. 5.- Examples of drawings that depict the S-shaped nephron as individual, or as only touching the collecting duct, instead of fully joined to it as shown in Golgi’s original definition (see Fig. 2) and in the micrographs in Fig. 3. Panel (a) is from Bard (1996), his Fig. 1; (b) is from El-Dahr (2017), their Fig. 1c; (c) is from Davidson (2009), his Fig. 6; (d) is from Hohenstein et al. (2015), their Fig. 2. These examples were chosen because of their Creative Commons licences, allowing simple reuse. Other examples include Saxén and Wartiovaara (1966), Patterson and Dressler (1994), Gill and Rosenblum (2006), Kreidberg (2010), Plenicéanu et al. (2010), Naylor and Davidson (2013), Schoenwolf (2015), Yosypiv (2017), Torban et al. (2021), and Nishimura et al. (2024).

REFERENCES

- BARD J (1996) A new role for the stromal cells in kidney development. *Bioessays*, 18(9): 705-707.
- BRUFORD EA, BRASCHI B, HAIM-VILMOVSKY L, JONES TEM, SEAL RL, TWEEDIE S (2022) The importance of being the HGNC. *Hum Genomics*, 16(1): 58.
- CHUNG E, DEACON P, PARK JS (2017) Notch is required for the formation of all nephron segments and primes nephron progenitors for differentiation. *Development*, 144: 4530-4539.
- DAVIDSON AJ (2009) Mouse kidney development. In: *StemBook* [Internet]. Cambridge (MA): Harvard Stem Cell Institute. Image copied 6th March 2025.
- DAVIES JA (1996) Mesenchyme to epithelium transition during development of the mammalian kidney tubule. *Acta Anat (Basel)*, 156(3): 187-201.
- DAVIES JA, FISHER CE (2002) Genes and proteins in renal development. *Exp Nephrol*, 10(2): 102-113.
- DISSE J (1902) Harn und Geschlechtsorgane. *Bardelebens Handbuch der Anatomie des Menschen*. Bd 7, Fischer, Jena.
- EL-DAHR S, HILLIARD S, SAIFUDEEN Z (2017) Regulation of kidney development by the Mdm2/Mdm4-p53 axis. *J Mol Cell Biol*, 9(1): 26-33.
- ÉMERY C (1883) Recherches embryologiques sur le rein des mammifères par C. *Arch Ital de Biol*, Turin 1883. Tomo iv, p 80.
- GILL PS, ROSENBLUM ND (2006) Control of murine kidney development by sonic hedgehog and its GLI effectors. *Cell Cycle*, 5(13): 1426-1430.
- GOLGI C (1889) Annotazioni intorno all'istologia dei reni dell'uomo e di altri mammiferi e sull'isto-genesi dei canalicoli uriniferi. *Rendiconti R Accad Lincei*, 5: 545-557.
- GROBSTEIN C (1956) Trans-filter induction of tubules in mouse metanephrogenic mesenchyme. *Exp Cell Res*, 10(2): 424-440.
- HERRING PT (1900) The development of the Malpighian bodies of the kidney, and its relation to pathological changes which occur in them. *J Path Bact*, 6: 459-496.
- HOHENSTEIN P, PRITCHARD-JONES K, CHARLTON J (2015) The yin and yang of kidney development and Wilms' tumors. *Genes Dev*, 29(5): 467-482.
- HUBER GC (1905) On the development and shape of uriniferous tubules of certain of the higher mammals. *Am J Anat Suppl to vol IV*, pp 1-98.
- HUBER SM, BRAUN GS, SEGERER S, VEH RW, HORSTER MF (2000) Metanephrogenic mesenchyme-to-epithelium transition induces profound expression changes of ion channels. *Am J Physiol Renal Physiol*, 279(1): F65-76.
- KREIDBERG JA (2010) WT1 and kidney progenitor cells. *Organogenesis*, 6(2): 61-70.
- LINDSTRÖM NO, LAWRENCE ML, BURN SF, JOHANSSON JA, BAKKER ER, RIDGWAY RA, CHANG CH, KAROLAK MJ, OXBURGH L, HEADON DJ, SANSOM OJ, SMITS R, DAVIES JA, HOHENSTEIN P (2015) Integrated β -catenin, BMP, PTEN, and Notch signalling patterns the nephron. *Elife*, 3: e04000.
- SCHOENWOLF GC, BLEYL SB, BRAUSER PR, FRANCIS-WEST PH (2015) *Larsen's Human Embryology* (fifth edition). Elsevier Saunders, Philadelphia, USA.
- LITTLE MH, BRENNAN J, GEORGAS K, DAVIES JA, DAVIDSON DR, BALDOCK RA, BEVERDAM A, BERTRAM JF, CAPEL B, CHIU HS, CLEMENTS D, CULLEN-MCEWEN L, FLEMING J, GILBERT T, HERZLINGER D, HOUGHTON D, KAUFMAN MH, KLEYMENOVA E, KOOPMAN PA, LEWIS AG, MCMAHON AP, MENDELSON CL, MITCHELL EK, RUMBALLE BA, SWEENEY DE, VALERIUS MT, YAMADA G, YANG Y, YU J (2007) A high-resolution anatomical ontology of the developing murine genitourinary tract. *Gene Expr Patterns*, 7(6): 680-699.
- NAYLOR RW, DAVIDSON AJ (2014) Hnf1beta and nephron segmentation. *Pediatr Nephrol*, 29(4): 659-64.
- NISHIMURA Y, HANADA S (2024) Origins and molecular mechanisms underlying renal vascular development. *Kidney* 360, 5(11): 1718-1726.
- PATTERSON LT, DRESSLER GR (1994) The regulation of kidney development: new insights from an old model. *Curr Opin Genet Dev*, 4(5): 696-702.
- PERANTONIO DO, DOVE LF, WILLIAMS CL (1991) Induction of tubules in rat metanephrogenic mesenchyme in the absence of an inductive tissue. *Differentiation*, 48(1): 25-31.
- PLENICEANU O, HARARI-STEINBERG O, DEKEL B (2010) Concise review: Kidney stem/progenitor cells: differentiate, sort out, or reprogram? *Stem Cells*, 28(9): 1649-1660.
- RIBBERT H (1900) Über die Entwicklung der bleibenden Niere und über die Entstehung der Cystenniere. *Verhandl Deutsch Path Gesselsch*, pp 187-203 (published 1900 but carrying an 1899 volume date).
- RIENHOFF WF (1922) Development and growth of the metanephros or permanent kidney in chick embryos. *Johns Hopkins Hosp Bull*, 33: 392-406.
- SAXÉN L, WARTIOVAARA J (1966) Cell contact and cell adhesion during tissue organization. *Int J Cancer*, 1(3): 271-290.
- SCHNELL J, ACHIENG M, LINDSTRÖM NO (2022) Principles of human and mouse nephron development. *Nat Rev Nephrol*, 18: 628-642.
- SCHREINER KE (1902) Über die Entwicklung der Amniotenniere. *Zeitsch Wissenschaft Zool*, bd 71, pp 1-228.
- STOERK O (1904) Beitrag zur Kenntnis Aufbaus der menschlichen Niere. *Anat Hefte*, bd 1, p 23. Pathologisch Anatomischen Institut Hofrat Weichselbaums, Wien (Vienna).
- TORBAN E, SOKOL SY (2021) Planar cell polarity pathway in kidney development, function and disease. *Nat Rev Nephrol*, 17(6): 369-385.
- YOSYPYV IV (2017) Prorenin receptor in kidney development. *Pediatr Nephrol*, 32(3): 383-392.