

History and highlights of the teratological collection in the *Museum Anatomicum* of Leiden University, The Netherlands

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The anatomical collection of the Anatomical Museum of Leiden University Medical Center (historically referred to as *Museum Anatomicum Academiae Lugduno-Batavae*) houses and maintains more than 13,000 unique anatomical, pathological and zoological specimens, and include the oldest teratological specimens of The Netherlands. Throughout four centuries hundreds of teratological specimens were acquired by more than a dozen collectors. Due to the rich history of this vast collection, teratological specimens can be investigated in a unique retrospective sight going back almost four centuries. The entire 19th century collection was described in full detail by Eduard Sandifort (1742–1814) and his son Gerard Sandifort (1779–1848). Efforts were made to re-describe, re-diagnose and re-categorize all present human teratological specimens, and to match them with historical descriptions. In the extant collection a total of 642 human teratological specimens were identified, including exceptional conditions such as faciocranioschisis and conjoined twins discordant for cyclopia, and sirenomelia. Both father and son Sandifort differed in their opinion regarding the causative explanation of congenital anomalies. Whereas, their contemporaries Wouter Van Doeveren (1730–1783) and Andreas Bonn (1738–1817) both presented an interesting view on how congenital anomalies were perceived and explained during the 18th and 19th centuries; the golden age of descriptive teratology. Although this enormous collection is almost 400 years old, it still impresses scientists, (bio)medical students, and laymen visiting and exploring the collections of the *Museum Anatomicum* in Leiden, The Netherlands.

KEYWORDS

conjoined twins, enchondromatosis, epigastric heteropagus, faciocranioschisis, holoprosencephaly, hypophosphatasia, Meckel syndrome, nasopharyngeal teratoma, orofaciocdigital syndrome, sirenomelia

1 | INTRODUCTION

The anatomical collection of the Anatomical Museum of the Leiden University Medical Center (historically referred to as *Museum*

Anatomicum Academiae Lugduno-Batavae) currently maintains and houses the oldest Dutch collection of both dried and embalmed, anatomical, pathological, embryological, and teratological human specimens. Founded in 1575, the University of Leiden is the oldest

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university in The Netherlands (Otterspeer, 2000). Over 350 years, many thousands of specimens were brought together and were either purchased from or donated by multiple private and several institutionalized collections (Elshout, 1952). Due to several obtained private collections of different scientists, all with their own specific interests, the anatomical museum of Leiden can be seen as a treasure-trove for both historical and contemporary (dys)morphological research (Smit, 1986).

The first publicly performed dissections at the University of Leiden are assigned to Geraert de Bondt (Gerardus Bontius, 1538–1599) who was professor of medicine, mathematics and astronomy. However, it was anatomy professor Pieter Pauw (Petrus Pavius, 1564–1617), an apprentice of Andries van Wesel (Andreas Vesalius, 1514–1564), who initiated anatomical education in Leiden between 1589 and 1617 (Muntendam, 1923). Pauw was one of the first Leiden professors who dissected human cadavers in order to use the thereby obtained anatomical specimens to educate anatomy on a grand scale; he publicly dissected more than 60 cadavers (Sandifort, 1793). Some of these dissections were described in his posthumously published *Anatomicæ Observationes Selectiores*, including that of a newborn child with an intracranial tumor (Pauw, 1657). Before the practical approach of using a *subjectum anatomicum*, anatomical education was mainly a theoretical exercise (Huisman, 2009). After several dissections, Pauw commanded the build of a *Theatrum Anatomicum* which subsequently opened its doors in 1594 as the first anatomical theater in The Netherlands. Allegorically arranged skeletons of both humans and animals were displayed on the balustrades and surrounded the anatomical theater in a circular manner. They were used for Pauw's lectures on osteology, although they probably also resembled emblems of *vanitas*; the skeletons were holding banners with Latin phrases about life, being indicative for mortality and fragility of (human) existence. The centerpiece consisted of the symbolized skeletons of Adam and Eve with the tree of knowledge in the foreground (Figure 1).

The first anatomical specimens were collected shortly after the establishment of this theater. The newly built theater, located in the Faliiede Bagijnchurch (Church of the Faille-Mantled Beguines) on the banks of the main canal (the Rapenburg) in downtown Leiden (The Netherlands), additionally housed the anatomical cabinet, the university library, the cabinet of natural curiosities and the botanical gardens; serving as an inspiring intertwined working place for both students and scientists around the turn of the 16th century (Huisman, 2009). Additionally, the church served as a tourist destination for it was publicly accessible and open seven days a week. Public dissections attracted people with diverse backgrounds and became frequent and well-visited events (Huistra, 2013). After Pauw's demise in 1617, professor in medicine Otto van Heurn (Otto Heurnius, 1577–1652) was the patriarch in the establishment of the anatomical collection which would subsequently become the *Museum Anatomicum* (Muntendam, 1923). In 1721 Bernard Siegfried Albinus (1697–1770) was appointed as professor of anatomy. Due to illness of his predecessor, Johannes Jacobus Rau (1668–1719), the collection had deteriorated. Albinus was instructed to restore

and make an inventory of Rau's collection. In 1725, Albinus published a catalogue entitled "*Index supelletilis anatomicae: quam academiae Batavae quae Leidae est legavit*" (Albinus, 1725) in which the collections of Rau are described. Bernard Siegfried Albinus enriched the collection with a great number of red injected alcohol-based specimens; some of these magnificent specimens are still present in the extant collection and show the refined technique of vascular injections from the 18th century. After Albinus passed away, his specimens were purchased by the Leiden University for 6,000 guilders in 1776. This collection, which consisted of 334 alcohol-based specimens and 418 dried specimens, was catalogued by his brother Frederik Bernard Albinus (1715–1778) and published as "*Supellex Anatomica Bernardi Siegfriedi Albinii*" (Albinus, 1775). Around 1772, the church of the Faille-Mantled Beguines was further extended to house its growing anatomical collections. In 1784, the anatomical collection expanded with the collection of Wouter van Doeveren (1730–1783) which contained a large number of teratological specimens (Elshout, 1952).

On the 12th of January 1807 a disastrous event in the history of the collection's integrity occurred when a gunpowder ship, carrying 18.5 tons of gun powder, exploded when floating on the main canal of Leiden. When this enormous explosion occurred, over 200 buildings were swept and blown away, including the church which housed the anatomical collections. This dramatic scene was the inspiration for a painting by Johannes Jelgerhuis (1770–1836) which shows the enormous ravage the explosion caused (Figure 2).

In subsequent years the damaged and decimated anatomical collection was re-extended by the purchase of the collection of Sebald Justinus Brugmans (1763–1819) in 1819, which consisted of 4,081 specimens, and parts of the collection of Andreas Bonn (1738–1817) in 1822. The now voluminous collection was described by Eduard Sandifort (1742–1814) and his son Gerard Sandifort (1779–1848) and resulted in an illustrated fourfold masterpiece entitled: *Museum Anatomicum Lugduno-Batavae Descriptum* (Sandifort, 1793, 1827, 1835). With this work both father and son became internationally renowned. In these catalogues the Leiden collection of the 19th century is described in full detail including the collections of contemporaries Johan Jacobus Rau, Bernard Siegfried Albinus, Wouter van Doeveren, Andreas Bonn, and Sebald Justinus Brugmans and indexes almost 7,500 specimens. Strangely, both Eduard's and Gerard's own collections were not indexed in these catalogues. During the 19th century the collection was further expanded by subsequently acquired specimen collections of several medical professors at the Leiden University including Jacobus Rocquette, Adrianus Marinus Ledebøer, Meinardus Simon du Pui, Jacobus Cornelis Broers, Gerardus Suringar, and Cornelis Swaving (Elshout, 1952; Huistra, 2013; Smit, 1986; Van der Boon, 1851).

After consecutive movements and threats throughout more than four decades, the anatomical museum is now situated inside the medical educational building of the University of Leiden and comprises more than 13,000 unique items. Predominantly, the collection functions as an inspiring place to educate medical students and is publicly accessible a few days throughout the year. The Anatomical Museum presently comprises specimens of the old anatomical

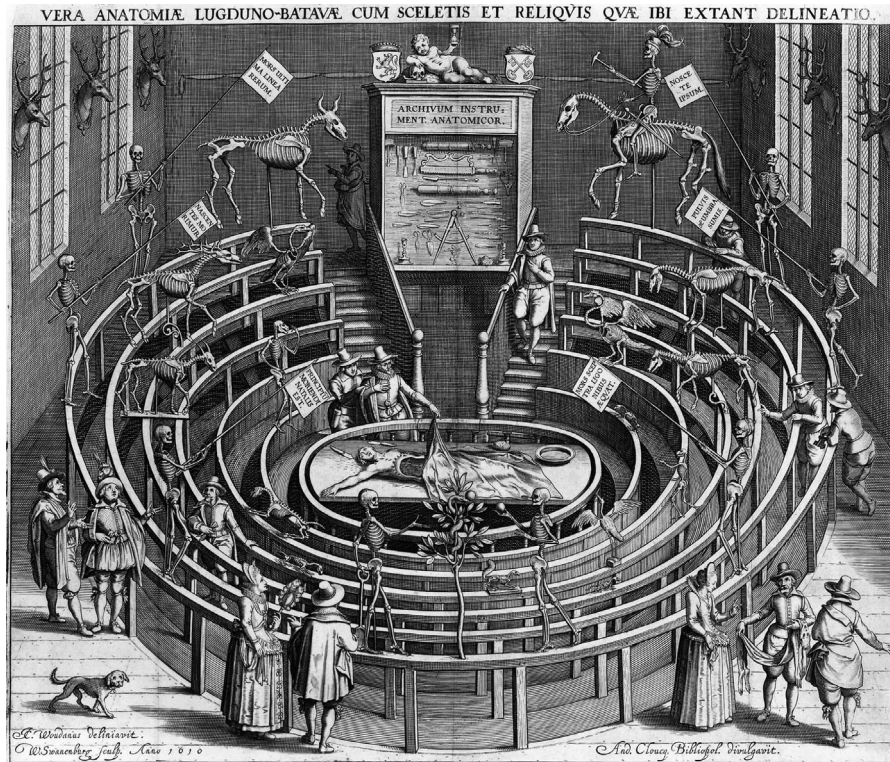


FIGURE 1 The *Theatrum Anatomicum* of Leiden University in the early 17th century, copperplate. Willem van Swanenburg, 1610

collections, the collections of the Department of Pathology (PA) and collections of the Department of Obstetrics & Gynecology (OG). We here report on the contemporary legacy of teratological specimens and descriptions of the *Museum Anatomicum* in Leiden and on the

diagnoses that we made. Additionally, we discuss the scientific opinions of father and son Sandifort together with those of their contemporaries towards congenital malformations and we reflect on the present day value of this legacy.



FIGURE 2 The Rapenburg, Leiden, three days after the explosion of the gunpowder ship on 12 January 1807. Johannes Jelgerhuis, 1807. Rijksmuseum, Amsterdam. [Color figure can be viewed at wileyonlinelibrary.com]

2 | MATERIALS AND METHODS

Our primary aim was to draw an inventory of the extant collection of human teratological specimens, to match them with (historical) descriptions from the *Museum Anatomicum* in Leiden, and to re-diagnose the conditions they presented with.

We first investigated all, currently present, teratological specimens by means of external inspection. Second, based on the available information and using contemporary pathognomonic insights and dysmorphological terminology, we tried for each specimen to determine whether the presented anomalies met the criteria for diagnosing monogenic and chromosomal syndromes, complex non-syndromic conditions, neural tube defects, conjoined, parasitic and acardiac twinning, primary and isolated congenital organ, and skeletal anomalies. If no diagnostic classification was applicable, we diagnosed the presenting sequence of anomalies as “isolated,” bearing in mind the restrictions of the investigation technique, that is, external inspection only. This restriction was due to the historic value of the specimens and therefore the impossibility for additional diagnostics.

Third, we explored the four Latin published *Museum Anatomicum Lugduno-Batavae* catalogues to find matching descriptions, pictures and annotations of the specimens (Sandifort, 1793, 1827, 1835). In these four catalogues the 19th century Leiden anatomical cabinets are described in full detail. The catalogues have been published as e-books on Google Books and can be inspected and downloaded for free. All inventoried existing teratological specimens were, when possible, assigned to a specific collector and were matched, where possible, to (historical) literature. As previously described (Boer, Radziun, & oostra, 2017a) all specimens and descriptions were reduced to “unique cases.” Finally, the most remarkable specimens were selected for a detailed description (See case 1–11) and the most influential collectors were described in detail (See Sections 4 and 5). Due to the magnitude of the found specimens and matching with historical descriptions, it is beyond the borders and scope of this paper to include all matching results. Details regarding the matched specimens can be obtained from the corresponding author.

3 | RESULTS

In the existing collection present at Leiden University, we identified 642 specimens that showed isolated or combined congenital anomalies, 556 cases comprised singleton related anomalies and 86 cases concerned conjoined twins, or twin-related anomalies. In 59 cases a monogenic or chromosomal syndrome was diagnosed or reasonably suspected. Isolated and complex non-syndromic conditions were diagnosed in 276 cases. One hundred and sixtyone cases concerned neural tube malformations (See Tables 1–4). Additionally, we found 60 specimens that were out of anatomical context or insufficiently accessible which we therefore excluded from the four defined tables. Moreover, 116 specimens could be assigned to a certain collector and 87 specimens to a certain institution, or department, whereas, 439 specimens could not be assigned (See

TABLE 1 Monogenic and chromosomal syndromes^a

Achondroplasia	7
Acrofacial dysostosis	1
Apert syndrome	3
Craniodiaphyseal dysplasia	1 (plaster cast)
Craniosynostoses	12
Enchondromatosis	1 (Case 1)
Hypophosphatasia	1 (Case 2)
Ichthyosis congenita gravis	2
Incontinentia pigmenti	1
Lysosomal storage disorder (Hurler)	1
Majewski syndrome	1
Meckel syndrome	3 (Case 3)
Osteogenesis imperfecta	6
Oral-facial-digital syndrome NOS	1 (Case 4)
Skeletal dysplasia NOS	2
Thanatophoric dysplasia	2
Tetra-amelia syndrome	1
Treacher Collins	1
Trisomy 13	2
Trisomy 18	10
Total	59

^aMonogenic and chromosomal syndromes are based on their external dysmorphological appearance. Unfortunately, the DNA quality of formalin- or alcohol-fixed specimens is insufficient for additional genetic testing. Most diagnoses are therefore tentative. Bold diagnoses are specimens which are described in more detail.

Table 5). Due to the magnitude of found specimens we decided to describe only 11 interesting cases in more detail (See cases 1–11).

3.1 | Enchondromatosis

Case 1: Specimen Pa0260 concerns a left skeletonized hand with multiple tumors arising from the metacarpals and both proximal and distal phalanges of the first, third, and fourth finger (Figure 3a) kept in fluid. Originally, this case was described by Andreas Bonn, as part of the *Hovius collection* most of which is presently situated in Museum Vrolik in Amsterdam (*Descriptio thesauri ossium morbosorum Hoviani*. p. 96, nr. CCCXXXV). Subsequently, the same case was (re)described and depicted (Figure 3b and c) by Gerard Sandifort (Mus. Anat. Vol. III. p. 349, nr. CCCI-CCCIX and p. 391, nr. DCXXXIX-DCXLV and Mus. Anat. Vol. IV. p. 81 and tabula CLXXXV and CLXXXVI). This case originally concerned 15 skeletal elements from a 27-year-old man who suffered, according to Bonn, from congenital rickets, leading to bony deposits and aberrant growth of the long bones. The men's posture, hands and legs were deformed, severely bent and swollen. According to the original description the malformed man fell from a great height which led to excessive bruises, edema, fever, and limping which eventually led to death. Autopsy revealed a retroperitoneal tumor which was attached to the lower lumbar vertebrae, sacrum and pelvic bones. At

TABLE 2 Isolated and complex non-syndromic conditions

Cranio cervical	
Arnold-Chiari malformation	1
Congenital struma	1
Hemifacial microsomia	1
Isolated cleft lip with or without cleft palate	19
Orbital tumor	1 (Case 5)
Pierre Robin sequence	1
Cardiovascular	
Coarctatio aortae	4
Congenital lymphedema	1
Cor uniloculare biatriatum	1
Cor trilobulare biatriatum	3
Ectopia cordis	1
Marfan syndrome (heart)	1
Persisting ductus Botalli	5
Septal defects heart	17
Tetralogy of Fallot	4 (Case 6)
Transposition of the great arteries	8
Gastrointestinal	
Appendix aplasia	1
Diaphragmatic hernia	7
Duodenal atresia/stenosis	3
Esophageal atresia/tracheal fistula	4
Gallbladder agenesis	1
Hirschsprung disease	4
Imperforated anus	7
Intestinal stenosis NOS	3
Meckel diverticulum	3
Umbilical hernia and omphalocele	14
Urogenital	
Ambiguous genitalia	2 (incl. 1 wax model)
Bladder- and cloacal exstrophy	14 (incl. 3 plaster casts)
Bladder diverticulum	1
Congenital hydronephrosis	4
Congenital megalourethra	1
Horseshoe kidney	5
Hypospadias	5
Persistent cloaca	1
Prune belly sequence	2
Sirenomelia sequence	8
(Unilateral) kidney agenesis	3
Ureteral duplication	8
Uterus bicornis	6
Uterus didelphys	3
Uterus unicornis	2

Musculoskeletal	
Congenital dislocation of the hip	24
Intercalary limb deficiencies NOS	2
Longitudinal limb deficiencies NOS	8
Pre- and/or postaxial polydactyly/syndactyly	10
Cystic organ conditions	
Congenital lung cysts	1
Congenital liver cysts	1
Congenital ovarian cysts	1
Congenital renal cysts	4
Disruptions	
Amniotic band sequence/vascular disruption	13
Isolated gastroschisis	2
Generalized conditions (incl. infections)	
Cowpox embropathy	1
Congenital syphilis	6
Hydrops fetalis / Cystic hygroma	11
Lithopaedion	2
Oligohydramnios sequence	2
Schisis association	
Encephalocele and omphalocele	1
Encephalocele, rachischis and omphalocele	1
Holoacrania, rachischis and omphalocele	3
Holoacrania, hypospadias and micropenis	1
Holoacrania and urinary tract malformations	1
Total	276

Bold diagnoses are specimens which are described in more detail.

the site where the tumor was attached, the normal bone was destroyed. Together with the overall clinical report, the engravings and the extant specimen this case can be diagnosed as multiple enchondromatosis (MIM:166000).

3.2 | Hypophosphatasia

Case 2: Specimens Pa0268 (Figure 4a) and Pb0260 (Figure 4b) concern a neonatal skeleton and skull originally collected by Andreas Bonn and described by Gerard Sandifort (Mus. Anat. III. p. 353. nr. CCCXV (skeleton), p. 389. nr. DCXXVIII, p. 390 nr.

DCXXXIII/DCXXXV and Mus. Anat. IV. p. 67–68 and tabula CLXXXIII and p.91–92 tabula CXCI). According to the description this child suffered from congenital rickets. During preparation of the skeleton (Figure 4c) the striking appearance of “soft” and “flexible” bones was mentioned. Moreover, it was mentioned that the periosteum could not be peeled off as easily as in other cases. The skull was described as being

TABLE 3 Neural tube malformations

Closure defects	
Craniorachischisis	15
Craniorachischisis totalis	8
Craniorachischisis with iniencephaly	11
Craniorachischisis posterior	1
Faciocranioschisis	1 (Case 7)
Holoacrania	20
Holoacrania with partial rachischisis	16
Iniencephaly	2
Iniencephaly with encephalocele	3
Lumbosacral spina bifida	23
Meroacrania	10
Occipital encephalocele	7
Occipito-cervical encephalocele	3
Occipital encephalocele with rachischisis	5
Parietal encephalocele	3
Spinal dysraphism	3
Thoracolumbar spina bifida	5
Holoprosencephaly	
Cyclopia	11
Ethmocephaly	3
Otocephaly	3
Combinations	
Closure defect + holoprosencephaly	8
Total	161

Bold diagnoses are specimens which are described in more detail.

affected by hydrocephaly and consisted of multiple fragmented bones (Figure 4d). The ribs showed multiple bony bulges; Sandifort described that these protruding deposits originated from healed fractures. Moreover, the ischial bones were located in close proximity and the acetabula were situated more ventrally than normal. The bones of all extremities, including the clavicles and shoulder blades were severely malformed and consisted of multiple bulges of bone deposits. According to Sandifort, the bones of the hands and feet were unaffected. Taking the soft and flexible bones in mind, we are inclined to diagnose this condition as infantile hypophosphatasia (MIM:241500), although the general appearance of the skeleton resembles osteogenesis imperfecta type 2. Interestingly, hypophosphatasia can produce rickets-like deformities as described here. Moreover, misshapen skulls, beading of costochondral junctions, enlarged joints from metaphyseal flaring and premature bony fusion of sutures can occur (Collmann, Mornet, Gattenlohner, Beck, & Girschick, 2009; Whyte, 2016), as well as, fractures and bone deformities (Whyte et al., 2012).

3.3 | Meckel syndrome

Case 3: Specimen Eb0220 (Figure 5) is a female neonate of unknown collector. On examination the head was very small, with a strongly

TABLE 4 Pathological twins

Symmetrical conjoined twins ^a	
Cephalothoracoileopagus	5
Dicephalus	5
Dicephalus discordant for cyclopia	1 (Case 8)
Diprosopus	7
Ileoischiopagus	1
Ischiopagus	1
Pygopagus	1
Thoracoileopagus	19
Thoracoileoischiopagus	1
Thoracoileopagus discordant for sirenomelia	1 (Case 9)
Parasitic conjoined twins and teratomas	
Epignathus/perioral-nasopharyngeal teratoma	6 (case 10)
Epigastrius/ventral teratoma	1 (case 11)
Pygopagus parasiticus/sacral teratoma	10
Acardiac twins	
Acardius anceps	4
Acardius acephalus	13
Acardius NOS ^b	2
Other twin related conditions	
foetus papyraceus	8
Total	86

Bold diagnoses are specimens which are described in more detail.

^aThe terminology we used to describe the various types of conjoined twinning is based on what is generally accepted. The thoracoileopagus category also comprised cases of ileopagus and xiphopagus, since we diagnosed the conditions on external criteria only. The infix -ileo- was used whenever the site of conjunction was continuous with a single umbilical insertion. Structures involved in the site of conjunction were considered as duplicated if they showed clear signs of complete or partial duplication. For instance, dicephalus conjoined twins, having a third median upper extremity with more than five digits, were specified with the suffix tetrabrachius. Discordant anomalies, when present, were mentioned separately.

^bAcardius NOS = Not otherwise specified, consisted of intestinal specimens originating from an acardiac twin.

sloping forehead, and a sac-like occipital encephalocele. The markedly distended abdomen was similar to a "prune belly;" presumably due to enlarged and cystic kidneys. The hands, as well as, the clubbed feet showed symmetrical postaxial hexadactyly. We diagnosed this condition as Meckel syndrome, which was also diagnosed in two other similar fetuses.

3.4 | Orofaciodigital syndrome

Case 4: Specimen Eb007 (Figure 6) concerns a term female neonate of unknown collector with hypertelorism, broad nasal bridge, bilateral cleft of the upper lip and cleft palate, lobulated tongue, both pre and post axial polydactyly on all four extremities and bilateral club foot. Based on the characteristic external characteristics we are inclined to diagnose this condition as orofaciadigital syndrome of unknown type.

TABLE 5 Identified teratological specimens from different collectors and institutions in the extant collection

Collector ^a	Found teratological specimens
Johannes Jacobus Rau (1668–1719)	2
Bernhardus Siegfried Albinus (1697–1770)	1
Wouter van Doeveren (1730–1783)	2
Andreas Bonn (1738–1817)	39
Eduard Sandifort (1742–1814)	8
Jacobus Rocquette (1744–1809)	4
Sebald Justinus Brugmans (1763–1819)	27
Gerard Sandifort (1779–1848)	2
Jacobus Cornelis Broers (1795–1847)	2
Adrianus Marinus Ledebøer (1797–1887)	3
Willem Vrolik (1801–1863)	1
Gerardus Conradus Bernardus Suringar (1802–1874)	19
Hidde Halbertsma (1820–1865)	1
Teunis Zaaijer (1837–1902)	1
Johannes Antonius James Barge (1884–1952)	4
Institutions	
Department of Obstetrics & Gynecology university of Leiden	54
Westeinde hospital, The Hague	33
Unknown	439
Total	642

^aCollectors are categorized by their date of birth followed by several institutions and the specimens of unknown collector. Names in bold refer to collectors that are described in more detail (See Discussion/Biographies).

3.5 | Orbital tumor

Case 5: Specimen Pb0207 concerns the macerated skull of a young child, aged only a couple of months (Figure 7a). The child suffered from a left sided intra-orbital tumor which pushed the left nostril closed and caused a depression of the left corner of the mouth. This is one of the very few 19th century, both pre-and postmortem annotated cases of a child with a complicated orbital tumor. This specimen was originally collected by Andreas Bonn and described and depicted (Mus. Anat. Vol. III. p. 379, nr. DLXIX and Mus. Anat. Vol. IV. p. 6 and tabula CXXVIII) in full detail by Gerard Sandifort (Figure 7b). According to the comprehensive description, the tumor was in coherence with the ocular muscles and the periosteum of the zygomatic bone. In the left canthus of the affected eye a misshapen lacrimal caruncle was noticeable, the conjunctiva were sebaceous, and the cornea indistinct. Moreover, the eye showed microphthalmia and proptosis. Shortly before the child died, the eye and surrounding tissue showed extensive putrefaction. The tumor, which mainly consisted of fat, pushed the left eye out of its socket making the eyelids unable to close. The upper eyelid was more affected than the lower eyelid due to a tubercular swelling. After the child died, the skull was dissected and depicted (Figure 7c). Unfortunately, the description did not mention if the tumor was present from birth. On exploration, the skull showed extensive orbital enlargement with deformities of the zygomatic bone and maxilla. The orbital bones were smooth, indicating the absence of any degenerative or infiltrative bone disease. The optic foramen and the superior orbital fissure were unaffected, the inferior orbital fissure was broadened and widened, the cranial vault was secondarily deformed. Although no other abnormalities regarding the autopsy were described the diagnoses orbital neuroblastoma, retinoblastoma, rhabdomyosarcoma, encephalocraniocutaneous lipomatosis, or oculocerebrocutaneous (Delleman) syndrome are the most obvious candidates. Unfortunately, there were no statements on brain and skin

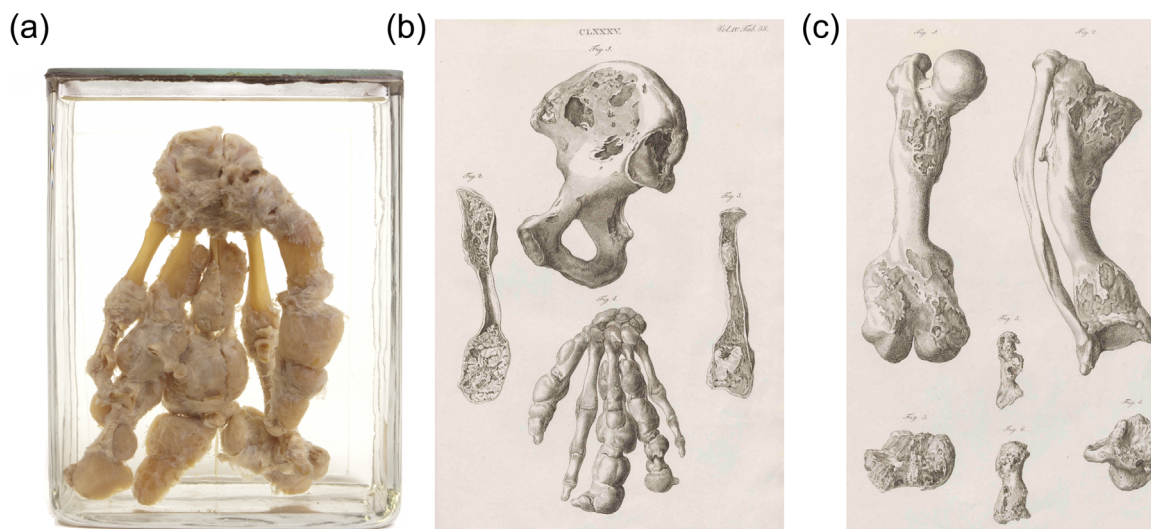


FIGURE 3 A. Case 1. Enchondromatosis. (a) Specimen Pa0260, hand affected by multiple enchondromata. From the collection of the Museum Anatomicum Leiden; The Netherlands. (b/c) Copperplate Sandifort (1835). [Color figure can be viewed at wileyonlinelibrary.com]

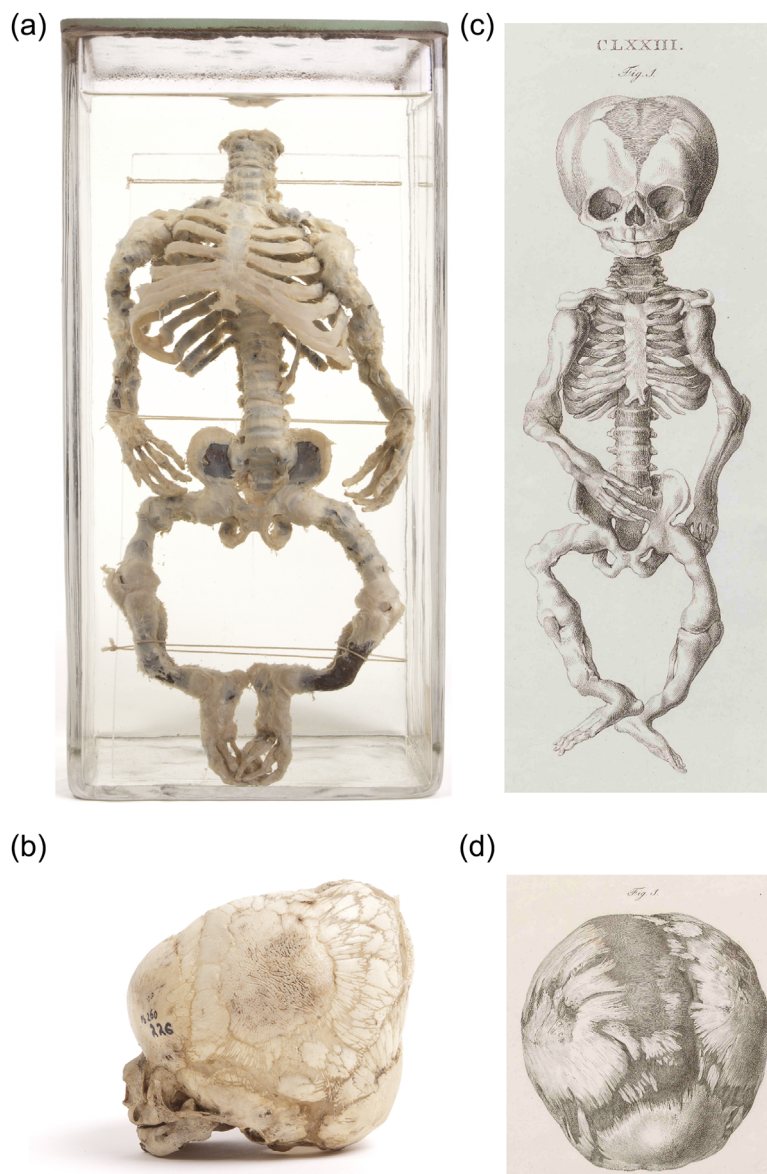


FIGURE 4 Case 2. Hypophosphatasia (a) Specimen Pb0260, skeleton affected by hypophosphatasia, and (b) specimen Pa0268, skull with multiple fragmented bones. From the collection of the Museum Anatomicum Leiden; The Netherlands. (c/d) Copperplate Sandifort (1835). [Color figure can be viewed at wileyonlinelibrary.com]

(accessory periocular cystic appendages) malformations which could make the diagnose of Delleman syndrome either more or less plausible.

3.6 | Tetralogy of fallot

Case 6: Specimen Ag0046 (Figure 8a) concerns a malformed skull of a neonate which was thoroughly described by Eduard Sandifort. The skull was part of a larger case report described in detail on page 1 till 41 in Part III of his *Observationes Anatomico-Pathologicae* (Sandifort, 1779). Additionally, Eduard depicted this case in several engravings (tabula I–VI starting on p. 171). These particular specimens and this case report were not mentioned in any of the *Museum Anatomicum* catalogues. However, the skull in this description is the only surviving specimen of this case. On examination the skull shows

excessively large parietal bones and a horizontal occipital bone. The engraving of the child from which this skull originated showed a thoracolumbar spina bifida, large omphalocele and distinct head abnormalities (Figure 8b). Moreover, the child suffered from multiple organ deformities including: cystic kidneys with distension of both ureters and tetralogy of Fallot. The combination of anomalies is not specific for any particular diagnosis but could match with an aneuploidic condition, that is, trisomy 18. Prior to the above attested case Eduard described, on page 1–38 of Part I of his *Observationes Anatomico-Pathologicae* (Sandifort, 1777), four characteristics (pulmonary stenosis, dextroposition of the aorta, interventricular septal defect, and hypertrophy of the right ventricle) in a heart of a cyanotic 12-year-old boy who complained of fatigue, headaches, fainting and edema, which fits perfectly with tetralogy of Fallot (Bennett, 1946). Both case reports predated the one by Arthur Fallot (1850–1911) in



FIGURE 5 Case 3. Specimen Eb0220, Meckel syndrome. From the collection of the Museum Anatomicum Leiden; The Netherlands. [Color figure can be viewed at wileyonlinelibrary.com]

Marseille Médical in 1888 (Fallot, 1888), although the condition was already described by Niels (Steno) Stensen (1638–1686) in 1671 (Stensen, 1671).

3.7 | Faciocranioschisis

Case 7: Specimen Eb0231 is one of the two specimens which could be assigned to Van Doeveren's original collection and concerns a male neonate with an exceptionally rare neural tube defect (Figure 9a). This case was described by Van Doeveren on page 46 of his *Specimen observationum* (Van Doeveren, 1765) and depicted this child in full detail (Figure 9b). In this description it was stated that the entire child was normally developed with exception of the severely malformed head with a cleft of the soft and hard palate. Subsequently, Eduard Sandifort described and depicted this



FIGURE 6 Case 4. Specimen Eb007, orofaciogigital syndrome. From the collection of the Museum Anatomicum Leiden; The Netherlands. [Color figure can be viewed at wileyonlinelibrary.com]

specimen (Mus. Anat. I. p. 300–301, nr. V and Mus. Anat. II. P. 119 and tabula CXXII). On examination, the microcephalic head showed a severe closure defect that extended mid-craniofacial from the upper lip through the entire face. We diagnosed this case as (isolated) faciocranioschisis.

3.8 | Conjoined twins

Case 8: Specimen Ac0107 (Figure 10) collected by Andreas Bonn concerns a female dicephalic conjoined twin originally described by Gerard Sandifort as "*Infans biceps. In capite uno oculi conjuncti sunt*" (Mus. Anat. Vol. III. p. 370–372. Nr. CDXC). This specific case was also described by Willem Vrolik (1801–1863) in 1836 (Vrolik, 1836). Unfortunately, this case was not depicted in the *Museum Anatomicum* catalogues. On external examination a rudimentary extremity in the medio-sacral area and an indeterminable malformation of the external genitalia is seen. Moreover, the right microcephalic head shows cyclopia (holoprosencephaly or aprosencephaly). We

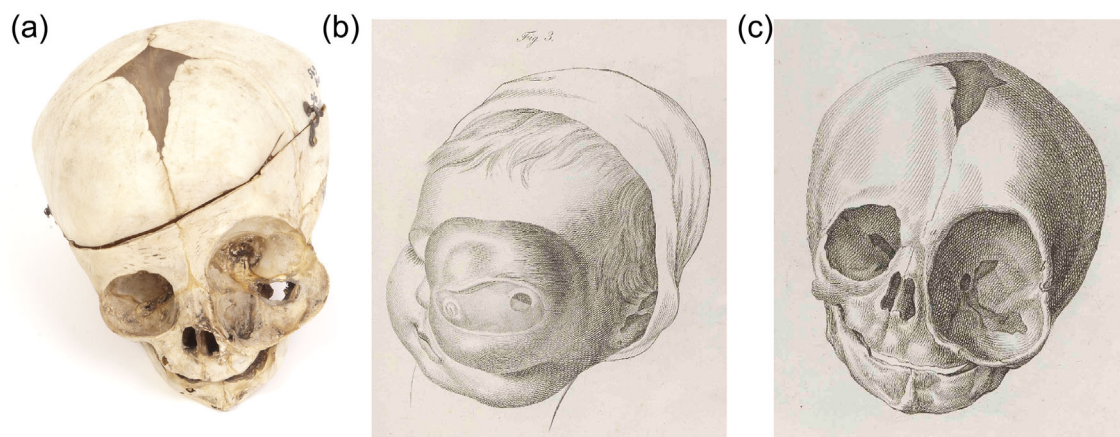


FIGURE 7 Case 5. Orbital tumor. (a) Specimen Pb0207, neonatal skull with an affected left orbit. From the collection of the Museum Anatomicum Leiden; The Netherlands. (b/c) Copperplate Sandifort (1835). [Color figure can be viewed at wileyonlinelibrary.com]

diagnosed this case as parapagus dicephalus dibrachius tripus discordant for cyclopia. This rare association is known to occur, albeit only sporadically described (Blaas et al., 2002).

3.9 | Conjoined twins

Case 9: Specimen Eb0020 (Figure 11) concerns a full-term female thoracoileopagus tetrabrachius tripus with a unilateral concomitant but discordant sirenomelia (sympus monopus) sequence of unknown collector. This specific discordance for thoracoileopagus tetrabrachius tripus was not found in the current available literature. The only found publication on this topic is from Tannuri, Batatinha, Velhote, & Tannuri, 2013 who described a craniopagus conjoined twin discordant for sirenomelia.

3.10 | Nasopharyngeal teratoma

Case 10: Specimen Eb0081 is one of the 39 existing teratological specimens assigned to Andreas Bonn and concerns a full-term female neonate which on external examination shows an intra-orally and intra-nasally located, non necrotizing, protruding mass (Figure 12a). According to Bonn the mouth was completely filled with the “polyp” which after progressive growth protruded from the mouth. Moreover, the tumor appeared to protrude from both nostrils. This case was only scantily described (Mus. Anat. Vol. III. p. 377–378, nr. DLVIII and Mus. Anat. Vol. IV. p. 98 and tabula CXCV) but was depicted in detail by Gerard Sandifort (Figure 12b). Based on the engravings and the specimen this case is diagnosed as an epignathus or nasopharyngeal teratoma. However, an oropharyngeal rhabdomyosarcoma cannot be ruled out without performing any further diagnostics.

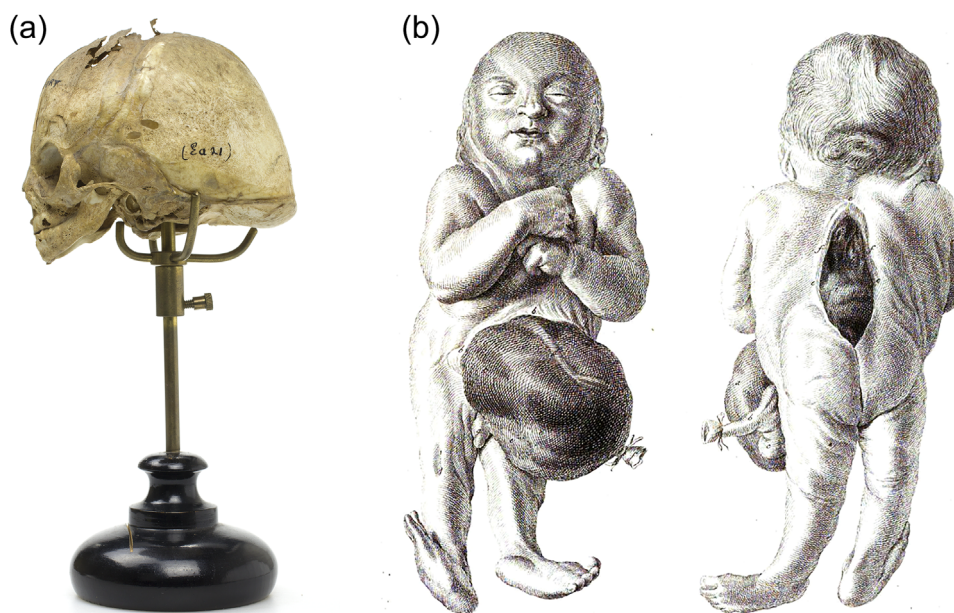


FIGURE 8 Case 6. Tetralogy of Fallot (a) Specimen Ag0046, skull of the child. From the collection of the Museum Anatomicum Leiden; The Netherlands. (b) Copperplate of the child with multiple congenital anomalies and tetralogy of Fallot Sandifort (1779). [Color figure can be viewed at wileyonlinelibrary.com]

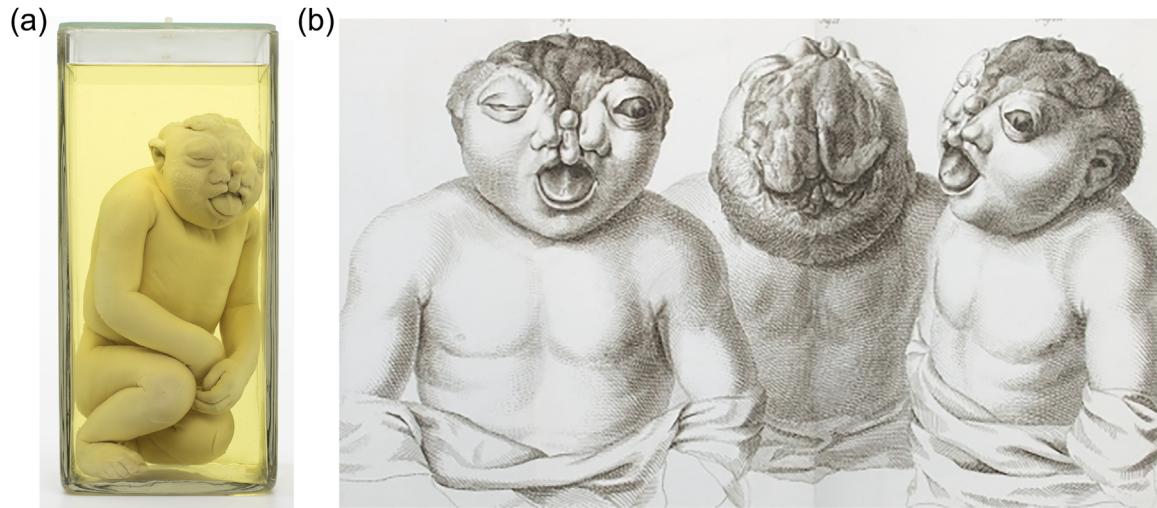


FIGURE 9 Case 7. Faciocranioschisis. (a) Specimen Eb0231 male neonate with faciocranioschisis. From the collection of the Museum Anatomicum Leiden; The Netherlands. (b) Copperplate Sandifort (1793). [Color figure can be viewed at wileyonlinelibrary.com]

3.11 | Epigastric heteropagus conjoined twin

Case 11: Specimen Eb0011 is the second of the two existing teratological specimens originating from Wouter van Doeveren. It was described by Eduard Sandifort as “*Infans monstrosus*” and

subsequently by the inventory of Elshout as “*Thoracopagus parasiticus masculinus*.” This case concerns a term male neonate with an incomplete smaller body attached to its thoraco-abdominal transition (Figure 13a). This case was described (Mus. Anat. I. p. 302–303, nr. XIII and Mus. Anat. II. P. 121 and tabula CXXV) and depicted (Figure 13b) by Eduard Sandifort. In this description he stated that a healthy 40-year-old woman, who delivered five healthy children previously, now delivered this unusual child which lived for three successive days before it died. We diagnosed this specimen as an epigastric heteropagus conjoined twin.



FIGURE 10 Case 8. Specimen Ac0107, parapagus dicephalus dibrachius tripus discordant for cyclopia. From the collection of the Museum Anatomicum Leiden; The Netherlands. [Color figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

Throughout the 17th and 18th centuries, teratological specimens were prominent parts of privately owned cabinets of curiosities; these specimens were first and foremost unique rarities. However, in the course of the 18th and 19th century, teratological specimens became more than singular cases of intriguing curiosities. Teratological specimens and collections became part of natural classifications and taxonomy. During the mid-18th century many privately owned collections were institutionalized after their collectors died. These institutionalized collections were often systematically arranged, in contrast to the mostly anecdotally collected morphology specimens many anatomists collected privately. The *Museum Anatomicum* of the Leiden University is a shining example of a vast and versatile collection which finds its origin in multiple privately owned collections and include teratological specimens which were collected over multiple centuries; collections were either purchased by the university or donated by their original collectors or their heirs. Due to the present day paucity of full-term fetuses with congenital anomalies, institutionalized teratological collections become more valuable over time. Nevertheless, these collections are prone to neglect and at risk for decline of its contents. This makes old teratological collections increasingly rare and often underrepresented in medical curricula.



FIGURE 11 Case 9. Specimen Eb0020, thoracoileopagus tetrabrachius tripus discordant for symphus monopus. From the collection of the Museum Anatomicum Leiden; The Netherlands. [Color figure can be viewed at wileyonlinelibrary.com]

On the other hand, several teratological collections in medical museums worldwide are still operational up to present day and are accessible for the general public and the medical student. These residual collections can be seen as “time capsules” full of nature's creations waiting to be explored with, for example, radiological or genetic techniques in order to exploit their excellent educational and scientific potentials (Boer et al., 2017b; Boer, Morava, Klein, Schepens-Franke, & Oostra, 2017c; Boer, Naue, de Rooy, & Oostra, 2017d).

The collection of the *Museum Anatomicum* can be used to retrospectively study how congenital anomalies were perceived during the heydays of collecting teratological specimens. Historical perspectives regarding the original collectors and their contemporaries can be studied and matched with their original specimens. Although large parts of the extant collection is described in four Latin published catalogues, by father and son Sandifort, it was merely impossible to match all existing specimens with these Latin descriptions. Many specimens

showed certain characteristics that were not mentioned in the specimen descriptions. It is conceivable that in the course of time specimens or specimen-numbers got changed, that new specimens were added and other specimens were discarded, making it impossible to assign them all to specific collectors or descriptions. Moreover, it is imaginable that specific specimens or preparation techniques were copied by other collectors and subsequently incorporated in the collection; again making it difficult to match all specimens to a specific collector. As it turns out we found 642 teratological specimens during re-examination, re-diagnosing and re-describing of the extant collection with some exceedingly rare conditions such as faciocranioschisis and conjoined twins discordant for holoprosencephaly and sirenomelia.

Although the collection of Sebald Justinus Brugmans consisted of 4,081 specimens (Sandifort, 1827), we only found 27 teratological specimens of his original collection. His collection was mainly characterized by comparative anatomy, pathological bones and fossils and included only 154 human specimens. Although, Brugmans did collect some teratological specimens, there was no additional literature found concerning this topic. The teratological specimens found in the extant collection consisted of congenital dislocations of the hip, hydrocephaly, anencephaly, cleft lip and palate, skeletal dysplasias, bladder exstrophy, sacralization, anal atresia, and some minor skeletal anomalies. The collection of Gerardus Suringar, donated to the museum in 1866, originally comprised more than 800 anatomical specimens, but we retrieved only 19 specimens which could be reasonably assigned to him. These included congenital luxations of the hip, hydrocephaly, neural tube defects (anencephaly and spina bifida), conjoined twins, cleft lip and palate, syndromes and some organ anomalies, none of which was described in more detail at the time.

5 | BIOGRAPHIES

The following section contains the biographies of Wouter van Doeveren, Andreas Bonn, Eduard Sandifort, and Gerard Sandifort. These four collectors were chosen because of their contributions to the teratological collection or their significant role in describing the specimens.

5.1 | Wouter Van Doeveren (1730–1783)

Wouter van Doeveren studied medicine in Leiden and obtained his doctor degree in the same city. In 1754, Van Doeveren was appointed professor in anatomy, surgery, and obstetrics in Groningen and became professor of medicine in Leiden in 1770 (Van der Zwaag, 1970). During his career in Groningen, Van Doeveren published his most admired work: “*Specimen observationum academicarum ad monstrorum historiam, anatomen, pathologiam, et artem obstetriciam, praecipue spectantium*” (Van Doeveren, 1765). In this masterpiece he described anomalies in both animals and humans. Teratology was a subject in which Van Doeveren was very interested and well ahead of his contemporaries; he was one of the first who attempted to build a systematic collection of teratological specimens, moving them from



FIGURE 12 Case 10. Nasopharyngeal teratoma. (a) Specimen Eb0081 female neonate with a nasopharyngeal teratoma. From the collection of the Museum Anatomicum Leiden; The Netherlands. (b) Copperplate Sandifort (1835). [Color figure can be viewed at wileyonlinelibrary.com]



FIGURE 13 Case 11. Epigastric heteropagus conjoined twin. (a) Specimen Eb0011: male neonate with asymmetric twin attached to the epigastric region. From the collection of the Museum Anatomicum Leiden; The Netherlands. (b) Copperplate Van Doeveren (1765). [Color figure can be viewed at wileyonlinelibrary.com]

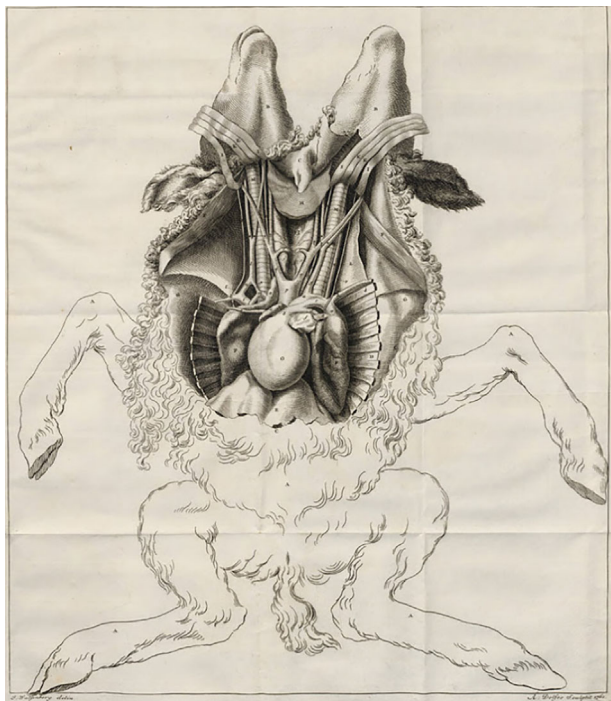


FIGURE 14 Siamese lamb, copperplate. Van Doeveren (1765). Leiden University Library. [Color figure can be viewed at wileyonlinelibrary.com]

the “sphere of wonder and curiosity” into the world of naturalization; as such, teratology became part of natural classifications and taxonomy (Hagner, 1999). Additionally, this systematic approach led to a paradigm shift that placed the “monstrous births” from a negative into a positive point of view. In the first chapter of his *Specimen observationum* Van Doeveren described the generally accepted opinions regarding the origin of congenital anomalies of his time. Two theories were described: 1) The “*monstra primigenia*,” a theory that explains anomalies as being present from the first conception without any involvement of exogenous factors; and 2) the “*monstra accidentalis*,” a theory stating that anomalies arise during development in utero; meaning that there was initially a normally developed embryo which became deformed under exogenous factors. In his description of a lamb with two heads (Figure 14) Van Doeveren stated that this beautifully formed Siamese lamb proved that “monsters” are meant to be the way they are and have a wonderful, symmetrical and purposefully built body. Moreover, he postulated that the lamb could not possibly be the result of two separate developed embryos which were fused secondarily, as the putative fusion should have been perfect and seamless. According to Van Doeveren this lamb was a perfect example of “*monstra primigenia*.” Conversely, on page 47 of the second chapter, he described a case of an anencephalic fetus with clefts of the nose, upper jaw and palate which he considered to result from an unknown accidental cause when the skull was still weak and soft during development, thereby confirming the “*monstra accidentalis*” concept. However, he stated that one should refrain from any opinion or verdict about the cause of an anomaly when one is in doubt. Moreover, Van Doeveren confirmed that dissecting and describing

congenital anomalies is useful and will eventually lead to more knowledge about how they arise. Van Doeveren believed that inside the anatomy of the “*monstra*,” the “*semina veri*” (seeds of truth) are located which are not unveiled in the normal anatomical situation of the human body. Although he admits that the exact cause is unknown, Van Doeveren prefers the theory of “*monstra primigenia*” (Van der Boon, 1851). Many contemporaries who believed in the “*monstra accidentalis*” theory, often had vague and abstruse ideas about the origin of anomalies, for example, “*imaginatio materna*” (maternal imagination). Van Doeveren’s aversion of these vaguely described factors were maybe due to the impossibility to place them into an exact and rational framework; an important factor for systematic research. According to Van Doeveren, maternal imagination was no satisfying explanation for anomalies found in humans, as plants and animals—which, after all, have no reason, morals or imagination—could also produce a monstrous progeny. In Van Doeveren’s opinion, this argument refutes maternal imagination as a cause of congenital anomalies.

Looking throughout the work of Van Doeveren it is clear that he raised two different theories (*monstra primigenia* or *monstra accidentalis*) as the cause of different congenital anomalies. It looks like Van Doeveren thought he had to choose one of the two theories to explain all congenital anomalies. It is conceivable that he saw anomalies which he could not explain and subsequently was indecisive in his conclusion that both theories could be applicable. The time spirit did not yet allow the awareness of the fact that both malformations and/or deformations can occur individually or in the same affected child. Malformations are homologous to *monstra primigenia* and deformations are homologous to *monstra accidentalis*.

After Van Doeveren’s death in 1783, his private collection was publically auctioned on the 18th of April 1785 and consisted over 3,000 items including zoological specimens, fossils, minerals, instruments and various scientific objects (Wijnperse & Brugmans, 1785). Part of the auctioned items were bought by the faculty board members for 4,300 guilders. Eduard Sandifort listed 441 specimens belonging to Van Doeveren’s collection in his *Museum Anatomicum* catalogue, which included 23 human anomalies and 15 animal anomalies. He depicted many of his specimens in the second part of the *Museum Anatomicum* catalogues (Sandifort, 1793). Unfortunately, the Van Doeveren collection was seriously damaged during the explosion of the gunpowder ship; only 32 specimens remained (Elshout, 1952). In the extant collection we found only two teratological specimens which could be reasonably assigned to Van Doeveren’s original collection (See cases 7 and 11). One of them is an exceptionally rare case of faciocranioschisis (Case 7). Only two descriptions of faciocranioschisis are described in the modern literature (Urioste & Rosa, 1998; Oostra, Baljet, & Hennekam, 1998). Oostra et al. (1998) who reviewed the teratological collection residing in Museum Vrolijk, described a 19th century case of faciocranioschisis in a female neonate. Our case dates back to 1765 a case description of faciocranioschisis published more than 100 years earlier, being the first historical description and the third attested case in modern literature so far.

5.2 | Andreas Bonn (1738–1817)

Andreas Bonn studied medicine in Amsterdam and Leiden. He obtained his doctor degree in Leiden with his dissertation named "*Specimen anatomico-medicum inaugurale, de continuationibus membranarum*" (Bonn, 1763). In this work Bonn described the morphology of the skin, joint capsules, periosteum and the membranes of the body cavities and the meninges; subjects in which Bonn was well ahead of his contemporaries (Van der Boon, 1851). In 1764 Bonn continued his study in Paris and became a well-known physician in Amsterdam in the same year. In 1771 he was appointed professor of anatomy and surgery at the *Atheneum Illustre* in Amsterdam (Elshout, 1952; Sandifort, 1827). In his younger years Bonn was engaged in describing the pathological bone collection of Amsterdam's physician and anatomist Jacobus Hovius (1710–1786). Bonn published this meticulously described collection in his "*Descriptio thesauri ossium morbosorum Hoviani*" (Bonn, 1783). Currently, the Hovius cabinet represents the oldest anatomical collection in Amsterdam and is still on display in Museum Vrolik (Figure 15). Bonn's personal collection contained beautiful and elegant red injected specimens of general and comparative anatomy and pathology. To make up for the losses that resulted from the exploded gunpowder ship the Bonn collection, amended with several Hovius specimens, was donated to the Leiden anatomical museum in 1822 with the specific clause that specimens of structures and conditions that already were present in the anatomical museum would be sent to other universities (Huistra, 2013). Gerard Sandifort assessed Bonn's specimens and selected 737 preparations which could be added to the anatomical museum. Sandifort stated that he was particularly pleased with the "monstra" and pathological bones since these were often underrepresented in anatomical collections (Sandifort, 1827). The remaining specimens were sent to the University of Ghent (Belgium), albeit that the present whereabouts of these specimens remains unknown.

Bonn's interest in congenital anomalies can be seen back throughout his career. He not only collected teratological specimens of human and zoological origin, but also specimens of deviant fruits. According to Bonn

these dysmorphic fruits were also to be ascribed as "monstra." Bonn published papers on congenital hip dysplasia's (Bonn, 1782a) and on urogenital anomalies in both sexes (Bonn, 1778, 1782b, 1791, 1818).

Bonn explained that the cause of congenital abnormalities (including spina bifida, bladder exstrophy, hypospadias and cleft lips/palates) all resulted from a mechanical injury during embryonic development. He thought that hypospadias was caused by a rupture of the urethral orifice and that the cause of an ectopic bladder was due to a rupture of the ventral body wall during birth. However, he admitted that these statements were inadequate and he confessed that the field of teratology was difficult to understand for himself and most of his contemporaries. However, in his paper about an acardiac twin (Bonn, 1794) he acknowledged that the cause of the acardiac was an "abnormal process" during embryological development rather than a mechanical injury. Bonn was, as was Van doeveren, indecisive in explaining all observed anomalies with the "*monstra accidentalis*" or the "*monstra primigenia*" theory. Moreover, he assumed that the cause of the acardiac twin was situated "inside" the embryo itself, although he was not familiar with what the exact "internal genesis" in the embryo could be. He described the absence of the heart and head as a "lack of human factors" and the partial absence of the abdominal organs—according to Bonn the "seat of desire and lust"—as a "lack of animal factors," thus taking a more or less mystical and vague point of view in the origin of malformations (Elshout, 1952). Additionally, Bonn quoted that the cause of the acardiac twin could be the result of a disturbed "*nisus formativus, vormdrift, or Bildungstrieb*;" again posing a different theory on the cause of an anomaly. He also stated that a woman cannot be designated to be the cause of the malformed child she gave birth to, confirming that the "*imaginatio materna*" theory was an unsatisfactory explanation. Looking at the many different theories Bonn described, he did not seem to be convinced himself that any of these explanations were true. The donated parts of the Bonn and Hovius collections are described by Gerard Sandifort in Vol. III and depicted in Vol. IV of the *Museum Anatomicum* catalogues (Sandifort, 1827,



FIGURE 15 The Hovius cabinet in the Vrolik Museum. Photo: Paul Bomers, Museum Vrolik, Academic Medical Centre, Amsterdam. [Color figure can be viewed at wileyonlinelibrary.com]

1835). In the extant collection we found a total of 39 teratological specimens which could reasonably be assigned to Bonn's original collection.

One of Bonn's specimens concerned a rare type of conjoined twinning: a parapagus dicephalus dibrachius tripus that was discordant for cyclopia (See case 8). It is known that concomitant anomalies have a much higher incidence in monozygotic twins compared to singletons and are even more frequent in conjoined twins. These anomalies can be designated as early structural defects with frequent discordance and mainly concerning midline structures as is the case in holoprosencephaly (Schinzel, Smith, & Miller, 1979). Unfortunately, due to the historic value of this specimen and therefore the absence of additional diagnostics, we were not able to make any statements about the internal morphology of the non-holoprosencephalic head in this specimen. Oostra, Baljet, Verbeeten, and Hennekam (1998b) described a case of a diprosopus tetraophthalmus distomia diotis with cebocephaly that was not apparent on external examination but was only noticeable after radiological imaging. One of the earliest known reports of a conjoined twin with concomitant holoprosencephaly is from Dutch professor h.c. Louis (Lodewijk) de Bils (1624–1669). De Bils was an autodidact without formal medical education who became renowned for his embalming and dissection techniques, for which he received the title “professor *honorarius anatomiae*” by the Illustrious School of 's Hertogenbosch (Jansma, 1919). De Bils described and depicted a dicephalus in which one head clearly showed a proboscis and synophthalmia (De Bils, 1661) (Figure 16). Rating (1933) reported a case of diprosopus which showed two separate eyes and a normal nose in the right face and synophthalmia and a proboscis in the left face. However, as mentioned some reports exist that describe holoprosencephaly in concomitance with conjoined twinning, although these associations remain exceedingly rare.

Another set of specimens of Bonn's collection concerned a case of multiple enchondromatosis wherein Bonn described the entire skeleton (Bonn, 1783). These specimens, either dried or fixated in ethanol were initially part of the Hovius collection. Part of this set moved with the Bonn collection to Leiden in 1822, whereas the remainder stayed in Amsterdam, where it still resides. Gerard Sandifort described 15 of these specimens (nr. CCCI–CCCIX were dried bones, specimens DCXXXIX–DCXLV were fixed and kept in alcohol). As it turns out the left femur, left tibia, left radius/ulna, left scapula, left clavicle, a sacrum with three lumbar vertebrae, a right finger and a left-sided hip bone were identified in the extant Hovius collection in Museum Vrolik. The right-sided skeletal elements but also the left hand and both fibular bones were described in the catalogue of the Leiden collection (Sandifort, 1827, 1835). The only specimen of this case which was identified in the extant Leiden collection is that of the left hand (See case 1). Bonn posed quite an interesting opinion regarding the cause of this rare bone dysplasia. He presumed that the cause of the tumors would have been present from birth or presented itself within the first year, because of their size. He considered the child to have suffered from congenital rickets (a default diagnose in the 18th and 19th century for many bone diseases which involved bending of tubular bones) which caused the distal ends of the bones to cease growing and to become malformed and replaced by nodular

proliferations. Bonn was right in that the tumors were, most probably, present around birth or in the first year as enchondromatosis is a rare primary bone dysplasia appearing in childhood (Kadar, Kleinstern, Morsy, Soreide, & Moran, 2016).

5.3 | Eduard Sandifort (1742–1814)

Eduard Sandifort studied medicine in Leiden and obtained his doctor degree in the same city with his dissertation entitled: “*Dissertatio anatomico-obstreticia de pelvi, ejusque in partu dilatatione*” (Sandifort, 1763). In this work he described the pelvic dilatation during parturition. In subsequent years Sandifort worked as a physician in The Hague (The Netherlands) and was engaged in the variolation against cattle-plague and smallpox (Smit, 1986). In 1765, at the age of twenty-three, Eduard began to publish his Nature- and Medical Library (Natuur –en Geneeskundige Bibliotheek) which appeared every year for ten successive years. In this compiled work hundreds of observations concerning botany, physics and medicine are described. In 1770 he became *Praelector Anatomiae et Chirurgiae* and only one year later he was appointed *Professor Anatomiae et Chirurgiae* at the University of Leiden. Between 1777 and 1781, Eduard Sandifort wrote four well-illustrated Latin catalogues, entitled “*Observationes Anatomico-Pathologicae*” (Sandifort, 1777, 1778, 1779, 1781a). In this work Sandifort included 47 descriptions of anatomical and pathological findings including some congenital anomalies. The aim of this work was twofold: 1) to register his pathological findings during dissections; and 2) to propagate his theories about pathology and congenital defects to

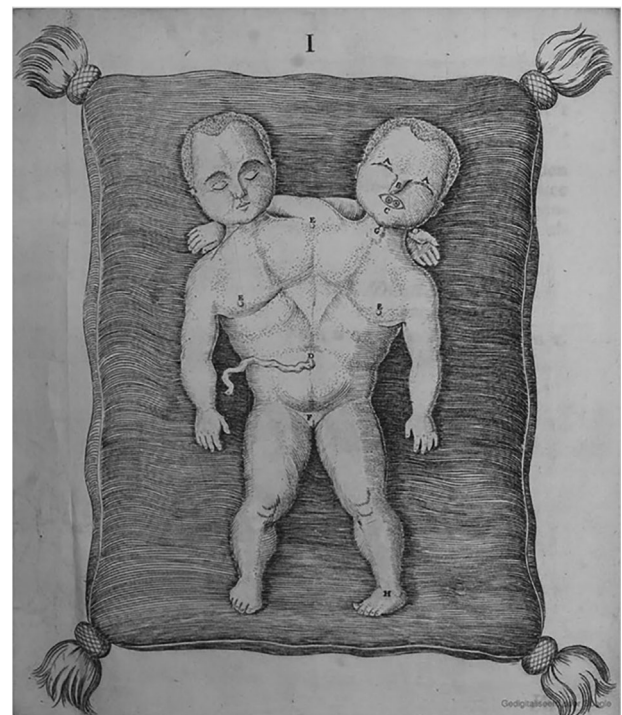


FIGURE 16 Copperplate of the conjoined twin with concomitant holoprosencephaly De Bils (1661). [Color figure can be viewed at wileyonlinelibrary.com]

a broad audience. Among others, he described a hydatiform mole, complex malformations, a horseshoe kidney, an acardiac twin, a duplicated ureter and bladder malformations. Noteworthy is the case on page 29 of the fourth book, entitled "*De labio leporino, congenito, duplici et complicato*" (Sandifort, 1781a). This description is one of the earliest extensively described cases, both pre- and postmortem, of a child with a complicated bilateral cleft lip, palate and nose (Figure 17A). Eduard Sandifort stated that this complex anomaly would be very difficult to operate and impossible to cure; his only intention was to describe the child's anomaly in full detail. Unfortunately, the child died of malnourishment when it was only 22 weeks old. Sandifort convinced the parents to donate the child's body for further research; he additionally gave a detailed description of the child's skull after he carefully dissected it (Figure 17B).

It was in 1793, that he became internationally renowned when he published the first two parts of the *Museum Anatomicum Lugduno-Batavae* catalogues (Sandifort, 1793). In these two volumes, written on request of the board of Leiden's University curators, Sandifort described the 17th and 18th century inherited anatomical collections of the *Museum Anatomicum* in their then present state and described the collections of contemporaries Johannes Jacobus Rau (1668–1719), Bernhardus Siegfried Albinus (1697–1770) and Wouter van Doeveren (1730–1783). In 1802 his private collection was bought by the anatomical museum (Smit, 1986). The collection of Eduard Sandifort is recognized by its exceptionally beautiful and elegant, with mercury and red-colored wax injected, specimens of the lymphatic system (Elshout, 1952). Another noteworthy script about congenital anomalies is his book entitled "*Icones herniae inguinalis congenitae*." In this book, he gave detailed information about congenital inguinal hernias accompanied by some fine engravings (Sandifort, 1781b). Furthermore, Eduard wrote a book entitled "*Anatome infantis cerebro destituti*." In this impressive work he described the morphology of the head, brain, skull, and vertebrae of the anencephalic child in great detail (Sandifort, 1784). Although Eduard primarily dedicated himself to careful descriptions rather than

speculative interpretations about the cause of congenital anomalies, he stated that the cause of anencephaly is a primary hydrocephalus. This hydrocephaly eventually degraded the brain and bones of the skull, resulting in an absent brain and hence confirming the "*monstra accidentalis*" theory. This in contrast to the indecisive opinions of his contemporaries Wouter van Doeveren and Andreas Bonn. He was one of the first to give a detailed description of a 12-year-old cyanotic boy who suffered from a cardiac malformation (See case 6), presently known as tetralogy of Fallot (Bennett, 1946; Sandifort, 1777). Furthermore, Eduard described many anomalies of the blood vessels (Van der Boon, 1851), again affirming his interest in congenital anomalies. In the extant collection we found a total of eight teratological specimens which could be reasonably assigned to Eduard's original collection.

5.4 | Gerard Sandifort (1779–1848)

Gerard Sandifort, son of Eduard Sandifort, was aged only thirteen when he began to help his father with dissecting anatomical specimens. He studied medicine and obtained his doctor's degree in Leiden with his dissertation called "*Dissertatio medica inauguralis, de pleuritide*" (Sandifort, 1824). In 1801 he was appointed professor of anatomy and subsequently became professor of anatomy, surgery and medicine in 1802. Gerard followed his father's footsteps and published part three and part four of the *Museum Anatomicum Lugduno-Batavae* catalogues (Sandifort, 1827, 1835). In these two works the collections of contemporaries Sebald Justinus Brugmans (1763–1819) and Andreas Bonn (1738–1817) are described. In the preface of part four Gerard noted that it was his main goal to describe the most important pathological specimens and included some exceptionally well-illustrated cases of congenital anomalies. Like his father, Gerard was renowned for his excellent observations and meticulous descriptions of both anatomical, pathological and teratological specimens. His expertise and opinion about the cause of congenital anomalies can be analyzed throughout his many treatises and

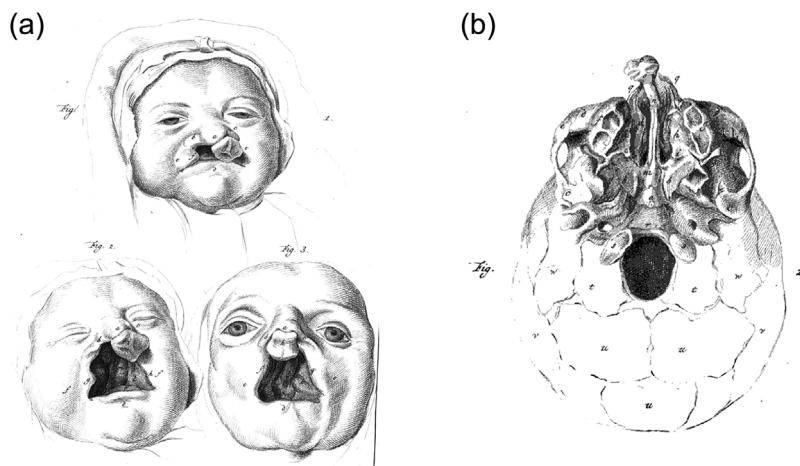


FIGURE 17 (a) Copperplate of the child with a complicated bilateral cleft lip, palate and nose. (b) Copperplate of the skull of the same child after Eduard Sandifort cleaned the skull after the child deceased

observations which were published between 1817 and 1848 for the "Royal Dutch Institute" (Koninklijk Nederlandsch Instituut). He wrote 46 treatises; however, only 15 concerned congenital defects in animals or humans. Gerard meticulously described and depicted the morphology of acardiac twins and anencephalic fetuses (Sandifort, 1820, 1823). In 7 of the 15 treatises concerning congenital anomalies, he gave his conception about the cause of an anomaly. In the early descriptions of Gerard (around 1820), he was convinced that an excess of nerves was the main cause of an anomaly. Around 1824, he changed his opinion and stated that the cause of an anomaly was the result of a disturbed "*nisus formativus*" (Van der Zwaag, 1970). This opinion shift could possibly have been triggered by a dissertation of the Leiden professor in pharmacy Gerardus Suringar (1802–1874) entitled: "*Dissertatio medica inauguralis de nisu formativo ejusque erroribus*" (An inaugural dissertation on the impulse of nature's formation and its mistakes) (Suringar, 1824). The overarching term "*nisus formativus*" can be seen as the source of all propagation, growth, and nourishment. The concept of "*nisus formativus*" was initially presented in 1781 by Johann Friedrich Blumenbach (1752–1840), who stated that this theory could explain the impulse of nature to create forms and how those forms were managed; every living organism was pre-formed and contained a kind of "potency" that only had to develop to its future shape (Blumenbach, 1781). For decades, this theory was the starting point to explain the formation of both normal and abnormal morphogenesis, as well as, the regeneration and conservation of all structures and included the origin and nature of congenital anomalies. This "*nisus formativus*" theory was sanctioned by Gerard until approximately 1839, when he stated in his treatise on rare malformations of the head in quadrupeds that the real cause of the anomalies was rather doubtful and still unknown (Sandifort, 1840). However, as late as 1847, he sometimes referred to an excess of nerves as the cause of certain anomalies (Numan, 1847). Comparable to his father, Gerard had a private collection of specimens that were not described in the *Museum Anatomicum* catalogues. After he died in 1849, these 432 anatomical specimens were publically auctioned (Anonymous, 1849); the present status and whereabouts of these specimens are unknown. Nevertheless, in the extant collection we found two specimens, both concerning the skeleton of an acardiac twin, that could be reasonably assigned to Gerard's original collection albeit not further elaborated, indicating that at least some of the auctioned specimens were purchased by the museum, at the time.

6 | CONCLUSION

The cause of congenital anomalies during the 18th and 19th centuries heydays of collecting teratological specimens was still debated and differently envisioned by several collectors. Subjects such as heredity and modern "concepts of developmental biology" were completely absent during the time in which these specimens were collected. Moreover, due to the absence of additional diagnostics such as genetics and radiology and the shortage of concrete causative theories it is rather astonishing that these old

collectors were already able to describe, and in many cases, diagnose a congenital anomaly. Many historically made diagnoses could not be changed after re-diagnosing the specimens with contemporary dysmorphological knowledge, actually confirming that these old collectors were perhaps the first dysmorphologists and can be seen as true pioneers in the field of teratology. The external descriptions these old collectors gave to these specimens were equivalent to concepts such as malformations and deformations we now abundantly use to describe congenital anomalies. Apparently, no collector was able to recognize that both expressions do not exclude each other and can be applicable individually to different conditions. Up to the present day teratology is still an elusive field of science with many open questions. However, historical theories about the cause of congenital anomalies can be used for further explorations into contemporary theories. Finally, exploiting old teratological collections can yield rare discordant associations, can give more insights in very rarely occurring birth defects and can be used to expand the clinical spectra of certain conditions. Therefore, old teratological collections have to be treasured for the future scientists in teratological research.

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CONFLICTS OF INTEREST

There is no conflict of interest reported.

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