THIEME Atlas of Anatomy

Latin Nomenclature

Internal Organs

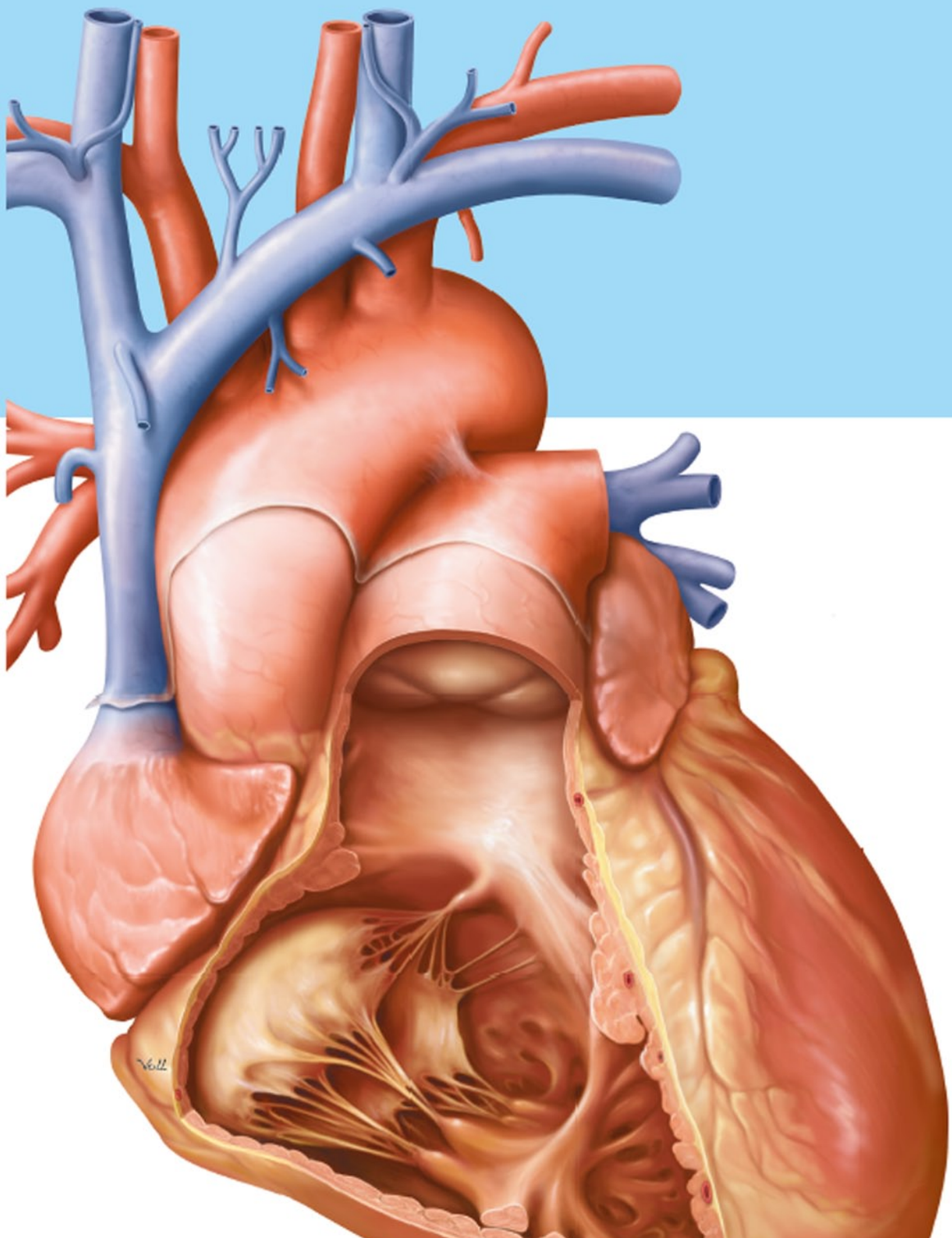
Third Edition

Michael Schuenke
Erik Schulte
Udo Schumacher

Consulting Editors
Wayne A. Cass
Hugo Zeberg

Illustrations by
Markus Voll
Karl Wesker

Foreword by
Anne M. Gilroy



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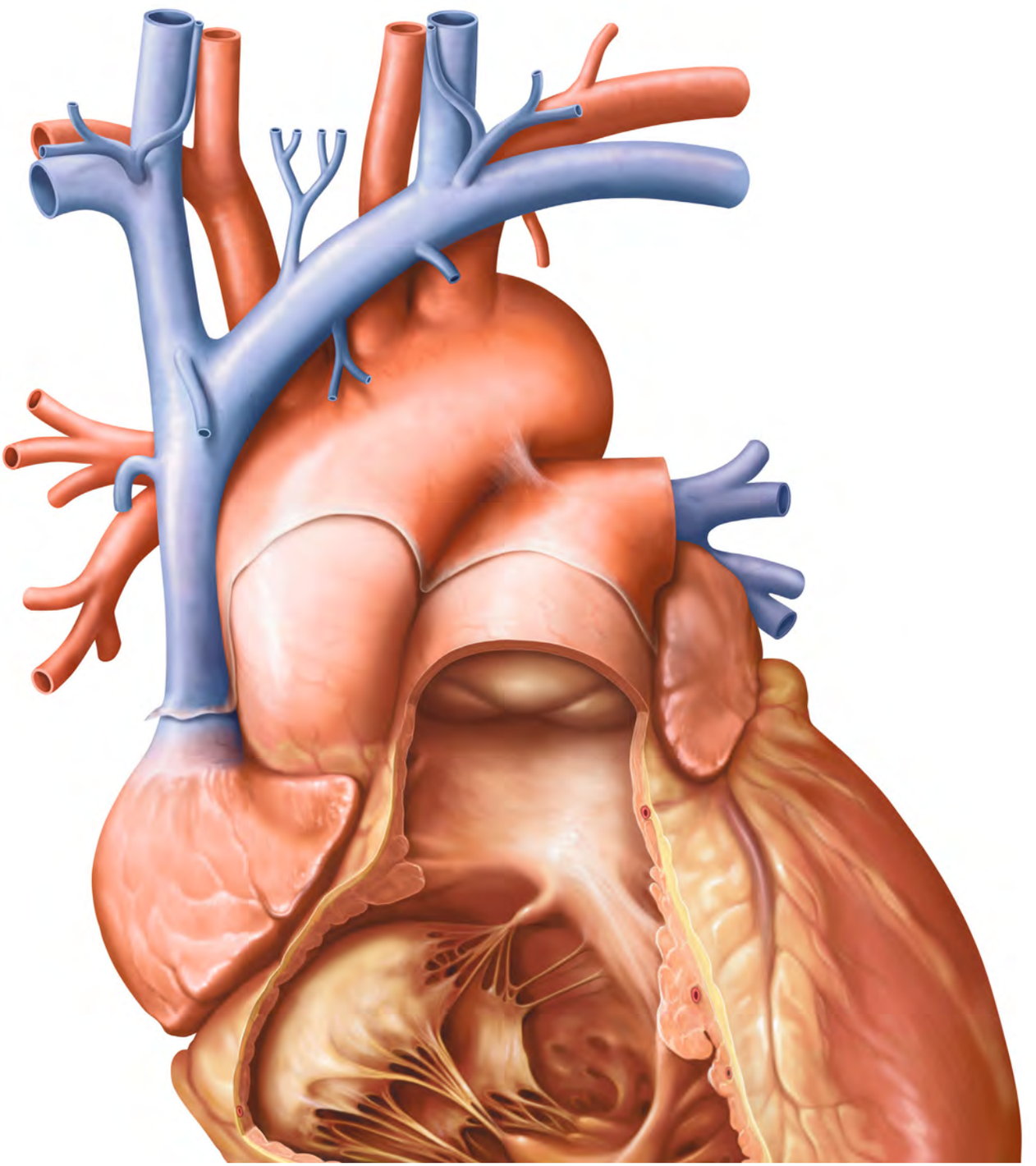

Internal Organs

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Latin Nomenclature

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New York • Stuttgart • Delhi • Rio de Janeiro

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Compositor: DiTech Process Solutions

Library of Congress Cataloging-in-Publication Data is available from the publisher.

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Thieme Medical Publishers, Inc.
333 Seventh Avenue, 18th Floor
New York, NY 10001, USA
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Printed in Germany by Appl

5 4 3 2 1

ISBN 978-1-68420-082-5

Also available as an e-book:
eISBN 978-1-68420-083-2

Foreword

Each of the authors of the single volume *Thieme Atlas of Anatomy* was impressed with the extraordinary detail, accuracy, and beauty of the illustrations that were created for the Thieme three volume series of anatomy atlases. We felt these images were one of the most significant additions to anatomic education in the past 50 years. The effective pedagogical approach of this series, with two-page learning units that combined the outstanding illustrations and captions that emphasized the functional and clinical significance of structures, coupled with the numerous tables summarizing key information, was unique. We also felt that the overall organization of each region, with structures presented first systemically — musculoskeletal, vascular, and nervous — and then topographically, supported classroom learning and active dissection in the laboratory.

This series combines the best of a clinically oriented text and an atlas. Its detail and pedagogical presentation make it a complete support for class and laboratory instruction and a reference for life in all the medical, dental, and allied health fields. Each of the volumes — *General Anatomy and Musculoskeletal System, Internal Organs,* and *Head, Neck, and Neuroanatomy* — can also be used as a stand-alone text/atlas for an in-depth study of systems often involved in the allied health/medical specialty fields.

We were delighted when Thieme asked us to work with them to create a single-volume atlas from this groundbreaking series, and we owe a great debt to the authors and illustrators of this series inasmuch as their materials and vision formed the general framework for the single volume *Thieme Atlas of Anatomy*.

We thank the authors and illustrators for this very special contribution to the teaching of anatomy and recommend it for thorough mastery of anatomy and its clinically functional importance in all fields of health care-related specialties.

Lawrence M. Ross, Brian R. MacPherson, and Anne M. Gilroy

A Note on the Use of Latin Terminology

To introduce the Latin nomenclature into an English-language textbook is a delicate task, particularly because many Latin loanwords have passed into general use. Some loanwords are so common that fluency of the text would be disturbed if they were to be translated back into Latin. These Latin loanwords have typically undergone several adaptations before becoming part of the English language. A term such as *sympathetic trunk* (lat. *truncus sympaticus*) has undergone morphological adaptation (through the loss of masculine suffix -us), orthographical adaptation (through the substitution of a "Germanic" k for a Latin c), and phonological adaptation (th and e instead of t and i). In addition, the word order has been reversed. The Latin term *sympaticus* is in fact borrowed from the late Greek word *sympathetikos* (from sympathes "having a fellow feeling, affected by like feelings"), thereby illustrating that words move between languages when cultures meet. Other anatomical terms are so colloquial (e.g. *hand*), that a Latin word (e.g. *manus*) would be inappropriate to use at all occasions. Clearly, the text would become unreadable if a strict translation of all English terms into Latin were imposed.

As a result, Latin has been used as long as it does not disrupt the flow of the text and whenever possible in figures and tables. In some cases, dual terminology has been used, with either the English or Latin word in parentheses. As much as possible, the terminology of *Terminolgia Anatomica* (1998) has been followed.

Hugo Zeberg

Preface of the Authors and Illustrators

When Thieme started planning the first edition of this atlas, they sought the opinions of students and instructors alike in both the United States and Europe on what constituted an "ideal" atlas of anatomy — ideal to learn from, to master extensive amounts of information while on a busy class schedule, and, in the process, to acquire sound, up-to-date knowledge. The result of our work in response to what Thieme had learned is this atlas. The *Thieme Atlas of Anatomy*, unlike most other atlases, is a comprehensive educational tool that combines illustrations with explanatory text and summary tables, introducing clinical applications throughout, and presenting anatomic concepts in a step-by-step sequence that includes system-by-system and topographical views.

For the first edition we had hoped that our *Atlas of Anatomy* would help the medical student to understand the anatomical basis of clinical medicine. This indeed was accepted by the students all over the world and soon a second edition had to come on the market in Germany, which was extensively extended and revised. More and more information had been added, including spreads on important foundational information on the common imaging planes for plain film, MRI, and CT scans, the structure of skeletal muscle fibers, the structure and chemical composition of hyaline cartilage, and the regeneration of peripheral nerves, bone marrow, and paraganglia, as well as new graphical summaries in neuroanatomy. Hence the fifth German edition looks ever more distinctly different from the first one. Of course, we have also checked, corrected, and updated all of the information in this atlas.

We are grateful to the American branch of Thieme that they have made this third English edition possible. We hope that this updated version will serve the medical students and practitioners of medicine alike in helping them to understand human morphology which is indispensable for diagnosis and therapy.

Michael Schünke, Erik Schulte, Udo Schumacher,
Markus Voll, and Karl Wesker

Acknowledgments

First we wish to thank our families. This atlas is dedicated to them.

Since the publication of the first volume of the *Thieme Atlas of Anatomy* in 2006, we have received numerous suggestions for refinements and additions. We would like to take this opportunity to express our sincere thanks to all those who through the years have helped us to improve the *Thieme Atlas of Anatomy* in one way or another. Specifically, this includes Kirsten Hattermann, Ph.D.; Runhild Lucius, D.D.S.; Prof. Renate Lüllmann-Rauch, M.D.; Prof. Jobst Sievers, M.D.; Ali Therany, D.D.S.; Prof. Thilo Wedel, M.D. (all at the Anatomic Institute of Christian Albrecht University of Kiel); as well as Christian Friedrichs, D.D.S. (Practice for Tooth Preservation and Endodontics, Kiel); Prof. Reinhart Gossrau, M.D. (Charité Berlin, Institute of Anatomy); Prof. Paul Peter Lunkenheimer, M.D. (Westphalian Wilhelm University Münster); Thomas Müller, M.D., associate professor (Institute of Functional and Clinical Anatomy of the Johannes Gutenberg University of Mainz); Kai-Hinrich Olms, M.D., Foot Surgery, Bad Schwartau; Daniel Paech, M.S. physics, medical student (Department of Neuroradiology of the University Medical Center, Heidelberg); Thilo Schwalenberg, M.D., supervising physician (Urologic Clinic of the University Medical Center, Leipzig); Prof. emeritus Katharina Spanel-Borowski, M.D. (University of Leipzig); Prof. Christoph Viebahn, M.D. (Georg August University of Göttingen). For their extensive proofreading we thank Gabriele Schünke, M.S. biology; Jakob Fay, M.D.; as well as medical students Claudia Dücker, Simin Rassouli, Heike Teichmann, Susanne Tippmann, and dental student Sylvia Zilles; also, Julia Jörns-Kuhnke, M.D., especially for her assistance with the figure labels.

We extend special thanks to Stephanie Gay and Bert Sender, who prepared the layouts. Their ability to arrange the text and illustrations on facing pages for maximum clarity has contributed greatly to the quality of the atlas.

We particularly acknowledge the efforts of those who handled this project on the publishing side:

Jürgen Lüthje, M.D., Ph.D., executive editor at Thieme Medical Publishers, has "made the impossible possible." He not only reconciled the wishes of the authors and artists with the demands of reality but also managed to keep a team of five people working together for years on a project whose goal was known to us from the beginning but whose full dimensions we only came to appreciate over time. He is deserving of our most sincere and heartfelt thanks once more this year, in which Jürgen Lüthje, M.D., Ph.D., is retiring. We welcome his successor Dr. Jochen Neuberger, who has shown great initiative is taking over the *Thieme Atlas of Anatomy* and will continue to lead and develop the existing team.

Sabine Bartl, developmental editor, became a touchstone for the authors in the best sense of the word. She was able to determine whether a beginning student, and thus one who is not (yet) a professional, could clearly appreciate the logic of the presentation. The authors are indebted to her.

We are grateful to Antje Bühl, who was there from the beginning as project assistant, working "behind the scenes" on numerous tasks such as repeated proofreading and helping to arrange the figure labels.

We owe a great debt of thanks to Martin Spencker, managing director of Educational Publications at Thieme, especially to his ability to make quick and unconventional decisions when dealing with problems and uncertainties. His openness to all the concerns of the authors and artists established conditions for a cooperative partnership.

We are also indebted to Yvonne Strassburg, Michael Zepf, and Laura Diemand who saw to it that the *Thieme Atlas of Anatomy* was printed and bound on schedule, and that the project benefited from the best practical expertise throughout the entire process of publication. We also thank Susanne Tochtermann-Wenzel and Anja Jahn for their assistance with technical issues involving every aspect of the illustrations; Julia Fersch who ensured that the *Thieme Atlas of Anatomy* is also accessible via eRef; Almut Leopold for the exceptional index; Marie-Luise Kürschner and Nina Jentschke for the appealing cover design; as well as Dr. Thomas Krimmer, Liesa Arendt, Birgit Carlsen, Stephanie Eilmann, and Anne Döbler, representing all those now and previously involved in the marketing, sale, and promotion of the *Thieme Atlas of Anatomy*.

The authors, October 2019

I thank my wife, Valerie, and son, Robert, for their love, support and understanding. Nothing means more to me than the two of you.

As consulting editor I was asked to review the English translation of *Thieme Atlas of Anatomy: Internal Organs*, third edition. My work involved reviewing and editing the translation and nomenclature conversion of the German text to currently used English terms. In addition, some minor changes in presentation were made to reflect commonly accepted approaches in North American educational programs. This task was facilitated by the clear organization of the original text and the exceptional work of the translators. Throughout this process I have tried to remain faithful to the intentions and insights of the authors and illustrators, whom I thank for this outstanding revision.

I would also like to thank the entire team at Thieme Medical Publishers who worked on this edition. In particular I would like to give special thanks to Delia DeTurris, Executive Editor, for inviting me to work on this atlas and for her continued support, and Torsten Scheihagen, Managing Editor, for his support and help throughout the process of completing this atlas. I also thank Brian R. MacPherson, Ph.D., Professor of Neuroscience at the University of Kentucky, for his support.

Wayne A. Cass

It has been a great honor to act as a consulting editor, with responsibility for the Latin nomenclature, for *Thieme Atlas of Anatomy: Internal Organs*, Third Edition. There were several people from whom I received a great deal of assistance and guidance, and must express my gratitude towards. Regarding the discussion of nomenclature, I would wish to thank my mentor Prof. Peter Århem, Ph.D., my father Lennart Zeberg, M.D., and Prof. Jonas Broman, Ph.D. In addition, I would also like to express my gratitude to Prof. Björn Meister, M.D., Ph.D., for putting forward my name for this task.

Moreover, I am deeply grateful to the staff at Thieme Medical Publishers that I have been in close contact with, in particular, the editorial director Anne Sydor, Ph.D., managing editor Judith Tomat, editorial assistant Huvie Weinreich, and marketing agent David Towle.

I would also like to acknowledge the Federative International Programme for Anatomical Terminology (FIPAT) for their work towards a standard nomenclature in the field of anatomy.

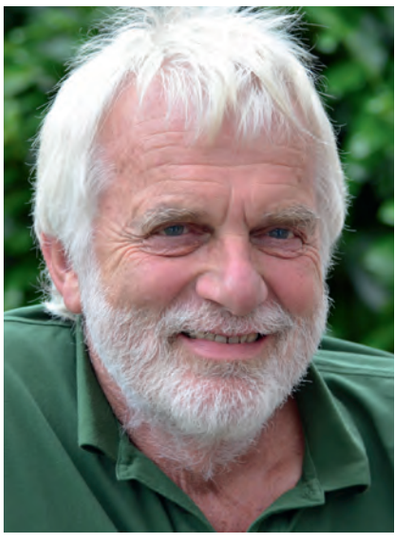
In addition, I would like to express my gratitude to my talented assistant teachers — C. Stening-Soppola, D.F. Åström, A. Javanmardi, E.N. Sögutlu, A. Sotoodeh, N. Aziz, A.-M. Al-Khabbaz, K. Ma, and T. Engström — for performing an initial review of the Latin nomenclature.

Hugo Zeberg

The people behind the *Thieme Atlas of Anatomy*

A work such as the *Thieme Atlas of Anatomy* can only arise when the people involved in the project work hand in hand. The integrated educational and artistic work you now hold in your hands is the product of an intensive discourse between anatomy professors Michael Schünke, Erik Schulte, and Udo Schumacher and anatomic illustrators Markus Voll and Karl Wesker.

Creating learning units that comprehensively treat a topic on a two-page spread is a challenge in itself. The authors must carefully select the content, assemble it, and add explanatory legends. Yet how this content is presented in the atlas, how appealing and memorable it is, depends largely on the illustrations. And the *Thieme Atlas of Anatomy* now includes a good 5000 of them. In creating them, Markus Voll and



Michael Scheunke, MD, PhD, professor

Institute of Anatomy of the University of Kiel, studied biology and medicine in Tübingen and Kiel, extensive teaching of medical students and physical therapists, author and translator of other textbooks.

Erik Schulte, MD, professor

Institute of Functional and Clinical Anatomy of the Johannes Gutenberg University of Mainz, studied medicine in Freiburg, extensive teaching of medical students, award for excellence in teaching in Mainz.

Udo Schumacher, MD, professor

Institute of Anatomy of the University of Hamburg; studied medicine in Kiel with one year of study at the Wistar Institute of Anatomy and Biology in Philadelphia; extensive teaching of medical students, physical therapists, and residents (FRCS). Spent several years in Southampton and gained experience in integrated interdisciplinary instruction.

Karl Wesker drew on many years of experience in anatomic illustration, visited anatomic collections, studied specimens, and immersed themselves in old and new works of anatomy. This was the foundation on which the *Thieme Atlas of Anatomy* arose.
It guides the reader through anatomy step by step, revealing what a crucial role anatomy will later play in medical practice. This was a particularly important consideration for the authors. Whether performing bowel surgery for a tumor, puncturing the tympanic membrane in a middle ear infection, or examining a pregnant patient, no physician lacking knowledge of anatomy is a good physician. Even the *Thieme Atlas of Anatomy* cannot spare you the effort of learning, yet the authors and illustrators can assure you that it will make it a lot more pleasant.

Markus Voll

Freelance illustrator and graphic artist in Munich, trained as an artist at the Blocherer School of Design in Munich, studied medicine at the University of Munich. He has worked as a scientific illustrator on numerous book projects for 25 years.

Karl Wesker

Freelance painter and graphic artist in Berlin. Apprenticeship as a plate etcher and lithographer, studied visual communication at the University of Applied Sciences in Münster and at the Berlin University of the Arts and art science at the Technical University of Berlin. For over 30 years he has been active as a freelance painter and graphic artist, including book projects in anatomy.

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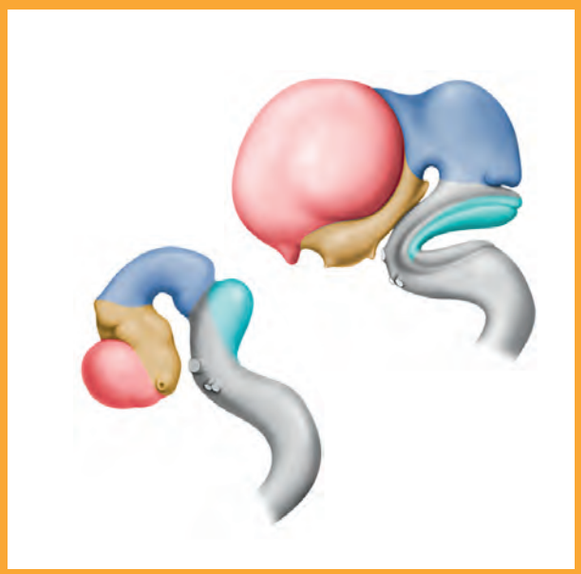
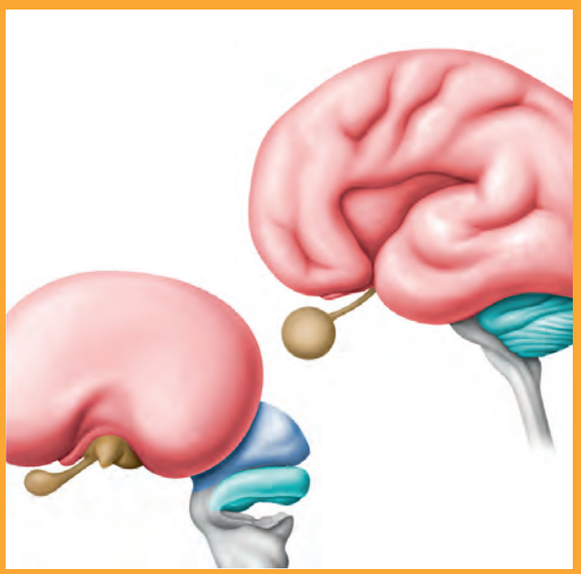
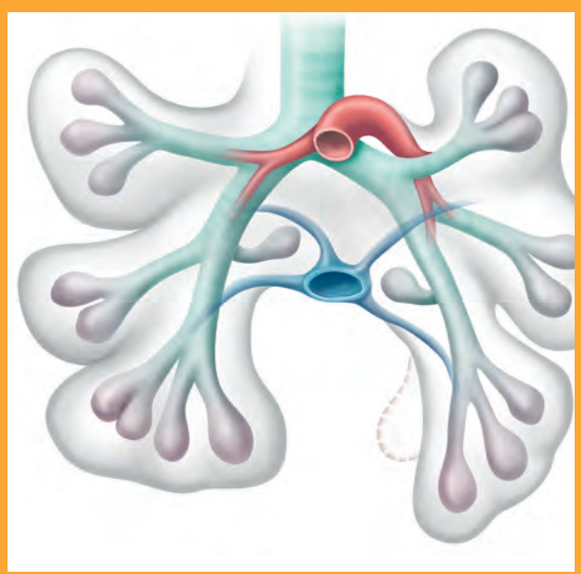
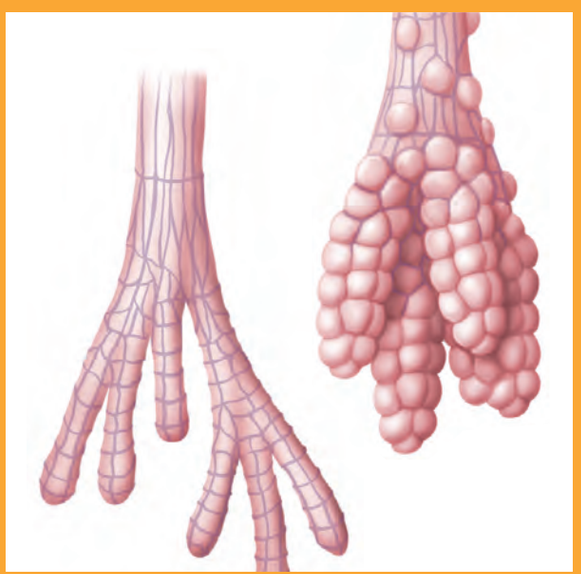








A Structure and Development of Organ Systems

1.1 Definitions, Overview, and Evolution of Body Cavities

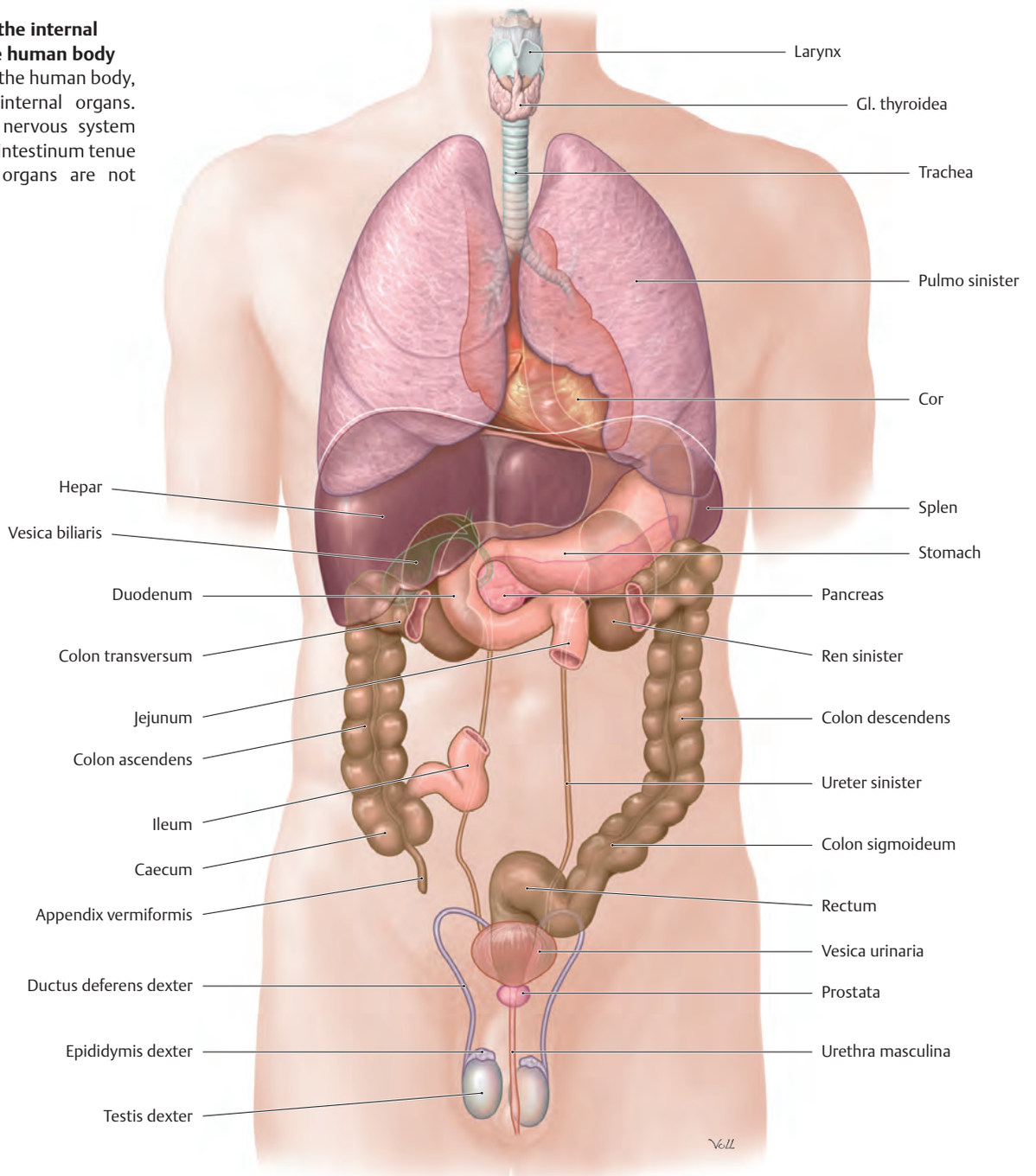
Definitions

The human body, similar to all higher organisms, is organized into a hierarchy of different levels:

- A **cell** is the smallest unit of life, that in principle can survive on its own.
- A **tissue** consists primarily of cells from the same origin, and the extracellular matrix they form. A tissue is an ensemble of cells, organized to do a specific job.
- An **organ** is a structural unit composed of different tissues. Thus, it combines the functions of the various tissue components.
- An **organ system** is made up of organs that function together to perform a specific function. For example, the digestive organs make up the *digestive system*. For the most part, the individual organs are related to each other morphologically.
- An **organism** is composed of several organ systems.

A Overview of the internal organs of the human body

Anterior view of the human body, displaying the internal organs. For clarity, the nervous system and most of the intestinum tenue and endocrine organs are not shown.



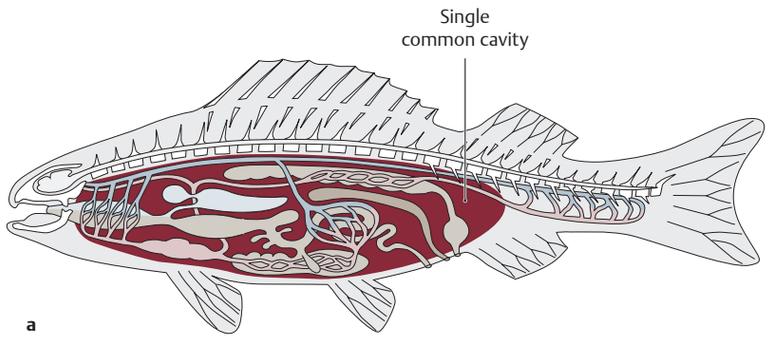
B Overview of organ systems

Since, by definition, every structural unit composed of different tissues is referred to as an organ (according to this definition, every muscle is an organ), the term is commonly used for structures in the cranium, neck, and body cavities. The organs situated inside the body cavities are referred to as internal organs or viscera. This atlas is a study aid for learning gross anatomy. Thus, the individual organs are discussed with respect to their topography. However, since groups of individual organs form morphological and functional systems, which due to evolutionary processes don't conform to topographical anatomy, those organ systems along with their embryology will be discussed first. This overview will aid in understanding the location, shape and function of the internal organs in the developing organism.

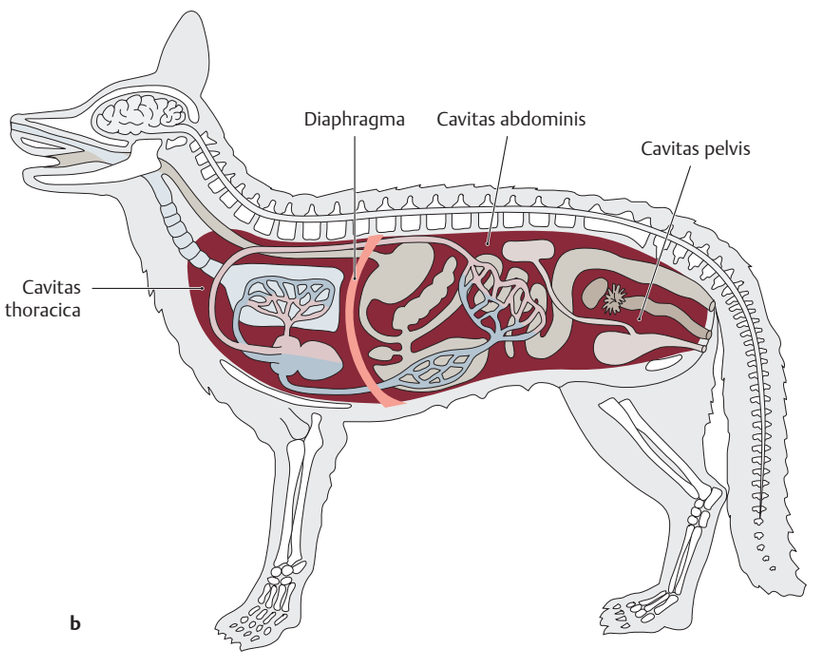
Note: Peripheral nerves, bone marrow, and blood are usually not referred to as "organs." For the sake of completeness, they will also be discussed since they are part of whole organ systems.

* Organs that are highlighted in italics are located in the neck or cranium and thus will not be discussed here.

System	Organs*
Systema digestorium	*Cavitas oris with dentes and gll. salivariae, pharynx,* oesophagus, stomach (gaster), intestinum tenue, intestinum crassum, rectum, pancreas, liver (hepar), and vesica fellea
Systema respiratorium	*Cavitas nasi and sinus paranasales, larynx,* trachea, pulmones
Systema urinarium	Kidneys (renes), ureteres, vesica urinaria, urethra
Systema genitale	♀ Uterus, tubae uterinae (salpinges), ovarium, vagina, gll. vestibulares majores ♂ Testes, epididymis, ductus deferens, vesiculae seminales, prostata, gl. bulbourethralis
Systema cardiovasculare	Heart (cor), vessels, blood, and *medulla ossium rubra*
Systema lymphoideum	*Medulla ossium, tonsillae,* thymus, splen, nodi lymphoidei, ductus thoracicus
Systema endocrinum	*Gl. thyroidea, gll. parathyroideae,* gll. suprarenales (adrenal), paraganglia, pancreas (islet cells), ovaria, testes, *hypophysis, hypothalamus*
Systema nervosum	*Encephalon, medulla spinalis,* systema nervosum periphericum (with *somatic* and autonomic components)



a



b

C Evolution of body cavities

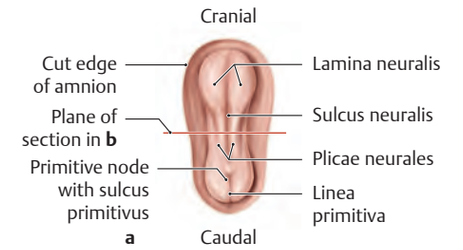
While in fish **(a)** all internal organs are situated in a single common body cavity, in mammals **(b)**, the diaphragma separates the cavitas thoracica from the cavitas abdominis. Due to shared evolutionary history, the structures of these two body cavities are basically identical. The different anatomical terms used for similar structures (e.g., pleura – peritoneum) are functionally meaningless. In mammals, there is no physical structure that separates the cavitas abdominis from the cavitas pelvis. They form a continuous space that in terms of its topographical anatomy is divided only by the superior border of the bony pelvis. The anatomical unit of the cavitates abdominis and pelvis is of clinical significance as there are no anatomical barriers to restrict the spread of inflammation or tumors between these two compartments. The diaphragma acts as a barrier to stop tumors or inflammation from spreading from the cavitas abdominis to the cavitas thoracica and vice versa.

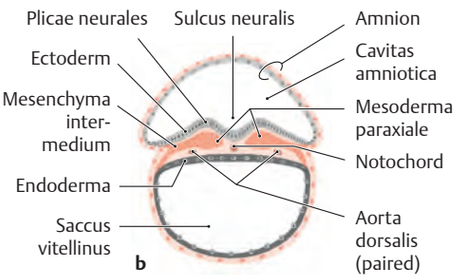
1.2 Organogenesis and the Development of Body Cavities

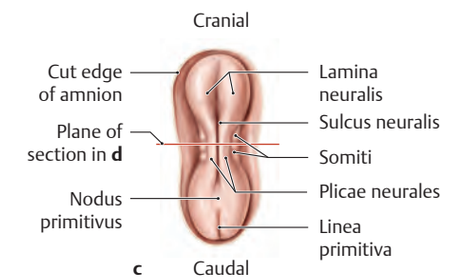
A Differentiation of the germ layers (after Christ and Wachtler)

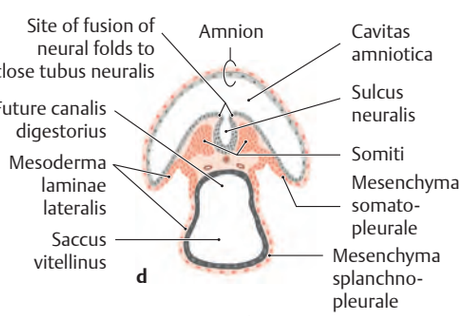
After the formation of the trilaminar discus embryonicus at the end of the third week (see **B**) the primordia (precursor cells destined to become a specific tissue or organ) of the different tissues and organs are arranged according to the body plan. In the subsequent embryonic period (weeks 4 to 8), the three germ layers (ectoderma, mesoderma, and endoderma) give rise to all major external and internal organs (organogenesis). At the same time, the trilaminar discus embryonicus begins to fold, resulting in major changes in body form and internal structure. By the end of the embryonic stage, the major features of the body are recognizable and the organs have moved into their eventual position within and outside of the body cavities.

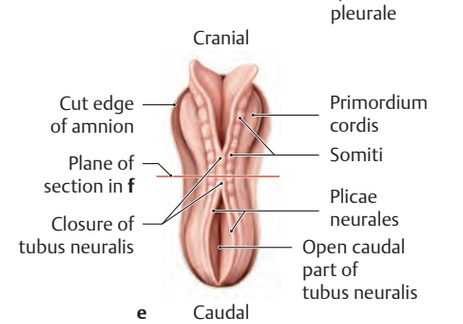
Ectoderma	Tubus neuralis		Encephalon, retina, medulla spinalis
	Crista neuralis	Crista neuralis cranialis	Ganglia sensoria and parasympathica, pars enterica systematis nervosi, thyrocyti C, textus muscularis levis, pigment cells, glomus caroticum, bone, cartilage, connective tissue, dentinum and cementum of the teeth, dermis, and tela subcutanea of the head
		Crista neuralis truncalis	Ganglia sensoria and autonomica, gliocyti peripherici, medulla suprarenalis, melanocyti, intramural plexuses
	Surface ectoderma	Ectodermal placodesae	Adenohypophysis, ganglia sensoria nervorum cranialium, epithelium olfactorium, auris interna, lens
			Enamelum of the teeth, epithelium cavitatis oris, gll. salivariae, cavitates nasi, sinus paranasales, lacrimal passages, porus acusticus externus, epidermis, hair, nails, cutaneous glands
Mesoderma	Axial	Notochorda, prechordal mesoderma	Musculi externi bulbi oculi
	Paraxiale		Columna vertebralis, costae, textus muscularis striatus, connective tissue, dermis and subcutis of the back and part of the head, smooth muscle, blood vessels
	Mesenchyma intermedium		Renes (kidneys), gonada, renal and genital excretory ducts
	Meso-derma laminae lateralis	Visceral (mesenchyma splanchnopleurale)	Cor (heart), vasa sanguinea, textus muscularis levis, bowel wall, blood, cortex suprarenalis, tunica serosa pleurae visceralis
		Parietal (mesenchyma somatopleurale)	Sternum, limbs (cartilage, bones, and ligaments), dermis and tela subcutanea of the anterolateral body wall, textus muscularis levis, connective tissue, tunica serosa pleurae parietalis
Endoderma			Epithelium of the bowel, respiratory tract, digestive glands, gll. pharyngeales, tuba auditiva, cavitas tympani, vesica urinaria, thymus, gll. parathyroideae, gl. thyroidea

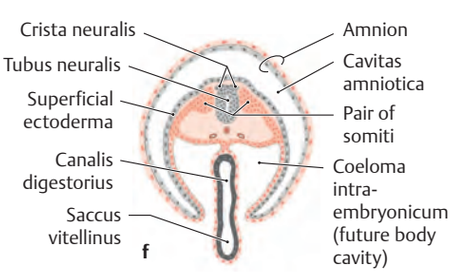












B Neurulation and Somitus Formation (after Sadler)

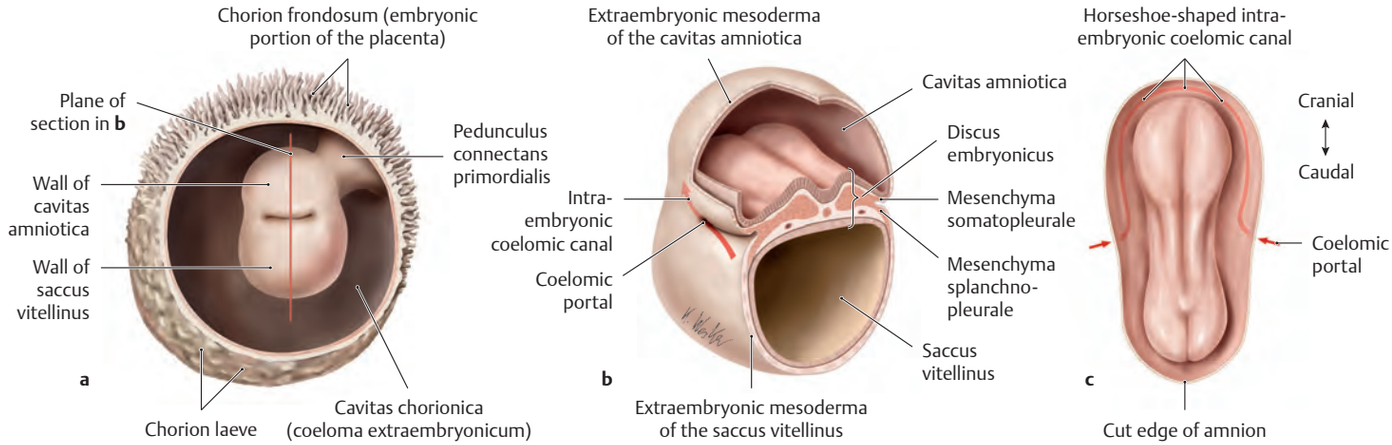
a, **c**, and **e** Dorsal views of the discus embryonicus after removal of the amnion;
b, **d**, and **f** Schematic cross-sections of the corresponding stages at the planes of section as marked in **a**, **c**, and **e**; Age is in postovulatory days.

During neurulation (formation of the tubus neuralis from the lamina neuralis), the neurectoderma differentiates from the surface ectoderma, due to inductive influences from the notochorda, and the tubus neuralis and crista neuralis cells move inside the embryo.

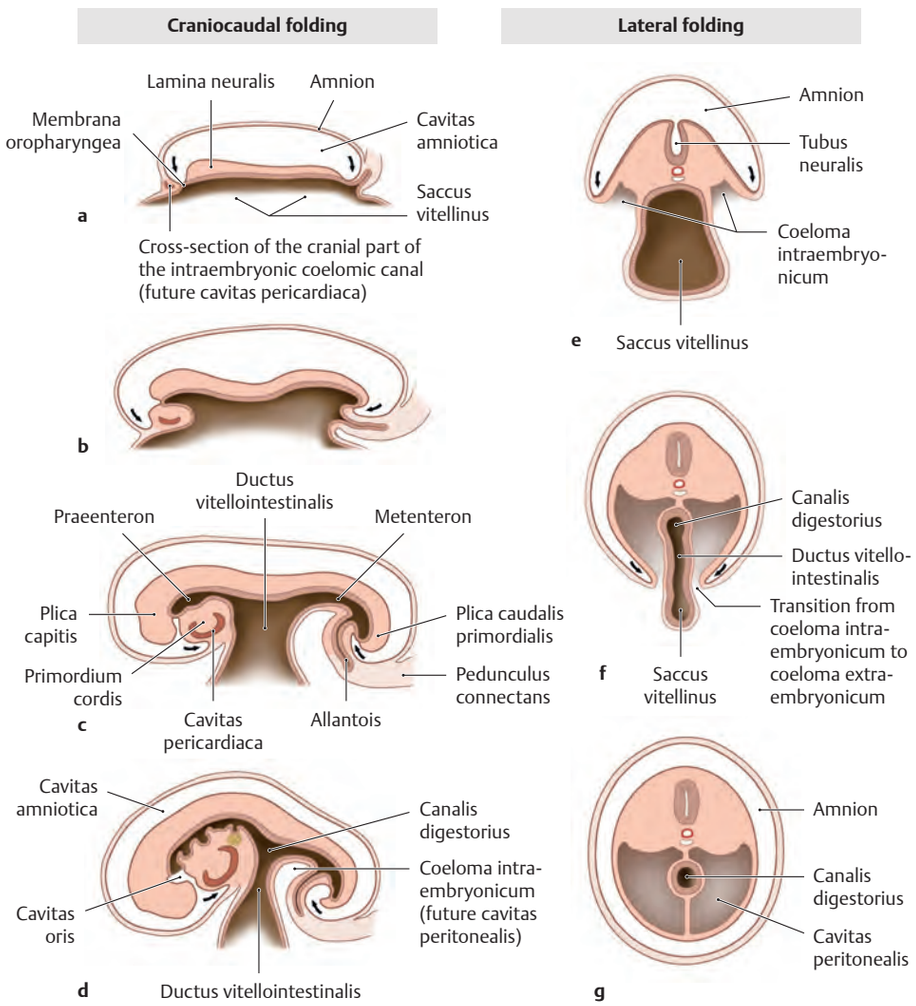
a and **b** Discus embryonicus at 19 days: The sulcus neuralis is developing in the area of the lamina neuralis.

c and **d** Discus embryonicus at 20 days: In the mesoderma paraxiale, flanking both sides of the sulcus neuralis and notochorda, the first somiti have formed (they contain cellular material assigned to form the columna vertebralis, muscles, and subcutaneous tissue). Immediately lateral to the mesoderma paraxiale is the mesenchyma intermedium, and lateral to that is the mesoderma laminae lateralis. The sulcus neuralis is beginning to close to form the tubus neuralis and the embryo begins to fold.

e and **f** Discus embryonicus at 22 days: Eight pairs of somiti are seen flanking the partially closed tubus neuralis which is sinking below the ectoderma. In the mesoderma laminae lateralis, the coeloma intraembryonicum, or future body cavity, arises. It will later develop both a parietal and a visceral layer (somatopleure and splanchnopleure). On the side facing the coeloma, a mesothelial lining develops from the somato- and splanchnopleure. It later forms the tunicae serosae lining the cavitates pericardiaca, pleurali, and peritonealis. The tubus neuralis migrates deeper into the mesoderma, and the somiti differentiate into sclerotomus, myotomus, and dermatome.

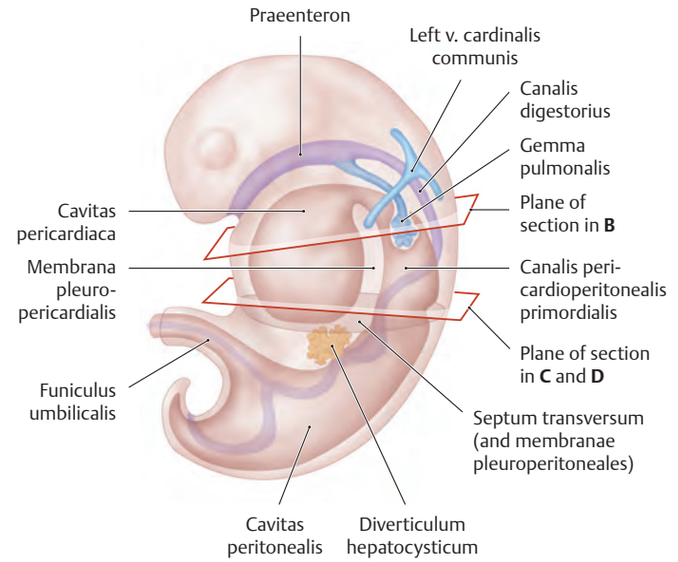


C Formation of the coeloma intraembryonicum (after Waldeyer)
a View into the chorionic cavity (coeloma extraembryonicum); **b** Cut through the cavitas amniotica, discus embryonicus and saccus vitellinus (the cavitas chorionica has been removed); **c** View of the discus embryonicus (the intraembryonic coelomic canal has been highlighted in red). The eventual definitive serous cavities (cavitates pericardiaca, pleuralis, and peritonealis) arise from the coeloma intraembryonicum which begins to form in week 4 when intercellular clefts (not shown) appear in the mesoderma laminae lateralis (see **B**). The coeloma intraembryonicum divides the mesoderma laminae lateralis into parietal and visceral layers (*mesenchymata somatopleurale* and *splanchnopleurale*). At the edges of the discus embryonicus, the mesenchyma somatopleurale adjacent to the surface ectoderm is continuous with the extraembryonic mesoderma of the amnion. The mesenchyma splanchnopleurale adjacent to the endoderma is continuous with the extraembryonic mesoderma of the saccus vitellinus. Thus, the coeloma intraembryonicum surrounds the opening of the saccus vitellinus like a ring (the *coelomic ring*). In the cranial part of the embryo, the coelomic ring closes off from the coeloma extraembryonicum (cavitas chorionica) and forms a horseshoe shaped intraembryonic *coelomic canal,* which is visible when viewed from above. The caudal coelomata intra and extraembryonicum (see **D**) continue to communicate with one another through the *coelomic portals*. Later, as a result of embryonic folding, the caudal coelomata intra- and extraembryonicum become separated from each other. During the course of embryonic development, the coeloma intraembryonicum compartmentalizes with the cavitas pericardiaca arising from the unpaired cranial part of the coeloma and the paired cavitates pleuralis and peritonealis arising from the lateral limbs of the coelom.

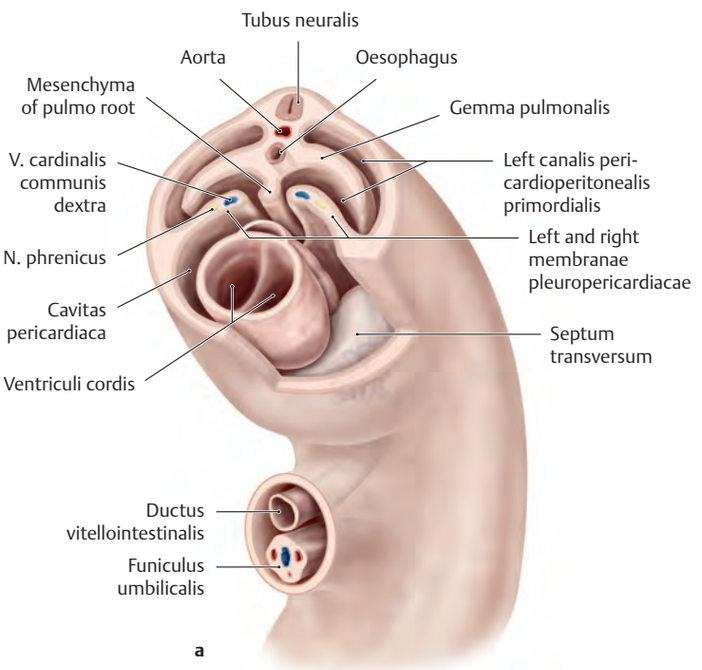


D Embryonic folding
a–**d** Midsagittal sections; **e**–**g** Frontal sections at the level of the saccus vitellinus.
During folding the embryo is rapidly growing and it rises up from the surface of the original discus. The lamina neuralis grows rapidly and extends in both the cranial and caudal directions. As a result, the embryo curves upon itself (**a**–**d**). The formation of somiti causes a lateral expansion (lateral folding) of the embryo in the area above the saccus vitellinus (**e**–**g**). As a result, the intraembryonic coelomic canal shifts ventrally. Due to cranial folding (head fold), the cranial portion of the coeloma intraembryonicum moves ventral to the praeenteron and broadens into the cavitas pericardiaca. The folding of the caudal tail moves the pedunculus connectans (the future funiculus umbilicalis) and the allantois to the ventral aspect of the embryo. While lateral folding occurs, the coeloma intraembryonicum progressively separates from the coelom extraembryonicum. These processes result in the junction between embryonic endoderma (primitive canalis digestorius) and saccus vitellinus (future pedunculus sacci vitellini) becoming increasingly narrow. At the same time, the left and right caudal parts of the coeloma intraembryonicum merge with one another forming a single large cavitas coelomica, which is the future cavitas peritonealis (for position of cavitates pleurales see p. 6).

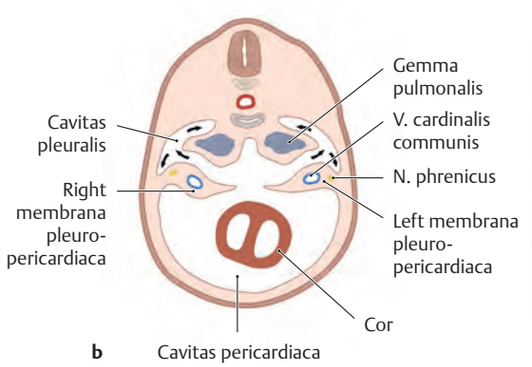
1.3 Compartmentalizatioan of the Coeloma Intraembryonicum

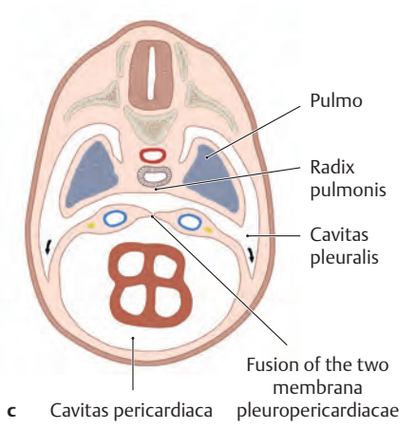


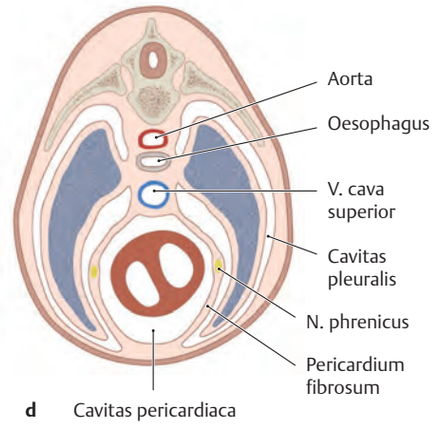
A Overview of the compartmentalization of the coeloma intraembryonicum (after Drews)
Embryo at 4 weeks (viewed from left side).
Due to cranial folding, the cranial portion of the coeloma intraembryonicum moves ventral to the praeenteron and broadens into the cavitas pericardiaca. The cavitas pericardiaca flanking the canalis digestorius (gut tube) communicates with the caudally located cavitas peritonealis through the canales pericardioperitoneales primordiales. The still unfolded parts of the future cavitas peritonealis initially open laterally into the cavitas chorionica. The gemmae pulmonales, which push from the canalis digestorius into the canales pericardioperitoneales, grow into the future paired cavitates pleurales. Through the formation of partitions, the pleural cavities separate from both the cavitas pericardiaca (membranae or plicae pleuropericardiacae) and the cavitas peritonealis (septum transversum and membranae or plicae pleuroperitoneales) (see **B**). In the frontal plane the plicae pleuropericardiacae originate on the craniolateral side of the two canales pericardioperitoneales primordiales in the area surrounding the vv. cardinales communes. They fuse with the mesoderma located ventral to the canalis digestorius (the future oesophagus). The plicae pleuroperitoneales develop in the caudolateral wall of the canales pericardioperitoneales and, together with the mesooesophagum dorsale and the septum transversum, form the future diaphragma (see **D**).

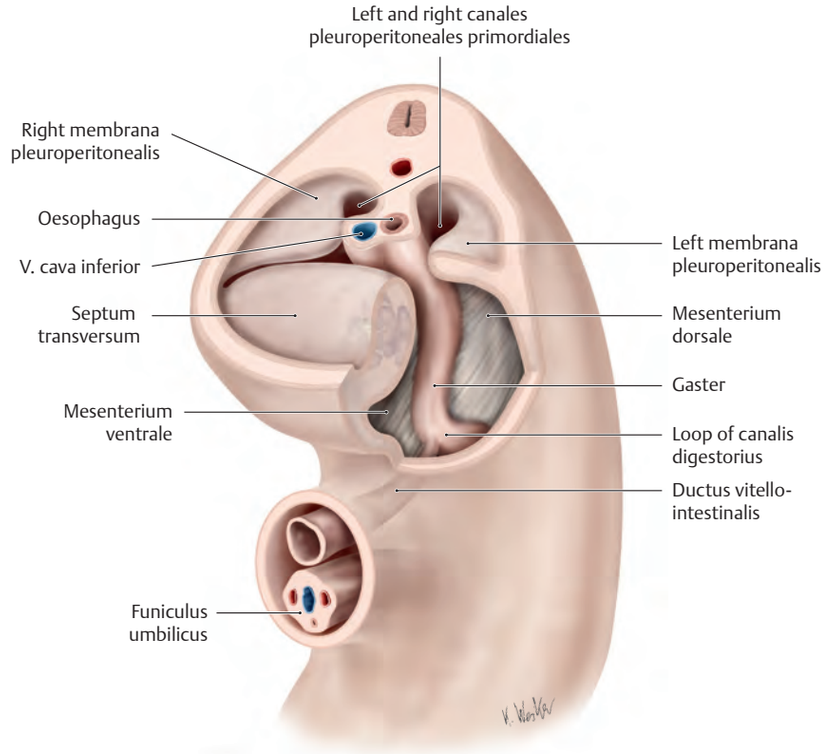


B Separation of the cavitas pericardiaca from the cavitates pleurales (after Sadler)
Embryo at 5 weeks. Frontal section at the level of the future cavitas pericardiaca; for plane of section see **A**.
In the 5th week, at the junction between the unpaired cavitas pericardiaca and the two canales pericardioperitoneales, two thin mesoderm folds (plicae pleuropericardiacae), coming from the lateral direction, grow toward one another. They contain the trunks of the vv. cardinales communes and the nn. phrenici. The cavitates pleurales form as a result of the gemmae pulmonales growing into the canales pleuroperitoneales (see p. 36 development of the pulmones). In the course of further development, the cavitates pleurales further expand and become separate from the cavitas pericardiaca. The separation is complete once both of the plicae pleuropericardiacae have fused with the mesenchyma at the root of the lungs. The anterior vv. cardinales merge to form the v. cava superior; and the two plicae pleuropericardiacae give rise to the future pericardium fibrosum (see p. 14, development of the heart).



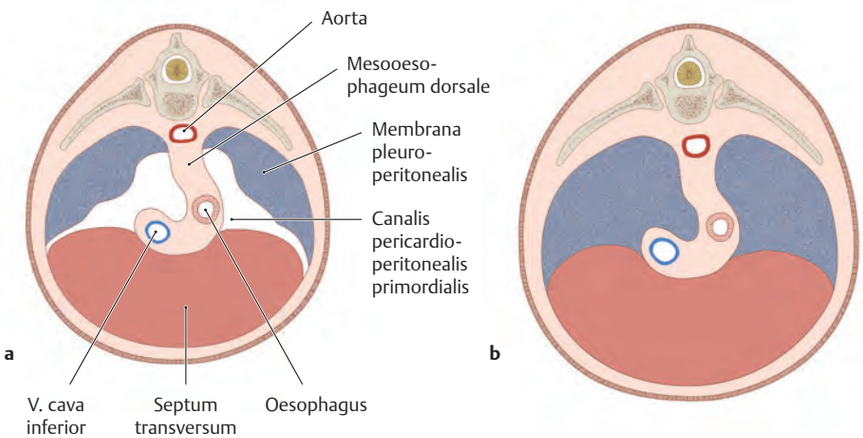






C Separation of the cavitates pleurales from the cavitas peritonealis
(after Sadler)

After the cavitates pleurales have separated from the cavitas pericardiaca, they are still temporarily connected to the cavitas peritonealis through the canales pericardioperitoneales. They become completely sealed off by the end of the 7th week with the development of the diaphragma, which is formed from several different structures (see **D**). Faulty closure of the canales pericardioperitoneales can lead to a *congenital hernia diaphragmatica* (e.g., Bochdalek hernia) allowing abdominal viscera to enter into the cavitates pleurales.



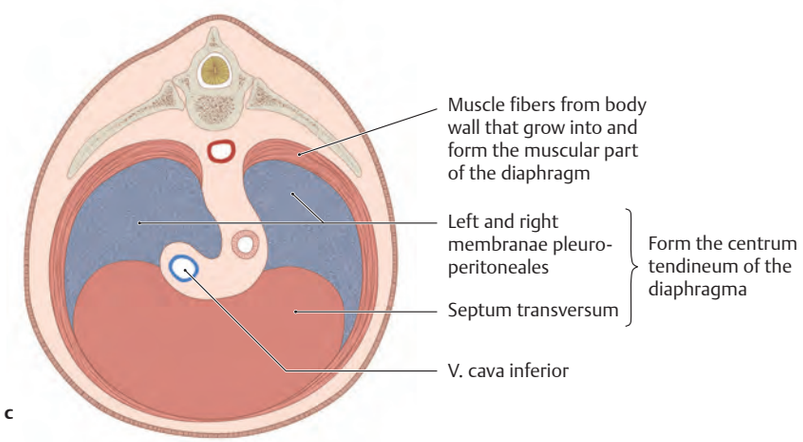
D Development of the diaphragma
(after Sadler)

The diaphragma is derived from four different structures:

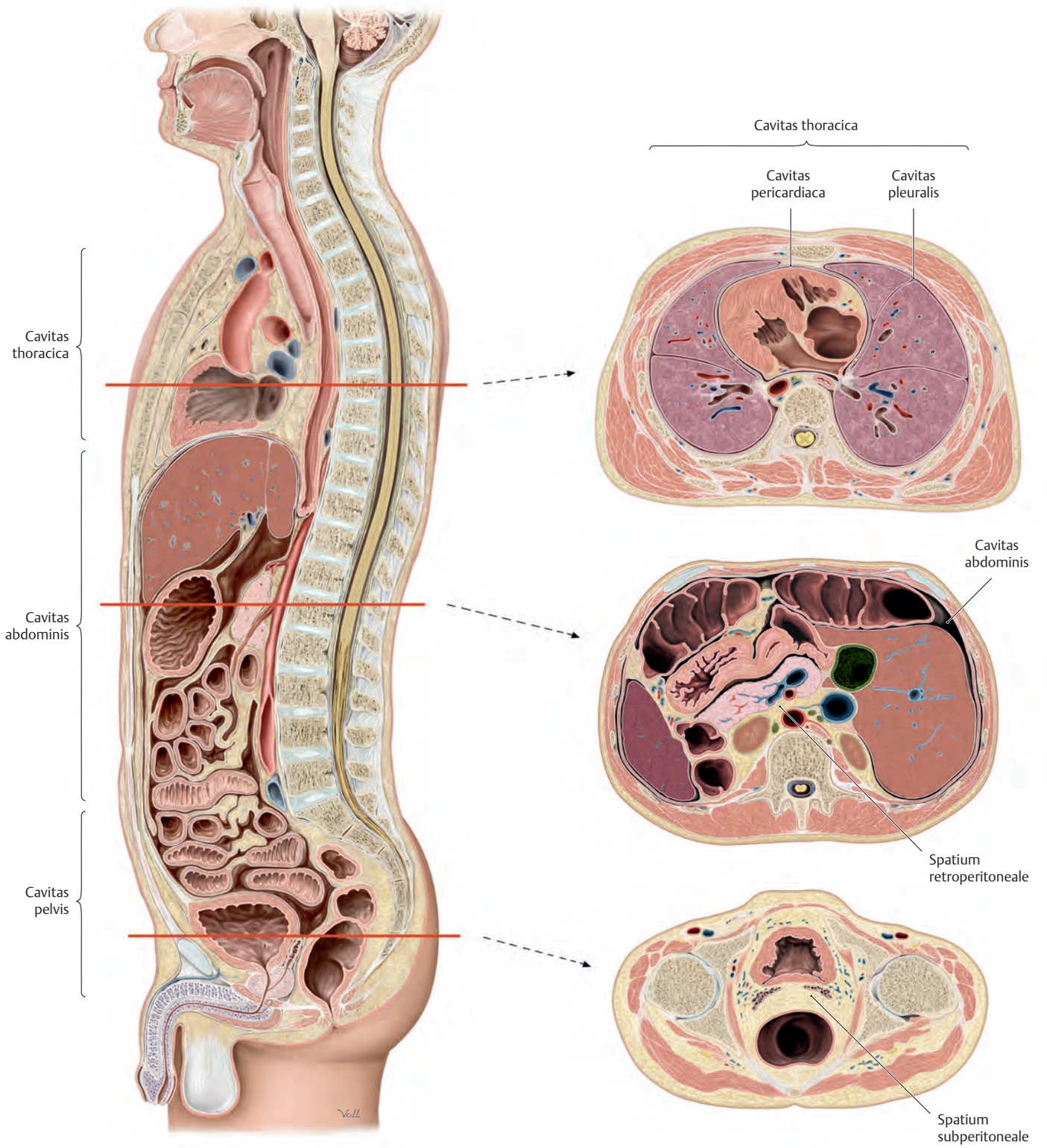
- the septum transversum
- the left and right plicae pleuroperitoneales
- the mesooesophagum dorsale
- body wall musculature

In the 4th week the septum transversum develops as a thick mesenchymal plate in the area between the cavitas pericardiaca and pedunculus sacci vitellini. In the 6th week, the septum transversum moves caudally (**a**). The hepar (liver) forms in the ventral mesenterium directly below it. During further development, the septum transversum fuses with both of the plicae pleuroperitoneales and forms the future *centrum tendineum* (**b**). The mesooesophagum dorsale and the adjacent body wall musculature give rise to the muscular part of the diaphragma (**c**).

Note: The nn. phrenici (C3, C4, and C5), located in the plicae pleuropericardiacae directly next to the trunks of the vv. cardinales communes, provide motor innervation to the diaphragma. The textus muscularis striatus of the diaphragm (from somiti), as well as the septum transversum, are originally from cervical regions. This explains why the nerve supply to the diaphragma (the nn. phrenici) comes from cervical medulla spinalis levels.



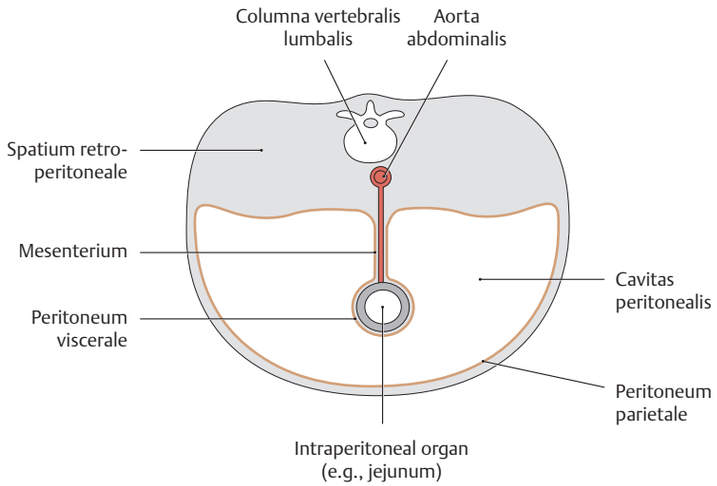
1.4 Organization and Architecture of Body Cavities



A Organization of the body cavities
Midsagittal section, viewed from the left side. Three large body cavities can be identified. From from the top down they are as follows

- Cavitas thoracica
- Cavitas abdominis
- Cavitas pelvis

These body cavities are completely surrounded by parts of the body wall. The majority of the walls consists of muscle and connective tissue. In addition, the thorax is surrounded by costae, and the pelvis by the ossa coxae. At its upper end, the connective tissue space of the cavitas thoracica is continuous with the connective tissue space of the neck. The diaphragma pelvis muscles close off the apertura pelvis inferior. Depending on their location in one of the three cavities, organs are referred to as thoracic, abdominal or pelvic organs (see **C**).



B Structure of the body cavities

Highly schematic cross-section of a human body; superior view. Every body cavity can be divided into two differently structured spaces:

- A **hollow space**: A smooth, moist epithelial layer, the serous membrane or tunica serosa, lines the inner wall of the cavity and the adjacent outer wall of the organs. The portion of the tunica serosa that covers the organ is called the *lamina visceralis* (viscera refers to internal organ). The portion lining the walls of the cavity is called the *lamina parietalis* (parietal refers to wall). The organs located in the cavity are movable. They are attached to the connective tissue space (see below) by a connective tissue bridge covered by a serous membrane (a mesenterium).
- A **connective tissue space** within which run the pathways leading to and from the organ. Organs situated in these spaces are surrounded by connective tissue and are more or less immovable.

While this general structure applies to all three body cavities, the terms for the individual regions vary (see **C**):

- In the **thorax**, most of the connective tissue is located in the central compartment of the cavitas thoracica, the mediastinum, in which the cavitas pericardiaca (a hollow space lined with a serous membrane) is embedded. The cavitates pleurales are located lateral to the mediastinum.
- In the **abdomen**, the connective tissue is situated behind the cavitas peritonealis in the spatium retroperitoneale (an extraperitoneal space).
- In the **pelvis**, the connective tissue is situated both behind and below the cavitas peritonealis in the spatia retroperitoneale and subperitoneale (spatia extraperitonealia).

Correspondingly, all organs in the thorax, abdomen and pelvis can be organized according to their location in the connective tissue space or in one of the serous-membrane lined cavities (see **C**).

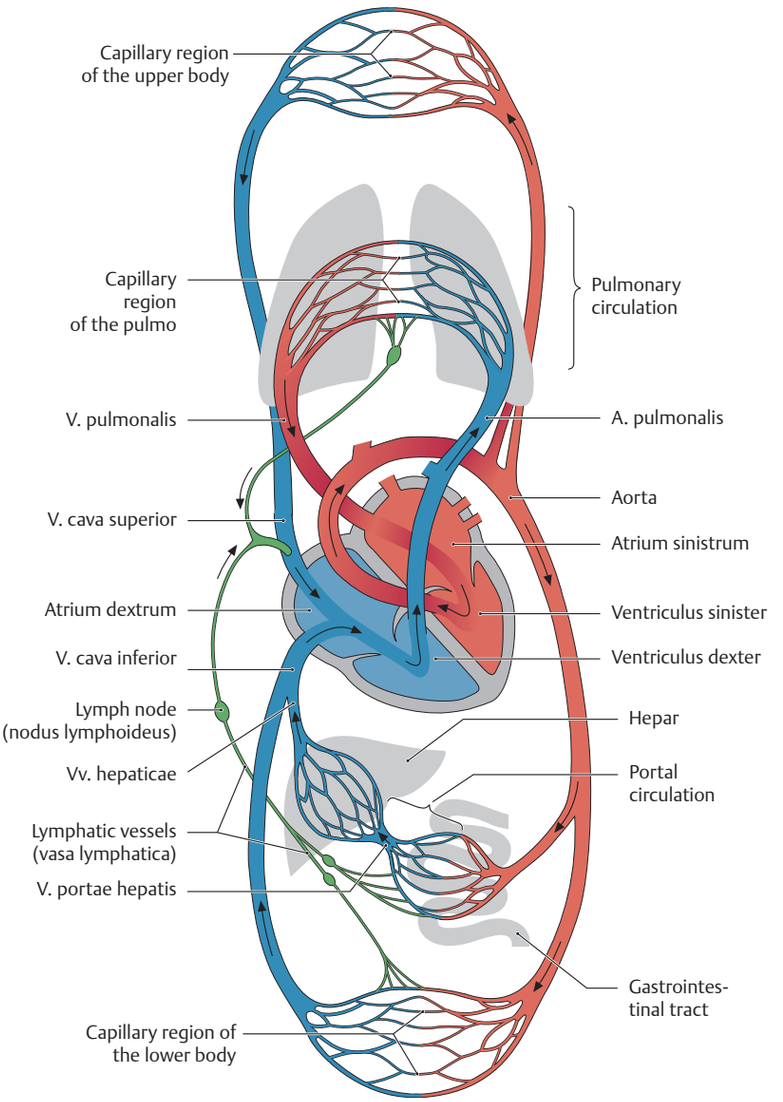
Note: While the partition between the cavitates thoracica and abdominis is clearly defined by the diaphragma, the separation between the cavitates abdominis and pelvis is often only demarcated by bony reference points on the body wall. Thus, the cavitates abdominis and pelvis essentially remain a single cavity, and therefore form a single region where disease processes can spread from one cavity to the other.

A mesenterium is a layer of connective tissue covered by peritoneum. Within it run the organ's neurovascular supply (vasa sanguinea and lymphatica, nervi). With reference to organs, the mesenterium is often identified with the prefix "meso" (e.g., mesocolon transversum).

C Spaces and body cavities and their respective organs in the thorax, abdomen, and pelvis

Body cavity and the organs it contains	Serous cavities and the organs they contain	Serous membrane	Connective tissue spaces and their embedded organs
Cavitas thoracica (thorax) Thoracic organs	• Paired cavitates pleurales with pulmones: *Intrapleural organs* • Cavitas pericardiaca *Intrapericardial organ*	• Pleura visceralis and parietalis • Laminae visceralis and parietal is pericardii serosi	• Mediastinum (middle section of the cavitas thoracica) between the cavitates pleurales as well as behind the unpaired cavitas pericardiaca with the mediastinal organs: oesophagus, trachea, and thymus as well as vessels and nerves: – *Mediastinal organs*
Cavitas abdominis (abdomen) Abdominal organs	• Abdominal cavitas peritonealis with gaster (stomach), parts of the intestina tenue and crassum, splen (spleen), hepar (liver), vesica biliaris, and caecum with appendix vermiformis: *Intraperitoneal organs*	• Peritoneum viscerale and parietale	• Spatium extraperitoneale behind the abdominal cavitas peritonealis (spatium retroperitoneale, retropubicum) with renes, ureteres, pancreas and parts of the duodenum, intestinum crassum, and rectum: – *Extraperitoneal organs*
Cavitas pelvis (pelvis) Pelvic organs	• Pelvic cavitas peritonealis with fundus and corpus uteri, ovaria, tubae uterinae, and upper rectum: *Intraperitoneal organs*	• Peritoneum viscerale and parietale	• Spatia extraperitonealia behind and below the pelvic cavitas peritonealis (spatia retroperitoneale and subperitoneale) with vesica urinaria and adjacent portions of the ureteres, prostata, gll. vesiculosae, cervix uteri, vagina, and parts of the rectum: – *Extraperitoneal organs*

2.1 Overview and Basic Wall Structure



A Overview of the cardiovascular system

The **cardiovascular system** is a closed system of vessels through which the blood is transported. This circulation is necessary to supply the organs with oxygen, nutrients, and hormones and to carry carbon dioxide and other metabolic waste products away to the excretory organs. Additionally, cells and proteins of the immune system travel through the bloodstream. Using blood as a transport medium, they "patrol" the body by constantly looking out for pathogens. The blood can also transport heat, so that circulation helps to regulate body temperature. In addition to these functions, the blood also helps to seal off leaks. It contains clotting factors that are activated when vessels gets damaged. The circulation is powered by the cor (heart) which functions as a pressure pump.

The circulatory system can be divided into two main circuits:

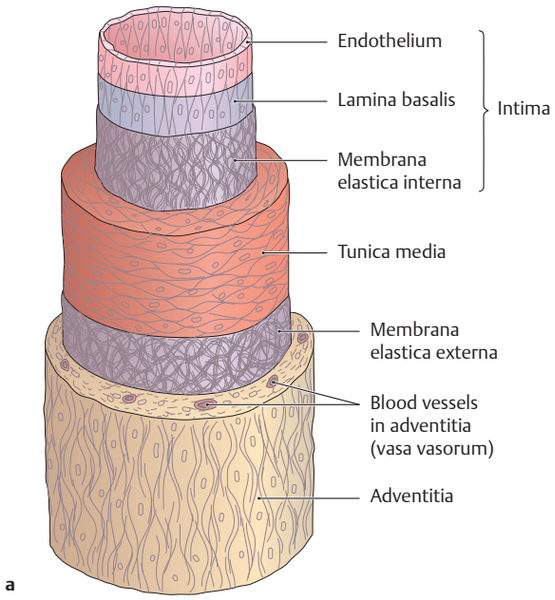
- the systemic circulation (high-pressure system, average blood pressure of 100mmHg in the major arteries) and
- the pulmonary circulation (low-pressure system, average blood pressure of 12mmHg; the difference in pressure from the systemic circulation is almost a factor of 10).

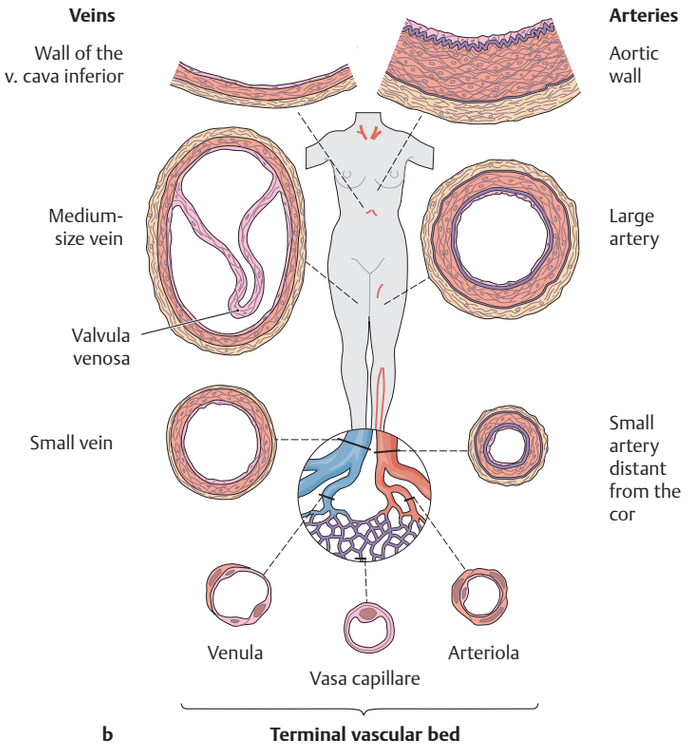
Regarding the vessels and pump, both circulatory systems can be divided into four parts:

- arteriae (aa.) and arteriolae: they lead away from the heart and distribute blood to the organs
- capillaries: they connect arterioles to venules and enable the exchange of substances in organs
- venulae and venae (vv.): receive blood from the capillaries and carry it back to the cor
- cor: functions as a circulation pump and transports the blood back to the arteriae

The **lymphatic system** is an additional vascular system that carries fluid away from the organs. It begins with lymphatic capillaries (vasa lymphocapillaria) in the organs and transports lymph back to the venous system.

Note: Whether to refer to a vessel as an artery or vein depends on the direction of blood flow, not on blood oxygen level. Arteriae carry blood away from the heart, and venae carry blood toward the heart. Hence, in the diagram, the a. pulmonaria contains oxygen-low blood (blue), while the v. pulmonaria contains oxygen-rich blood (red).





B Basic wall structure of large blood vessels

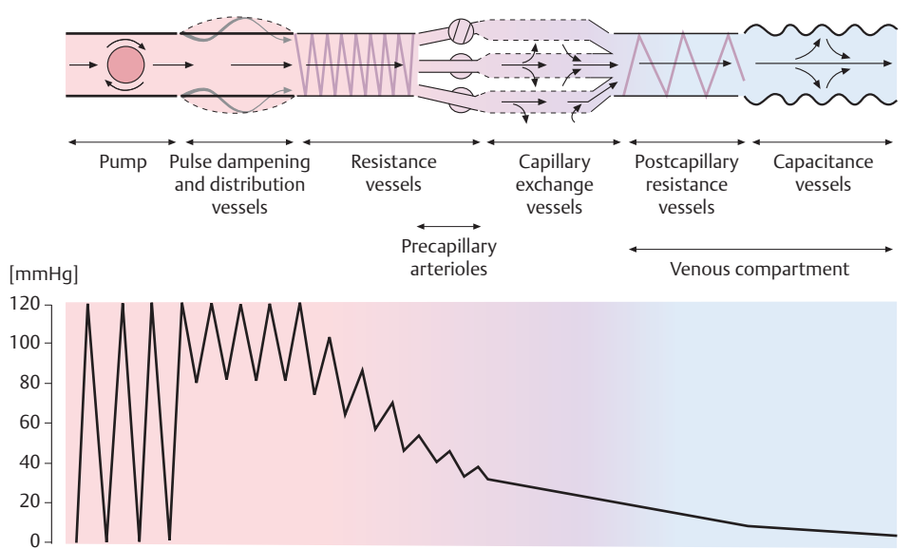
a The major blood vessels (arteries and veins) generally consist of three layers:

- The tunica intima (intima): an endothelium consisting of a single layer of squamous epithelial cells, with the cells elongated in the direction of blood flow, and a thin layer of subendothelial connective tissue
- The tunica media (media): consisting of a circular arrangement of smooth muscle cells, and elastic fibers of the internal elastic membrane (which separates the intima from the media) and external elastic membrane (which separates the media from the adventitia)
- The tunica adventitia (adventitia): consisting mainly of loose connective tissue, which integrates the blood vessel into its surroundings and allows for movement of vessels with organ movements. It can contain blood and lymphatic vessels as well as nerves.

b While veins have a similar three-layered structure as arteries, they have fewer and less dense layers of smooth muscle cells, giving the media of veins a looser structure. These structural characteristics are the result of lower venous blood pressure compared to arterial blood pressure. The peripheral veins in limbs contain valves to help direct blood flow back to the cor. The small exchange vessels, the capillaries, have no muscle tissue and consist only of endothelium and basement membrane.

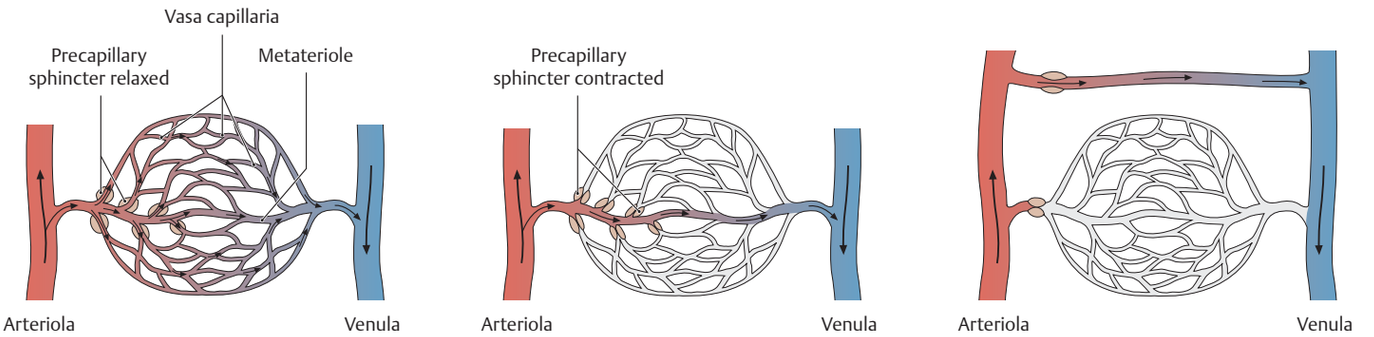
C Blood pressure in different regions of the cardiovascular system

The function and structure of the cardiovascular system are closely interconnected, as higher blood pressure leads to the thickening of blood vessel walls and lower blood pressure allows walls to thin. Thus, knowledge of blood pressures is important when interpreting morphology. In the cor and major arteries closest to the cor, blood pressure fluctuates substantially with each cardiac cycle. While blood pressure in the ventriculus sinister reaches 120 mmHg during systole, during diastole it drops to 0 mmHg. Due to the vessel wall properties of the arteriae close to the heart, blood pressure fluctuations in them during the cardiac cycle are less extreme. Resistance vessels further help regulation so that capillary pressure remains constant. Pressure is lowest in the central veins closest to the heart. Because of their thin walls, they can expand and store blood.



Note: The different regions of the vascular system are assigned specific functions, which are described in the illustration above.

2.2 Terminal Vessels and Overview of the Major Blood Vessels



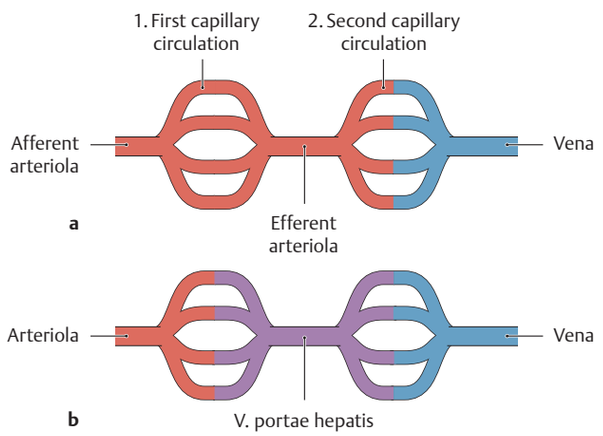
A Terminal vessels

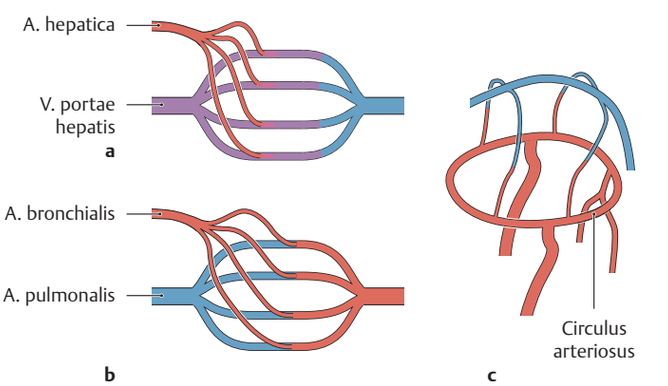
a The primary function of the arteries and veins is to transport blood. Terminal vessels are concerned with the exchange of substances between blood and tissue. This is often called the *microcirculation.* The terminal vascular bed consists of

- Arteriolae
- Capillaries
- Venulae

b It is important to point out that capillary perfusion can vary within organs. Precapillary sphincters, which consist of smooth muscle cells, help to regulate perfusion in *one* capillary. Terminal vessel perfusion within a specific organ is related to the organ's function and varies from organ to organ.

c Additionally, arteriovenous anastomoses help regulate the circulation in a group of neighboring capillaries that have formed one functional unit. Thus, entire capillary beds can be shut down.
Disruption of the fine regulation of the microcirculation is a major problem when patients go into shock because blood can pool in capillaries.





B Vascular relationships

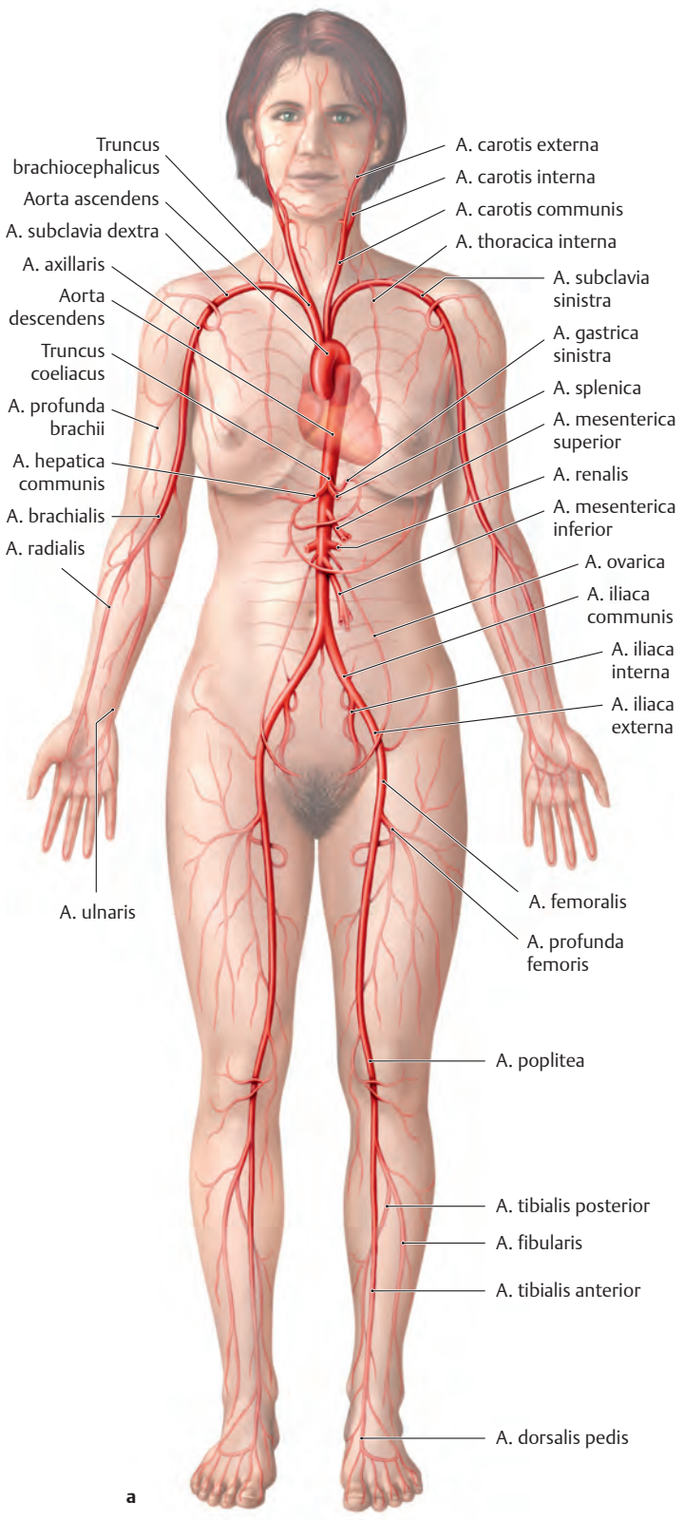
In addition to the above mentioned descriptions of typical organ circulation: artery – capillary – vein, there are additional blood flow patterns in some organs.

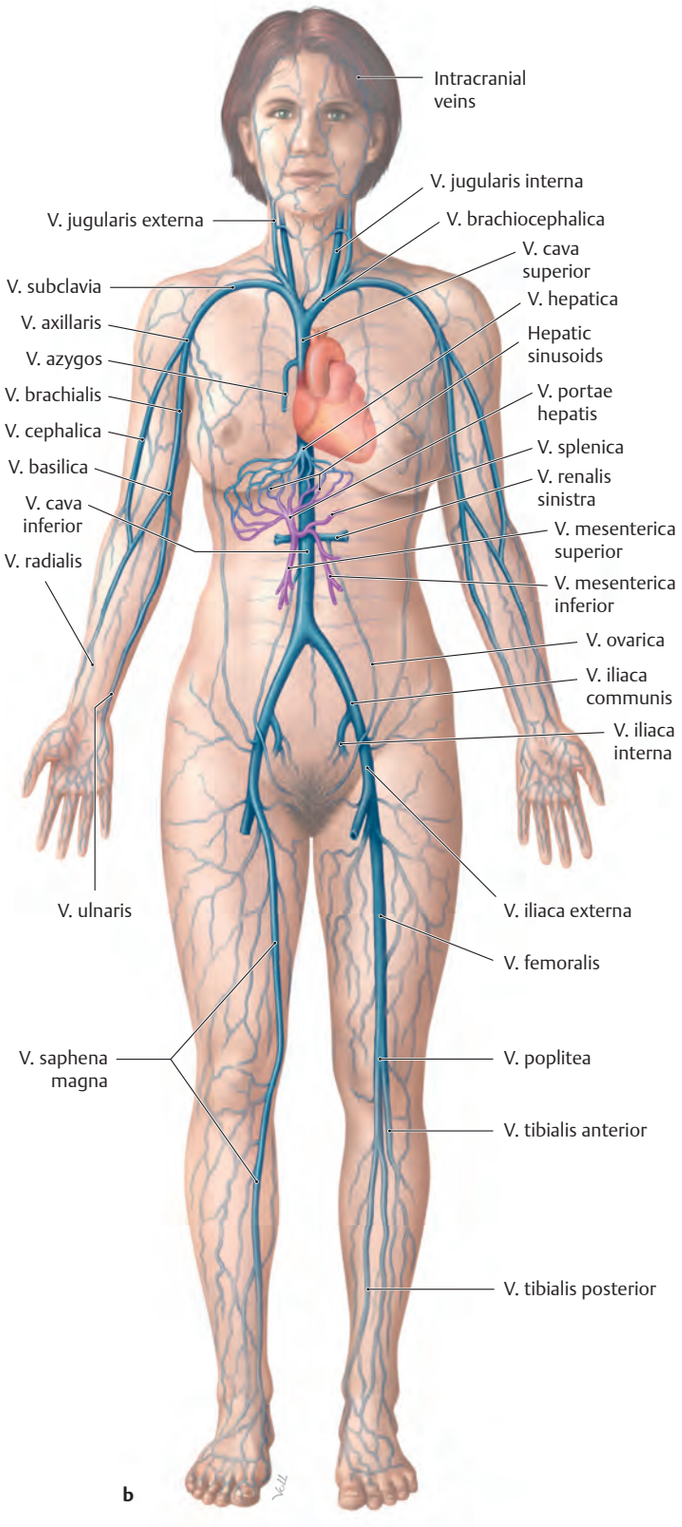
a Flow of arterial blood through two serially connected capillary beds: Two serially connected capillary beds are found in the ren (kidney) where arterial blood initially flows through the corpuscula renalia (glomeruli) and then into the capillaries of the medulla renalis.

b Flow through two venous circuits (portal venous system): Venous blood flowing through two serially connected capillary beds is known as a portal venous system. For clarification, the blood in the first capillary bed is colored purple because it is not yet completely deoxygenated. Such a portal venous system exists in the digestive tract, where the v. portae hepatis collects the venous blood from the unpaired abdominal organs (gaster, intestina, splen). From there it flows to the capillaries of the hepar.

C Dual organ circulation

The **hepar (liver)** receives its blood supply from the a. hepatica propria and the v. portae hepatis (**a**). The vessel responsible for suppling oxygenated blood to the liver tissue is the a. hepatica propria. The vessel that contains the blood with the substances to be metabolized in the liver is the v. portae hepatis. The **pulmones** also have a dual arterial supply (**b**). Here, the aa. pulmonariae contain deoxygenated blood and the rr. bronchiales contain oxygenated blood. Another pattern of multiple blood supply can be found in the **encephalon**. Four arteriae form a closed ring (the circulus arteriosus cerebri, circle of Willis) from which other vessels supply the encephalon (**c**). All three forms of blood supply through multiple vessels allow for a certain degree of compensation in case one of the supplying vessels fails.





D Major blood vessels
This overview depicts the major arteriae (**a**) and venae (**b**) in the human body. In the following organ descriptions, knowledge of the major vascular trunks is assumed, and the smaller organ-supplying vessels will be discussed with the respective organs.

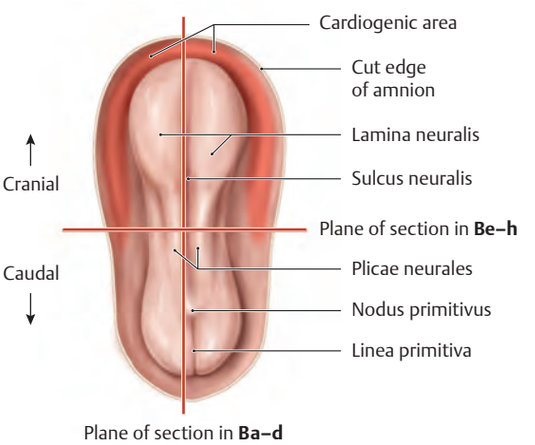
2.3 Cardiogenic Area, Development of the Heart Tube

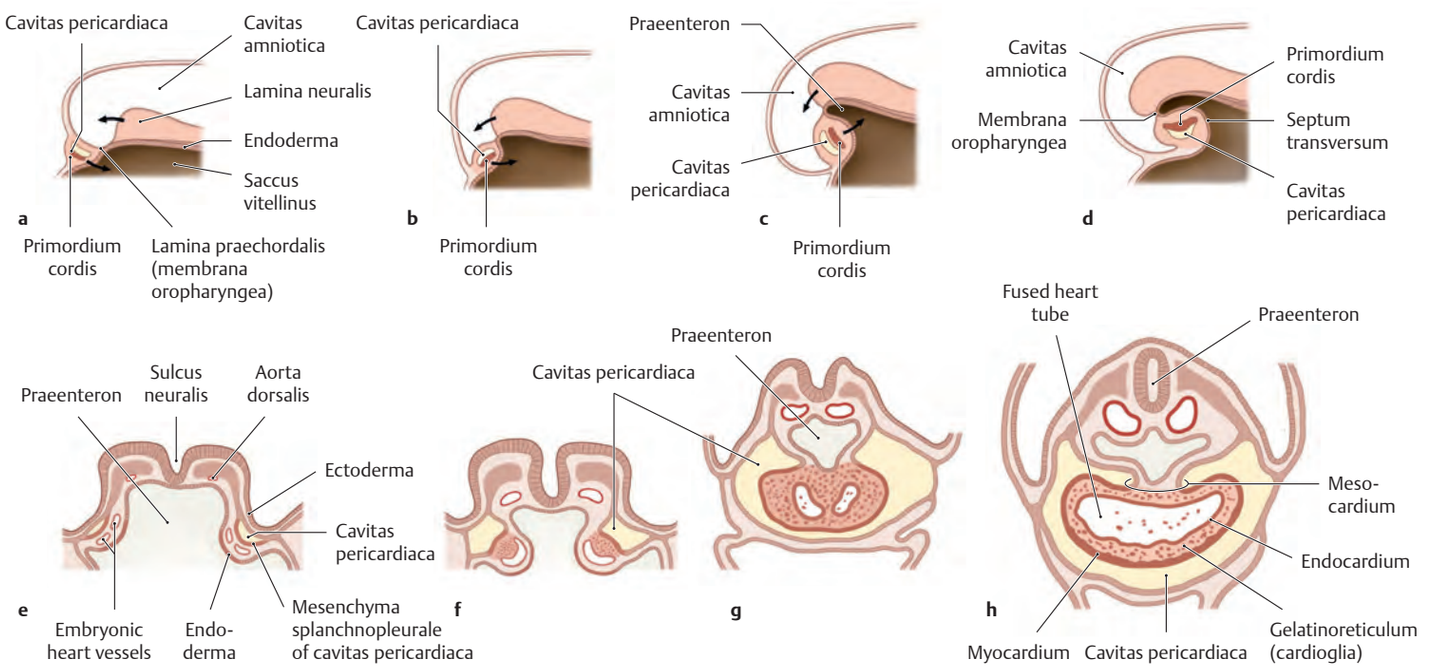
Characteristics

In many respects, the cardiovascular system is extraordinary. It is the first system to function in the human embryo; it is already functional by the end of the third week (first contractions of the primitive cor tubulare). Additionally, the cardiac loop (see below) is the body's first asymmetrical structure. Since the human embryo is poorly supplied with yolk, which ensures nutrition by diffusion for a limited time only, it depends on extraembryonic circulation from a very early stage. While the saccus vitellinus circulation appears earlier, it is the placental circulation that ultimately provides nutrients and removes waste over the course of embryonic and fetal development (see **D**).

A Origins of the cardiac tissue (cardiogenic area)

Dorsal view of the discus embryonicus from the cavitas amniotica. During the third week of development (presomite stage), the mesenchyma cardiogenicum, from which the cor develops, forms a horseshoe-shaped area (campus cordis primus) that consists of a thickened layer of mesenchymal cells. It lies anterolateral to the lamina neuralis. At this stage in development, the mesenchyme is still located under the similarly horseshoe-shaped intraembryonic cavitas coelomica. The campus cordis primus is composed of mesenchyma splanchnopleurale (the layer of mesoderma laminae lateralis facing the viscera) and it borders the future cavitas pericardiaca (see **Be**). During craniocaudal and lateral embryonic folding, the campus cordis primus, which originally lies in the anterolateral portion of the discus embryonicus, moves ventrally under the developing praeenteron along with the adjacent coelomic cleft (see **Bc**).

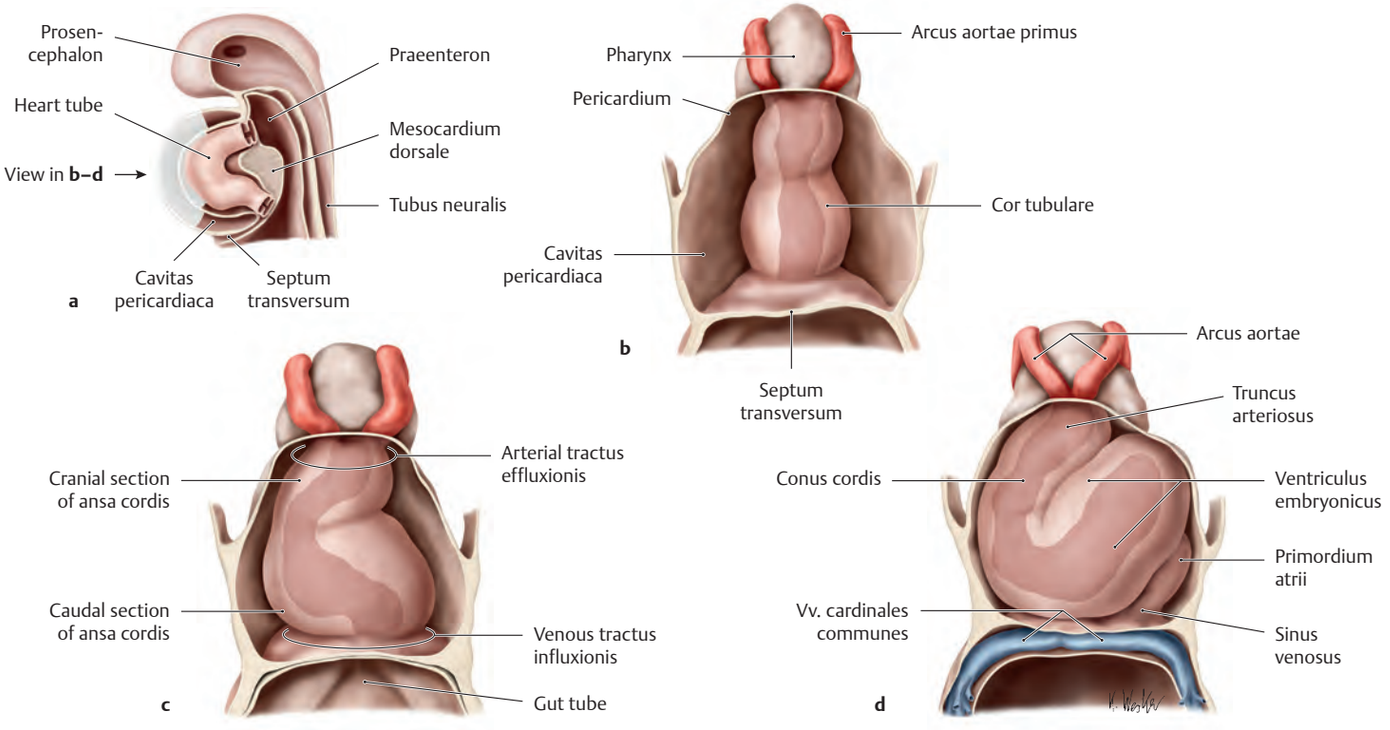




B Formation of the heart

a–**d** Sagittal sections; **e**–**h** Cross-sections (21–23 days / 4–12 somites); Lateral (**a**–**d**) and rostral (**e**–**h**) views; For location of the respective plane of section see **A**.

As a result of craniocaudal folding (**a**–**d**) the primordium cordis and the adjacent cavitas pericardiaca rotate 180 degrees and move under the praeenteron (descent of the heart). The lamina praechordalis (the future site of the cavitas oris), which previously was located caudally, is now rostral to the developing cor. The septum transversum (future centrum tendineum of the diaphragma) also moves caudally under the cor and cavitas pericardiaca. During the slightly delayed process of lateral folding (**e**–**h**) the initially paired primordia cordis fuse to form the unpaired cor tubulare (**h**). During this fusion, endothelial-lined embryonic vessels (endocardial tubes) that developed from angioblasts in the cardiogenic area fuse to form a single cavity in the cor tubulare. After fusing with the opposite side, the adjoining mesenchyma splanchnopleurale thickens and develops into cardiac muscle (myocardium). Between the endocardial and myocardial layers develops a basement membrane-like structure consisting of a gelantinous extracellular matrix (gelatinoreticulum). Thus, the fused embryonic heart tube consists of three layers—from inside to outside: endocardium, gelatinoreticulum, and myocardium. The visceral layer of the pericardium, the epicardium, develops from progenitor cells in the area around the sinus venosus, which then overgrow the myocardium.

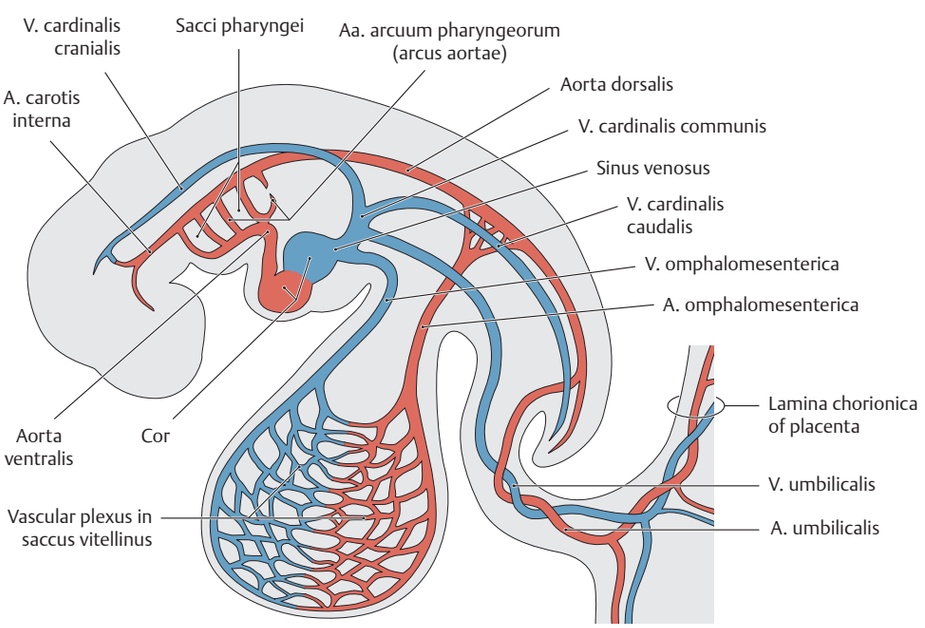


C Formation of the ansa cordis dextra

a Left lateral view; **b**–**d** Anterior view (with the cavitas pericardiaca opened).

During cranial embryonic folding, the developing cor and cavitas pericardiaca shift in a ventral and caudal direction. With the start of the fourth week, the cor tubulare elongates and curves to form the ansa cordis, which at this stage is attached by a mesocardium dorsale to the posterior wall of the cavitas pericardiaca. Over the course of development, this connection regresses (allowing formation of the sinus transversus pericardii), so that only the tractus influxionis (venosus) and effluxionis (arteriosus) attach the cor tubulare to the pericardium (see **c**). During formation of the ansa cordis, the cranial portion of the cor tubulare shifts ventrocaudally and to the right, while the caudal portion moves dorsocranially and to the left (**d**). Thus, the tractus influxionis lies dorsal and the tractus effluxionis ventral. At the same time, the ansa cordis dextra subdivides into multiple portions as a result of constriction and expansion, forming the following regions:

- truncus arteriosus
- conus cordis
- ventriculus embryonicus
- primordium atrii
- sinus venosus



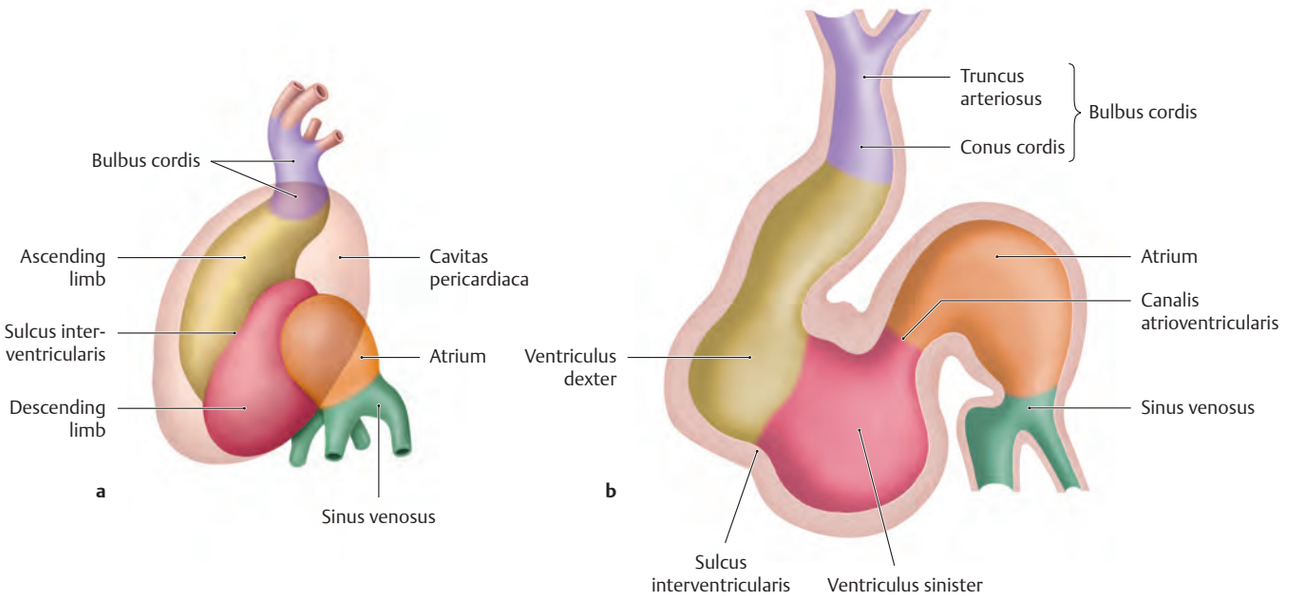
D Early embryonic circulation (after Drews)

Lateral view. The cardiovascular system of a 3 to 4 week old embryo consists of a contractile muscular cor tubulare and three distinct circulatory systems:

- An **intraembryonic systemic circulation** (aorta ascendens and aorta dorsalis, aa. arcuum pharyngeorum and arcus aortae, vv. praecardinales and postcardinales)
- An **extraembryonic vitelline circulation** (aa. and vv. omphalomesentericae)
- A **placental circulation** (aa. and vv. umbilicales).

Deoxygenated blood in the six major venous trunks (two vv. vitellinae or omphalomesentericae, two vv. umbilicales, and two vv. cardinales communes) flows into a common, venous cavity close to the heart called the sinus venosus. It then flows through the cor tubularis and out the aortae dorsales pares to enter the systemic circulation, saccus vitellinus or placenta (for development of the sinus venosus see p. 17).

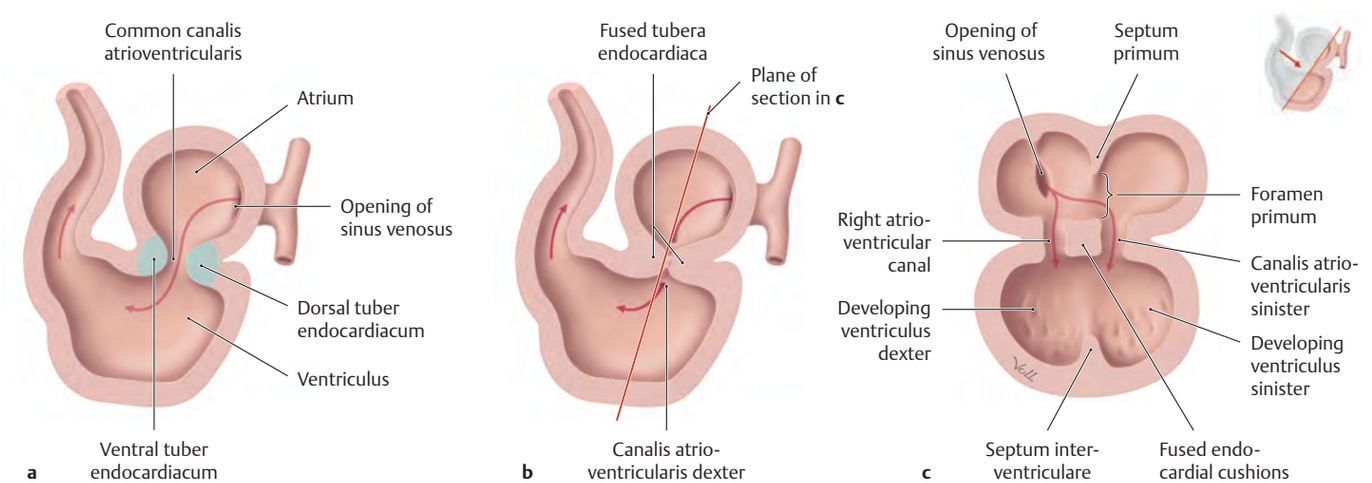
2.4 Development of the Inner Chambers of the Heart and Fate of the Sinus Venosus



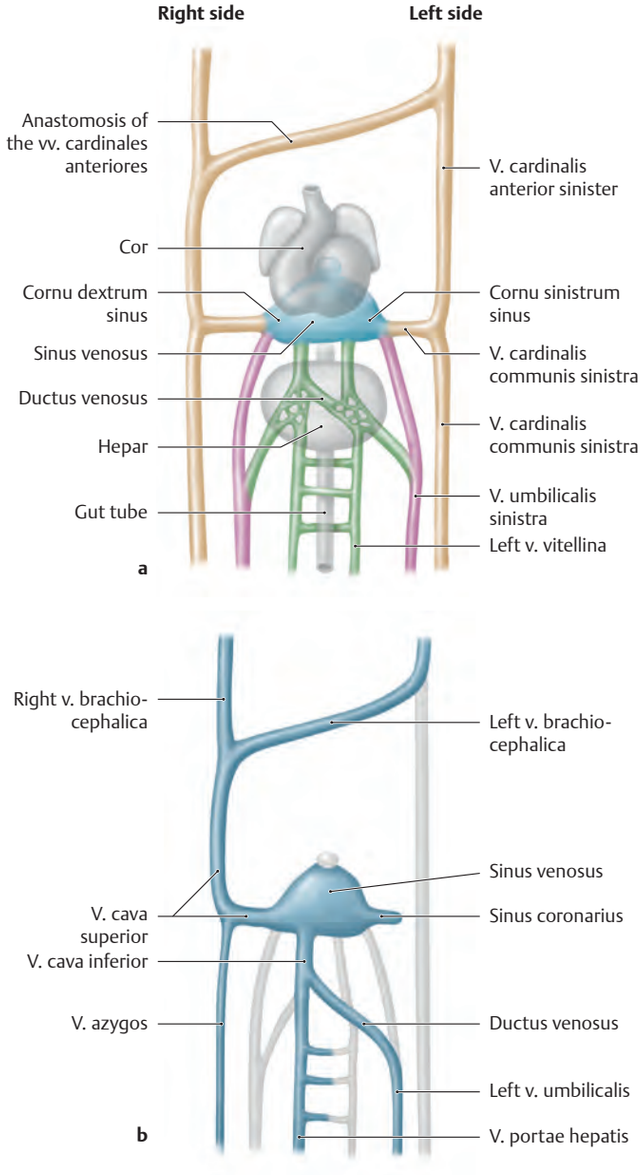
A The ansa cordis and the parts of the cor that develop from it
a Ansa cordis, left lateral view; **b** Sagittal section of the ansa cordis.
By the end of the 3rd or beginning of the 4th week, the precursors of the definitive parts of the cor are clearly visible:

- The bulbus cordis (truncus arteriosus and conus cordis) differentiates into the smooth-walled tractus effluxionis of the ventriculi sinister and dexter as well as the proximal portion of the aorta ascendens and truncus pulmonalis.
- The ascending limb of the ansa cordis forms the ventriculus dexter.
- The descending limb of the ansa cordis forms the ventriculus sinister.
- The sulcus interventricularis marks the boundary between the definitive ventriculi sinister and dexter.
- The future valvae atrioventriculares will form at the level of the canalis atrioventricularis.

Between the 27th and 37th day of development, a complex series of steps occurs in the ansa cordis to form septa in the atrium, ventriculus and tractus effluxionis (see p. 18) to divide the cor into right and left sides.



B Formation of the tubera endocardiaca and development of the cor's internal chambers
a and **b** Sagittal section of the ansa cordis; **c** Anterior view at the level of the tubera endocardiaca (for plane of section see **b**).
During the 4th week, the cor tubulare narrows at the junction of the atrium, ventriculus and canalis atrioventricularis (AV canal). This narrowing is a result of the formation of dorsal and ventral tubera endocardiaca. These are thickened areas of mesenchyma that develop in the region of the gelatinoreticulum. The tubera fuse, and with continued development divide the AV canal into right and left sides (right and left canales atrioventriculares). Later, the fused tubera endocardiaca give rise to the valvae atrioventriculares (valvae tricuspidalis and mitralis), which separate the atria from the ventriculi. Simultaneously, the atrium begins to separate into two chambers (see p.18).

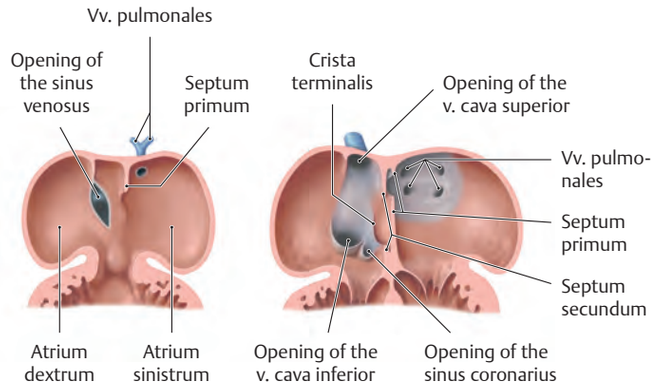


C Fate of the sinus venosus and the veins opening into it

a 4th week; **b** 3rd month; ventral view.

By the beginning of the 4th week, the sinus venosus is a separate part of the heart at the opening of the venous tractus influxionis. It opens into the still undivided atrium. Three large paired veins open into each side of the atrium through the cornua sinistrum and dextrum of the sinus venosus. These are the vv. vitellinae, vv. umbilicales, and vv. cardinales communes. Through two *left-right circuits* (see below), the tractus influxionis increasingly shifts to the right side of the body. On the left side, the majority of these veins disappear (see **E**):

1. **Left-right circuit:** Blood flowing from the placenta passes through the v. umbilicalis sinistra and ductus venosus and enters the hepar on the right side. From there it passes through the proximal portion of the right *v. vitellina* (future v. cava inferior) and then to the cornu dextrum sinus.
2. **Left-right circuit:** Both of the vv. praecardinales become connected by an anastomosis. Blood flowing through the systemic circulation enters the cornu dextrum sinus through the right *v. cardinalis communis* (future v. cava superior). The cornu dextrum sinus enlarges and is gradually incorporated into the right atrial wall (**b**). The *cornu sinistrum sinus,* however, increasingly regresses and forms the sinus coronarius.



D Transformation of the atria

The separation of the common atrium into atria sinistrum and dextrum begins in the 5th week with the formation of the septum primum (see p. 18). Around the same time the chambers of the atria enlarge by incorporating venous wall tissue. On the right side, parts of the cornu dextrum sinus are incorporated into the atrial wall. On the left side, a large part of the atrium sinistrum develops by incorporating the primitive vv. pulmonales. The origins of the parts of the atria are still detectable in the mature heart:

- The partes leves atriorum developed from venous wall tissue (sinus venosus, vv. pulmonales)
- The partes trabeculatae atriorum (mainly the auriculae sinistra and dextra) developed from the former common atrium

In the atrium dextrum, the border between the partes levis and trabeculata is demarcated by a vertical ridge, the crista terminalis. Its cranial portion is the former valva venosa dextra; its caudal portion is the valvulae venae cavae inferioris and sinus coronarii.

E Transformation of the sinus venosus and veins opening into it by the end of the 4th week (see also Cb)

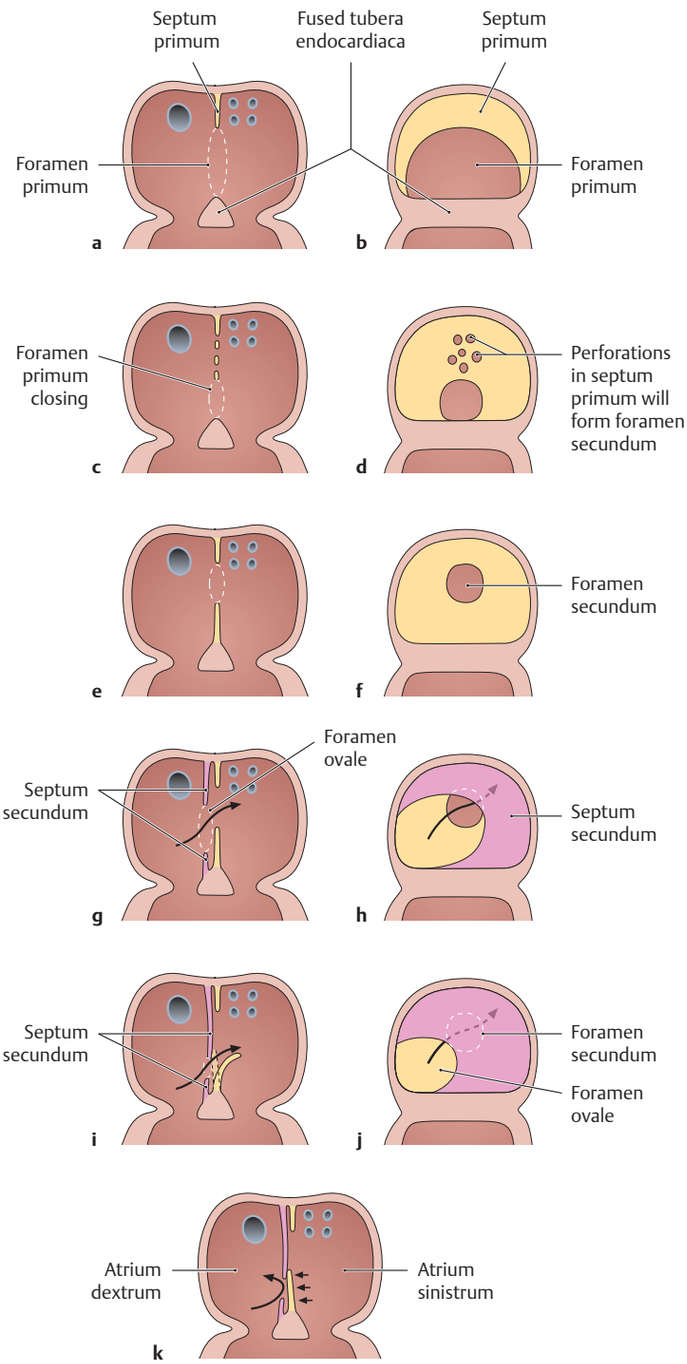
Sinus venosus and veins opening into it through the 4th week	Structures that remain on the right side of the body after the 4th week	Structures that remain on the left side of the body after the 4th week
Cornua dextrum and sinistrum sinus	Pars levis atrii dextri	Sinus coronarius
Vv. cardinales communes dextra and sinistra	Right vein develops into part of the v. cava superior	Left vein becomes part of the sinus coronarius
Vv. praecardinales dextra and sinistra	Right vein also develops into part of the v. cava superior	Left vein regresses
Right and left posterior cardinal veins	Right vein develops into the v. azygos	Left vein regresses
Vv. umbilicales dextra and sinistra	Right vein regresses	Left distal portion remains until birth
Vv. vitellinae dextra and sinistra	• Proximal portion of the right vein develops into part of the v. cava inferior • Distal portion of the right vein develops into the v. portae hepatis	Left vein regresses

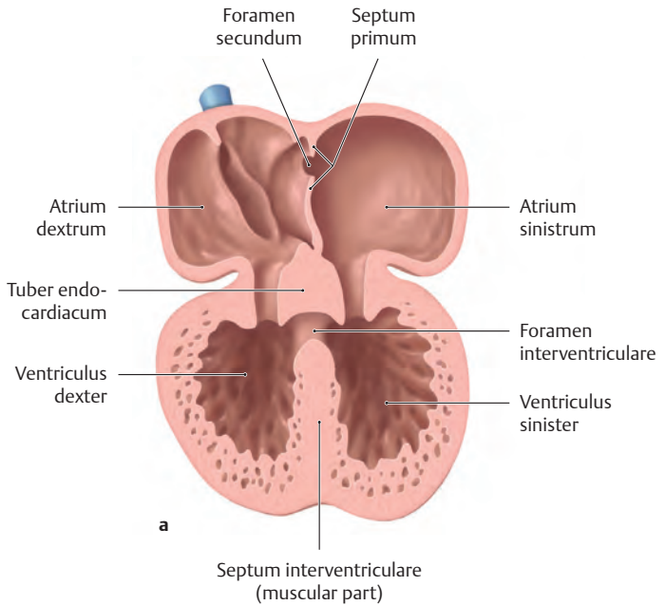
2.5 Cardiac Septation (Formation of Septa Interatriale, Interventriculare, and Aorticopulmonale)

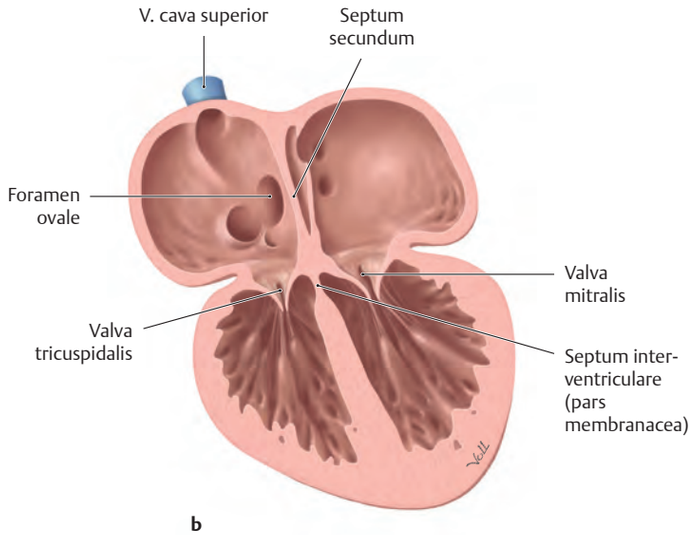
Development of cardiac septa—the basics
Cardiac septation begins at the end of the 4th week and is completed over the next three weeks. Over this period, the embryo grows in length from 5 mm to 17 mm. As a result of the development of the various cardiac septa, the cor tubulare separates into two sides with a circuit for the left heart and another for the right heart. The two circuits are completely separated from one another at the time of birth with the closure of the foramen ovale (see p. 20). This closure is due in part to increased blood flow to the infant's lungs and the resulting decrease in pressure in the right heart circuit.
Note: Septation defects play a key role in many heart malformations (eg. atrial and ventricular septal defects, transposition of large vessels, tetralogy of Fallot, see p. 21). The incidence rate of heart malformations among newborns is 7.5/1000 making them the most frequent congenital diseases. In Germany, 6000 children are born with a heart defect every year.

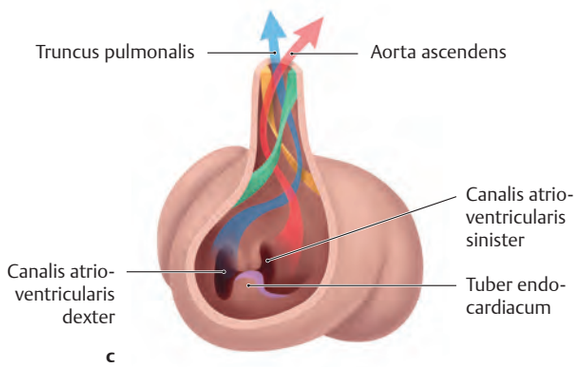
A Atrial septation (formation of the atrial septum)
a, c, e, g, i, k Frontal sections, ventral view; **b, d, f, h, j** Sagittal section, viewed from the right side.

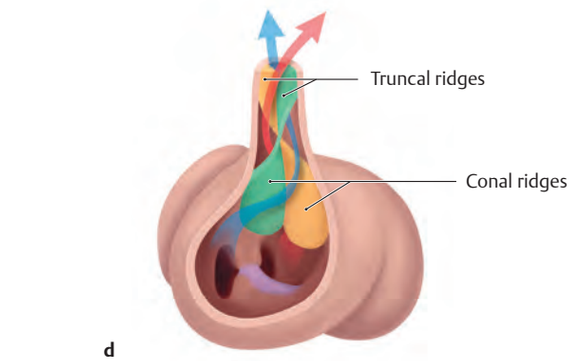
Septum primum and foramen secundum: After the 4th week the common atrium gradually gets divided into two chambers. From the roof of the still undivided atrium, the crescent-shaped *septum primum* grows and extends toward the already fused tubera endocardiaca of the canalis atrioventricularis (**a** and **b**). Between the margin of the septum and the tuber endocardiacum remains an opening, the *foramen primum*. It becomes progressively smaller and finally disappears as the septum primum continues to grow. At the same time, perforations produced by apoptosis appear in the central part of the septum primum. The perforations coalesce to form a new, large opening between the two atria, the *foramen secundum* (**c** and **d**). From now until birth, this new opening ensures continuous flow of oxygenated blood from the atrium dextrum to the atrium sinistrum.
Septum secundum and foramen ovale: By the end of the 5th week, a second crescent-shaped septum called the septum secundum grows from the ventrocranial wall of the atrium dextrum toward the fused tubera endocardiaca (**g** and **h**). The *septum secundum* does not completely reach the tubera endocardiaca and an opening, the *foramen ovale*, remains in the septum. The extending septum secundum progressively overgrows the *foramen secundum* in the *septum primum* (**i** and **j**). However, blood can continue to flow from the atrium dextrum to the atrium sinistrum due to differing blood pressures in the two sides. Before birth, pressure in the atrium dextrum is higher than in the atrium sinistrum and blood entering the atrium dextrum from the v. cava inferior passes into the atrium sinistrum. This is because the blood pressure is sufficient to push the septum primum aside and open it like a door. In this way, blood can pass through the foramen ovale, into the gap between the septum secundum and septum primum, and through the foramen secundum to enter the atrium sinistrum (**i** and **j**).
Closure of the foramen ovale and the definitive separation of the atria: Due to changes in the pulmonary circulation at birth, blood pressure in the atrium sinistrum increases. As a result, the septum primum is pushed against the septum secundum. The foramen ovale closes and the two atria are separate from one another (**k**). The septum primum forms the future fossa ovalis, and the free edge of the septum secundum develops into the limbus (border) of the fossa ovalis. Once these two septa fuse the foramen ovale remains permanently closed.
Note: Failure of the septa to fuse results in the foramen ovale remaining open (patent foramen ovale [PFO]). However, this is of little significance due to the pressure differences in the atria (see p. 21). The higher pressure in the atrium sinistrum pushes the septum primum firmly against the septum secundum.

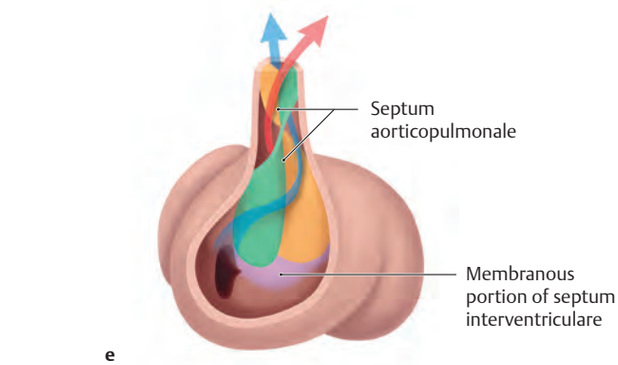












B Septation of the ventriculi and the tractus effluxionis (formation of the septa interventriculare and aorticopulmonale)
(after Sadler)

Ventricular septation also begins by the end of the 4th week with the formation of a myocardial wall between the ascending and descending limbs of the ansa cordis.

Ventricular septation (a and b): A crescent-shaped muscular ridge called the pars muscularis of the *septum interventriculare* develops from the wall of the ventriculus and projects into the ventricular lumen. With continued development, its two limbs fuse with the tubera endocardiaca of the canalis atrioventricularis (however, the bottom of the crescent-shaped ridge does not fuse with the tubera). The remaining opening between the two ventriculi is called the *foramen interventriculare*. In the 7th week, it is completely closed by the *pars membranacea* of the septum interventriculare, which comes from the tubera endocardiaca and the proximal end of the conal ridges (see below).

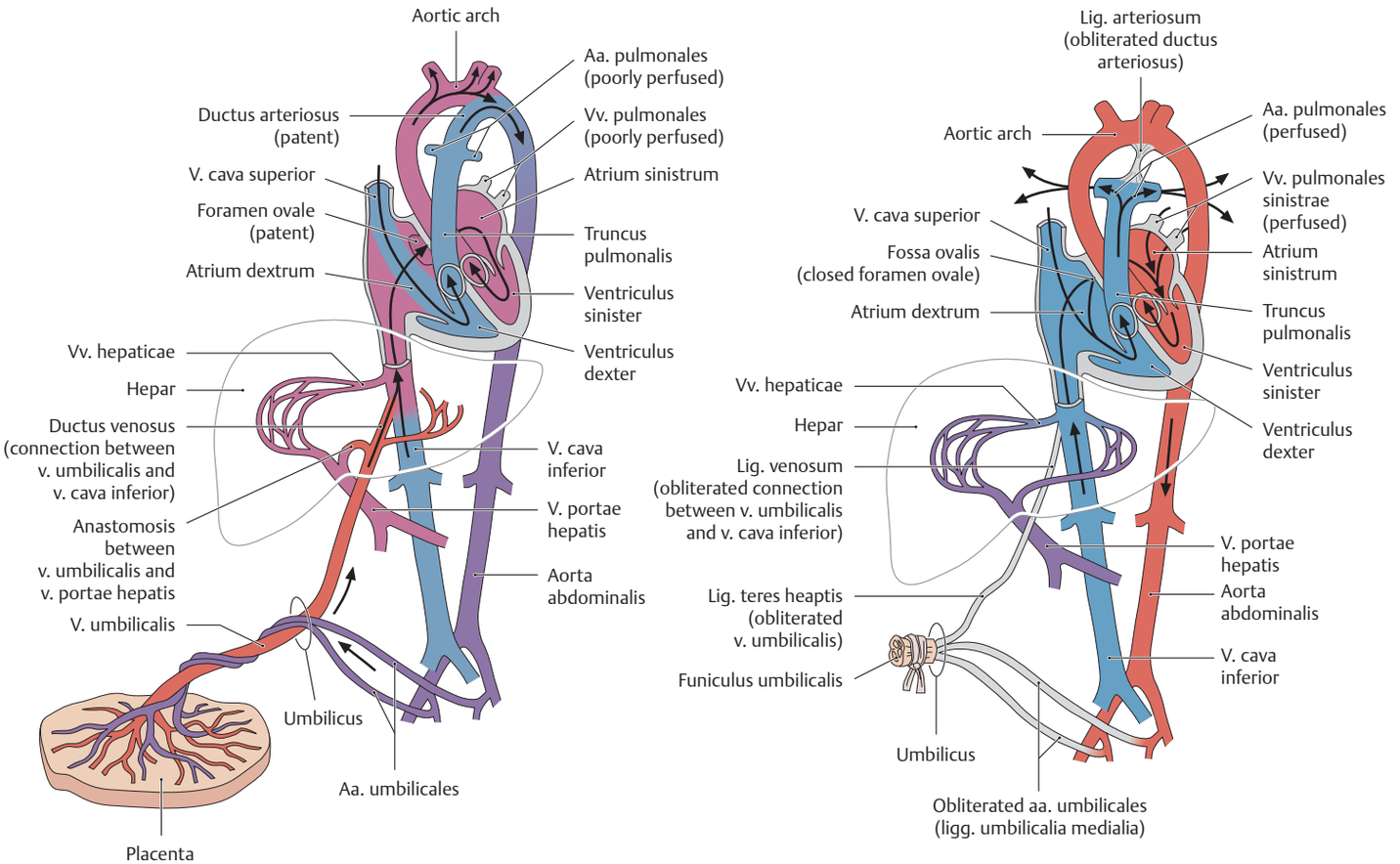
Outflow tract septation (c–e): While the septum interventriculare forms, the common tractus effluxionis of both ventriculi (bulbus cordis) begins to differentiate into the aorta ascendens and *truncus pulmonalis*. This is the result of the formation of two opposite longitudinal ridges in the lower (conus cordis) and upper (truncus arteriosus) parts of the tractus effluxionis. These conal and truncal ridges develop through increased proliferation of mesenchyma. Their progenitor cells migrated from cranial crista neuralis cells in the arcus pharyngei.

Note: Crista neuralis cells give rise to most of the peripheral nervous system, but also contribute to cardiovascular development. Thus, cranial crista neuralis cells are of central importance for the normal development of the cardiac tractus effluxionis.

Over the course of septum formation, the conal and truncal ridges complete a rotation of 180 degrees. This pattern of fusion leads to the formation of the spiral-shaped *septum aorticopulmonale*, which separates the common tractus effluxionis of the two ventriculi.

Heart valve formation: Formation of the valvae aortae and trunci pulmonalis is related to formation of the *septum aorticopulmonalis*. The valves develop from three subendocardial ridges (tubera endocardiaca) located at the junction of the conus cordis and truncus arteriosus (thus at the root of the aorta and truncus pulmonalis).

2.6 Pre- and Postnatal Circulation and Common Congenital Heart Defects



A Prenatal circulation (after Fritsch and Kühnel)
The prenatal circulation is characterized by the following:

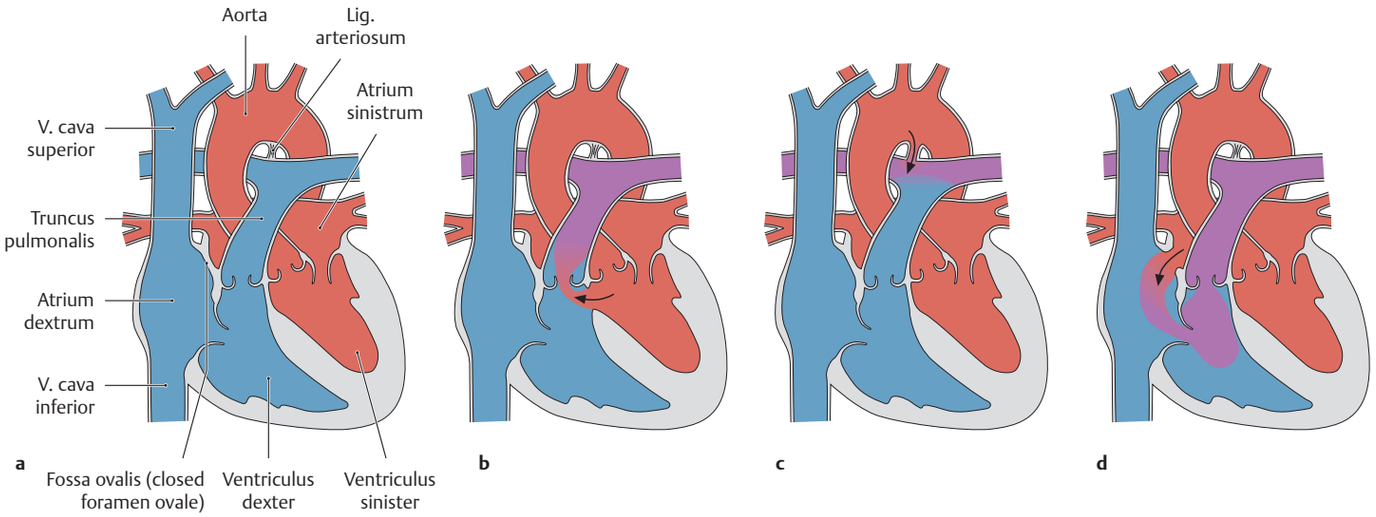
- Very little pulmonary blood flow
- Gas exchange in the placenta
- Delivery of oxygen and nutrients to the fetus through the placenta
- A right-to-left shunt in the heart

The fetal **lungs** have not yet expanded, are not aerated and have minimal blood flow. Consequently exchange of O_2 and CO_2 takes place outside the fetus in the placenta. Oxygenated and nutrient-rich fetal blood from the placenta passes to the fetus through the unpaired v. umbilicalis. Near the liver, the v. umbilicalis empties into the v. cava inferior through the ductus venosus (a venovenous anastomosis). There, oxygen-rich blood (from the v. umbilicalis) mixes with oxygen-poor blood (from the v. cava inferior). At the same time, the v. umbilicalis passes nutrient-rich blood, via another venous anastomosis, to the v. portae hepatis which transports it to the hepar for metabolic processing.
Blood flow in the **cor** is characterized by a right-to-left shunt. Blood from both vv. cavae flows into the atrium dextra. Blood from the v. cava inferior passes into the atrium sinistra through the foramen ovale (see p. 18). Most of the blood from the v. cava superior passes through the atrium dextrum to the ventriculus dexter and then enters the truncus pulmonalis. However, it does not enter the unexpanded fetal lungs but passes via the ductus arteriosus (an arterioarterial anastomosis) into the aorta and then to peripheral fetal vessels. Blood returns to the placenta through the paired aa. umbilicales (branches of the aa. iliacae internae). Since the pulmonary circulation is greatly reduced, very little blood is returned to the atrium sinistrum through the vv. pulmonales.

B Postnatal circulation (after Fritsch and Kühnel)
At birth, gas exchange and blood flow undergo a radical change. The postnatal circulation is characterized by the following:

- Loss of the placental circulation
- Pulmonary respiration with pulmonary gas exchange
- Functional occlusion of the right-to-left shunt and all fetal anastomoses

When respiration begins, the lungs are expanded, aerated and become responsible for gas exchange. Vascular resistance in the expanded lungs drops abruptly. The sudden drop in blood pressure in the atrium dextrum (pressure in the atrium sinistrum is now higher than in the atrium dextrum) causes the foramen ovale to close (see p. 18). Contraction of vascular smooth muscle in the ductus arteriosus functionally closes that anastomosis. Later it closes completely by scarring and forms the lig. arteriosum. The ventriculus dexter pumps blood through the aa. pulmonales into the expanded lungs. Blood from the ventriculus sinister is distributed through the aorta to all body regions and returns to the atrium dextrum through the vv. cavae superior and inferior. Both sides of the heart are now hemodynamically separate. The v. umbilicalis is no longer perfused and the ductus venosus connecting it to the v. cava inferior occludes and eventually scars to form the lig. venosum. The v. umbilicalis also becomes occluded and fibrous over its entire length, forming the lig. teres hepatis. The proximal portions of the aa. umbilicales remain patent, while the distal portions become occluded and form the lig. umbilicale mediale on each side.



C Congenital heart defects

Heart defects are the most common birth defects (incidence in live-born infants is 7.5/1000). The factors are usually genetic (trisomy 21) or exogenous (e.g., virus infections/rubella, alcohol, medications, cytostatics, ionizing radiation).

Note: The cor is most sensitive to teratogen exposure between the 4th and 7th weeks, a time period in which a woman may not know yet that she is pregnant.

Thanks to enormous progress in diagnosis and therapy, more than 85% of children born today with congenital heart disease survive and reach adult age. Among the most common congenital heart defects are *acyanotic heart defects* (cyanosis: bluish discoloration of the skin/mucosae due to low oxygen saturation). They are ventricular septal defects (31%), atrial septal defects (10%) and patent ductus arteriosus (9%), in which a non-physiological connection exists between the left and right sides of the heart. Since blood always flows from high pressure to low pressure, and the left side of the heart has the higher pressure in postnatal circulation, the heart abnormalities described are characterized by an initial left-to-right shunt. The shunt leads to higher pressure in the right side of the heart. In response to the increased pressure, the walls of the ventriculus dexter and aa. pulmonales thicken which results in continuously increasing resistance and pressure in the pulmonary circulation (pulmonary hypertension). Over time the pressure in the pulmonary circulation becomes higher than the pressure in the systemic circulation, which leads to a shunt reversal (now right-to-left shunt [Eisenmenger reaction]) and decompensated right-sided failure. As less blood flows through the aa. pulmonales, the oxygen saturation decreases leading secondarily to cyanosis. During childhood, acyanotic heart defects are usually well tolerated and become symptomatic only later in life. If a patent ductus arteriosus is surgically closed (e.g., using an endoscopic catheter) before complications occur, life expectancy is normal.

a Normal postnatal heart: The foramen ovale closes, the ductus arteriosus atrophies, and systemic and pulmonary circulation are completely separated.

b Ventricular septal defect (VSD): VSDs are usually located in the pars membranacea of the septum interventriculare and arise from failure of fusion of the pars muscularis of the septum interventriculare with the proximal septum aorticopulmonale. As a result, the foramen interventriculare remains open, and with each contraction blood from the ventriculus sinister enters the ventriculus dexter. Ventricular septal defects are frequently associated with an asymmetric septation of the outflow tract such as a narrowed truncus pulmonalis (stenosis), an "overriding" aorta on the ventricular septum, and right ventricular hypertrophy caused by the pulmonary stenosis (*tetralogy of Fallot*, the most common cyanotic heart defect. An infant's mucous membranes, lips, and fingers have a bluish color because too little blood is pumped through the pulmonary circulation for adequate oxygenation).

c Patent ductus arteriosus (PDA): frequently occurs in premature infants (75% will spontaneously close within one week). Symptoms are the result of increased backflow of aortic blood into the truncus pulmonalis, which leads to volume overload on the pulmonary circulation (see above). If the ductus arteriosus is closed (e.g., using an endoscopic catheter), life expectancy is normal.

d Atrial septal defects (ASD): depending on location, these defects are subdivided into three types: primum atrial septal defects (ASD I), secundum atrial septal defects (ASD II) and sinus venosus atrial septal defects (SV). The most common type is the secundum atrial septal defect (75% of all cases), characterized by the excessive resorption of septum primum tissue at the site of the foramen ovale (foramen secundum is too large) or inadequate growth of the septum secundum (foramen secundum is not sufficiently covered, see p. 18). As a result, in postnatal circulation, blood flows from the atrium sinistrum to the atrium dextrum which, depending on the shunt volume, leads to volume overload in the pulmonary circulation. Significant symptoms can occur later in life once the shunt has reached a certain size. Thus, ASD II defects are corrected even though patients have not yet shown symptoms. Closure of secundum atrial septal defects is generally performed by using an interventional approach with a stent and a self-expanding double-umbrella device made of a nickel titanium alloy.

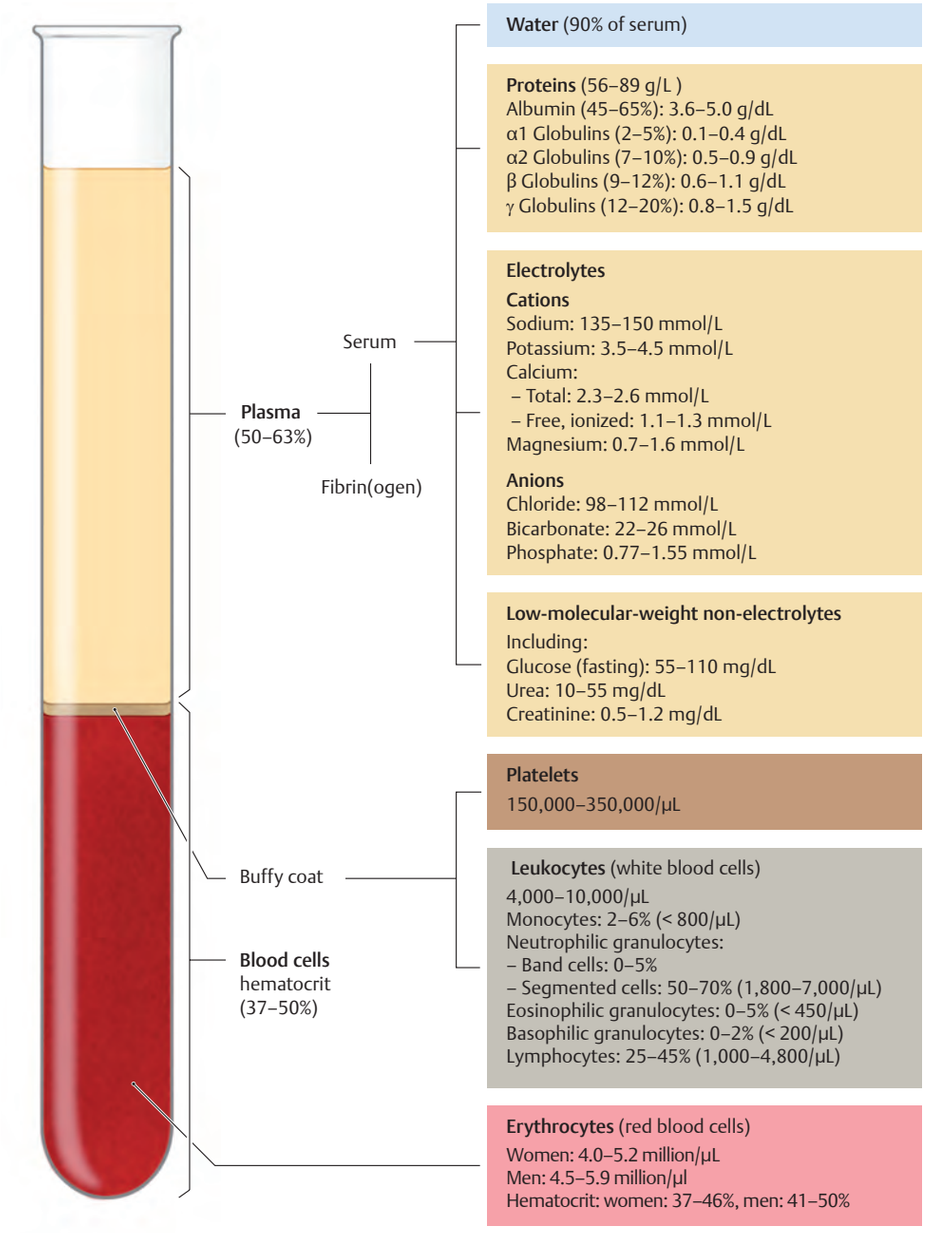
Note: Failure of the septum primum to fuse with the septum secundum after birth leads to an anatomically open (through which a probe could be passed) foramen ovale ("probe" patent foramen ovale [PFO]). Due to the valve mechanisms and the existing pressure differences, it is clinically insignificant (see p. 18) and thus is not a true heart defect but rather a normal variant (almost 30% of adults are affected). Pathological conditions, (e.g., resulting from an acute hemodynamically relevant pulmonary embolism) can lead to the formation of a right-to-left shunt. As a result, blood clots (thrombi), which are usually filtered out in the lungs, can enter the systemic circulation causing an ischemic stroke (a paradoxical or crossed embolism). Even smaller clots can be potentially life-threatening. Even routine activities (lifting heavy loads, coughing, etc.) can lead to quick changes in intrathoracic pressures so that a PFO can temporarily cause a right-to-left shunt.

3.1 Blood: Components

A Composition of blood

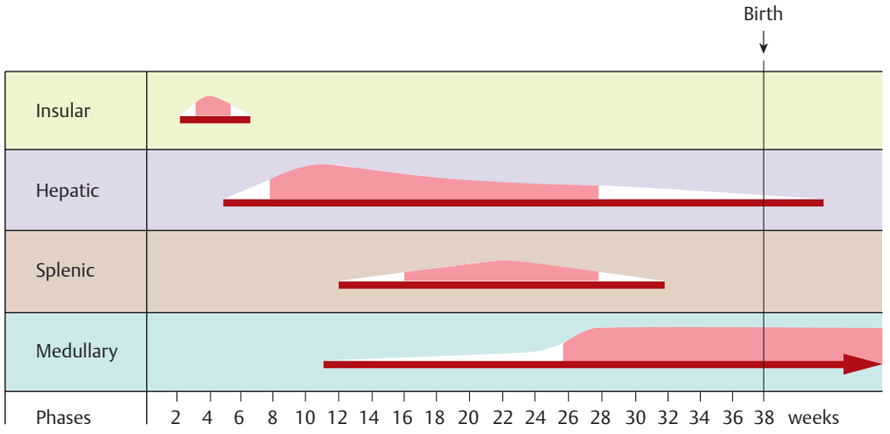
Blood is a unique tissue in that it is liquid. Yet like every other tissue it consists of an extracellular matrix (plasma) and cellular components (red and white blood cells as well as platelets). A transport and communication organ, it is contained within a closed vascular system that interconnects all organ systems. Its functions are accordingly diverse: transport of gases and substances, protection, thermoregulation, regulation of pH value, and coagulation. Coagulation prevents all of the blood from draining out of the cardiovascular system when its walls have been damaged.

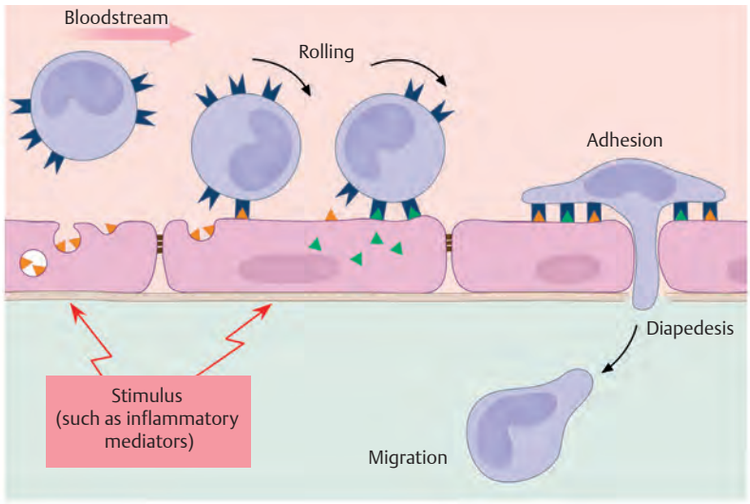
A protein-containing fluid (plasma) accounts for 50–63% of the blood volume; 37–50% is blood cells. The ratio of the volume of red blood cells to the total volume of blood is referred to as hematocrit. **Plasma** is obtained by centrifuging whole blood which has been prevented from coagulating by the addition of a substance such as heparin. **Serum** is obtained by initially allowing the blood to coagulate and then centrifuging it. Serum is thus plasma minus clotting factors. About 90% of plasma consists of water; the rest includes proteins, electrolytes, and low-molecular-weight substances of metabolism and metabolic regulation (hormones). Most plasma proteins are synthesized by the liver. Accounting for a full 99% of the hematocrit, the vast majority of **blood cells** (see p. 24) are the non-nucleated red blood cells. Their cytoplasm is filled with hemoglobin, which serves to transport oxygen and buffer the blood. The white blood cells have a protective function; the platelets promote blood coagulation. All blood cells come from stem cells of the red bone marrow (see p. 27) where they are constantly produced.



B Phases of blood formation during development

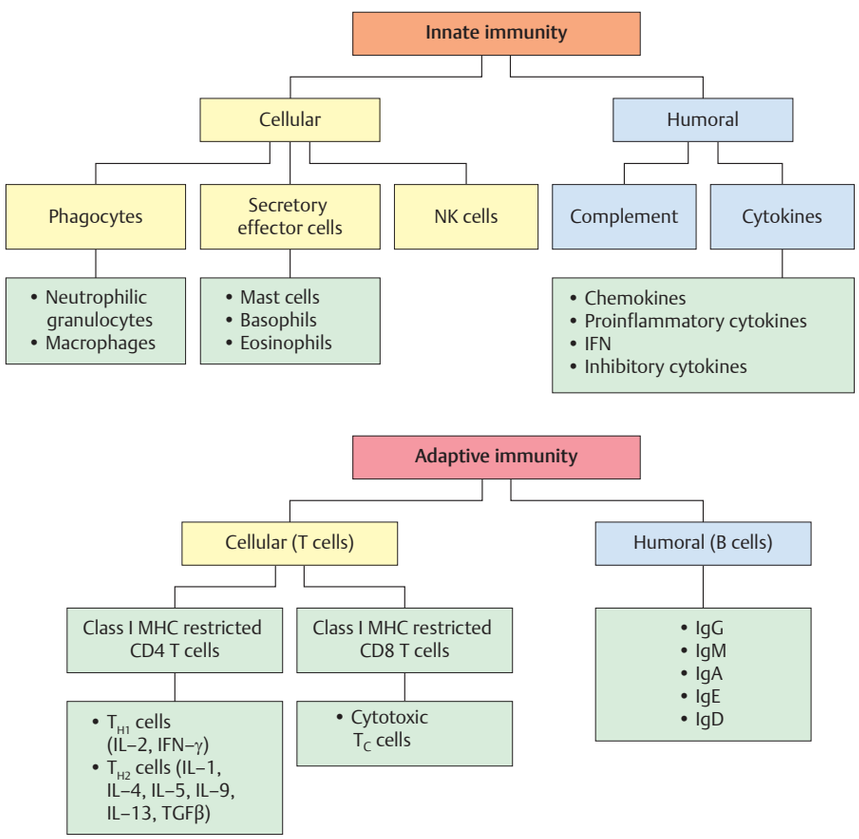
Blood is required before birth even prior to the development of red bone marrow. As a result, blood is initially formed elsewhere: in the yolk sac (insular), in the liver (hepatic), in the spleen (splenic), and finally in the secondary bone marrow (medullary). Malignant systemic diseases of the blood and the immune system "remember" these sites that provide favorable conditions for growth, and certain forms of these diseases then colonize the liver and spleen.





C Blood as a transport medium for blood cells

(modified from Lüllmann-Rauch, Thieme; 2012) White blood cells circulate through the blood and as a result are distributed throughout the body. They constantly migrate out of the blood stream and into the connective tissue of the organs where they attack bacteria or cancer cells. Migration (diapedesis) occurs via the leukocyte adhesion cascade. Upon receiving a stimulus, endothelial cells express cell adhesion molecules on their luminal surface. These molecules either come to the surface immediately through vesicles in the cytoplasm or they are synthesized in response. Ligands on the cell membrane of the leukocytes bind to these molecules. This binding (keying) causes the leukocytes to roll along the endothelium. Sometimes they come to a stop and sometimes they disconnect and rejoin the bloodstream. When they stop, the endothelial cells reduce their intercellular cohesion to allow the leukocytes to pass through the gap between them.



D Innate and adaptive immunity

As the blood has access to all organs, it plays an important role in the immune system in defending against infections and malignant cells. The immune system and the blood are thus tightly integrated. The innate immune system responds immediately to an appropriate stimulus and is nonspecific as it must respond to many possible attacks. Cellular components (cells are transported by the blood) and humoral components are differentiated. Humoral ("liquid") components include complement and cytokines in the blood. Adaptive immunity is specific and is directed toward a specific noxious agent such as a certain virus. The adaptive immune system includes T and B cells, which also circulate in the blood. T cells kill cancer cells or cells infected by viruses by direct contact (cellular immunity); B cells secrete various classes of antibodies (humoral immunity).

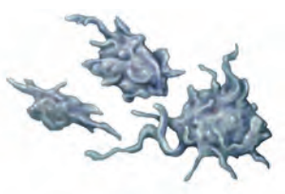
E Lifespan facts of certain blood cells

Type of cell	Retention time in blood	Lifetime in interstitium	Creation of new cells in bone marrow
Erythrocyte	120 days	—	About 8 days
Platelet	10 days unless consumed earlier	—	About 8 days
Neutrophilic granulocyte	< 1 day	1–2 days	About 8 days
Monocyte	About 1–3 days	Months (as a macrophage)	About 8 days

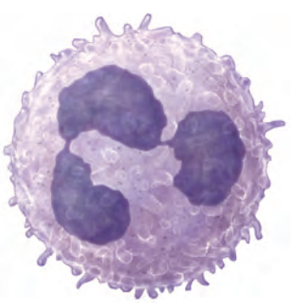
3.2 Blood: Cells

This unit discusses the cells of the blood that can be morphologically distinguished in a normal blood smear. The classic blood smear is colored with Pappenheim stain. Red and white blood cells as well as platelets are readily identifiable. See p. 22 for their normal values in blood.

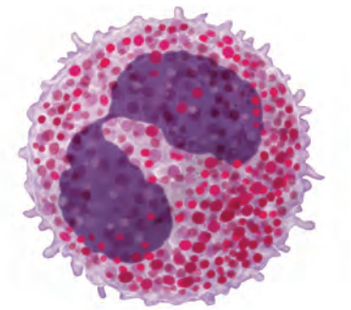
A Red blood cells (erythrocytes)
Erythrocytes (approx. 5 million/µL) are large, biconcave cells measuring about 7.5 µm in diameter. In mammals they contain no nucleus or cytoplasmic organelles. Their lack of organelles and their specially reinforced cell membrane allow erythrocytes to adapt particularly well to different flow characteristics in blood so that they can even squeeze through narrow capillaries. This adaptability allows them to survive in the blood about 120 days. After this, erythrocytes are eliminated by macrophages in the liver and spleen. Because they lack mitochondria, they must obtain their energy from anaerobic glycolysis. As a result they are dependent on glucose as a source of energy. Ninety-five percent of the interior of erythrocytes is filled with the protein hemoglobin, which binds O_2 and, to a lesser extent, CO_2. Erythrocytes are created in a series of morphologically distinct stages from a precursor cell containing a nucleus (see page 27). Reticulocytes represent the stage immediately preceding mature erythrocytes. They can be demonstrated with Cresyl violet stain. This stain binds to the RNA of the rough endoplasmic reticulum of erythrocytes, whose precursor cells ejected their nuclei 1–2 days previously and still contain residual traces of the endoplasmic reticulum. About 2.5 million reticulocytes leave the bone marrow per second. They mature into erythrocytes within a day. About 1% of erythrocytes are reticulocytes. As a result, reticulocytes are particularly suitable for monitoring erythropoiesis. When the number of reticulocytes increases, as can occur after acute bleeding, it is referred to as a reticulocyte crisis. This indicates that the bone marrow has responded to the blood loss by increasing the production of new erythrocytes. Here, the term crisis is used in a positive sense to indicate the regenerative output of the bone marrow.
Note: As the average diameter of erythrocytes is a reliably constant 7.5 µm, it can be used in histologic sections as an intrinsic scale for the size of a histologic structure.



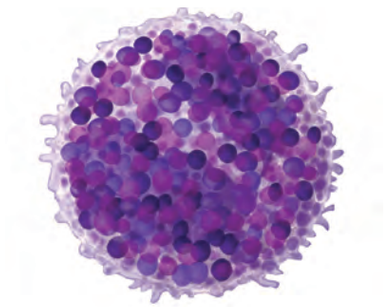
B Platelets (thrombocytes)
Platelets (about 250,000/µL) are non-nucleated fragments of megakaryocytes, multinuclear giant cells that reside in the bone marrow. They survive in blood for about 10 days after which they are phagocytized by macrophages in the liver and spleen, so new cells must be generated constantly. In flowing blood they assume the shape of a biconcave disk measuring 2.5 µm in diameter. Platelets are an essential component of blood coagulation. Increases, decreases, and anomalies of platelets can be diagnosed in blood smears. Below 30,000/µL fine capillary hemorrhaging known as petechial bleeding occurs. Below 10,000/µL life-threatening bleeding occurs. A change in the platelet count is a sensitive indicator of bone marrow function. A decreased platelet count can be an early indicator of worsening bone marrow function. Conversely, an increased platelet count can be an early indicator of increased bone marrow function.



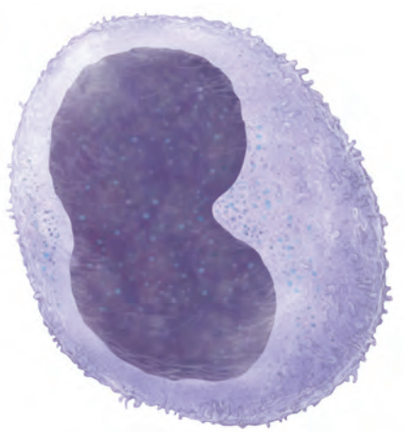
C Neutrophilic granulocytes
Neutrophils (the commonly used short form of neutrophilic granulocytes) represent the largest share of leukocytes in blood (4,000–10,000/µL), accounting for about 60%. A neutrophil measures 10–12 µm in diameter and remains in the blood for less than a day. It is characterized by a cell nucleus consisting of 3–4 segments connected to one another by narrow nucleic bridges. As a result it is also referred to as polymorphonuclear. Granulocytes take their respective name from how their granules stain with Pappenheim dye. The term neutrophilic comes from the fact that their cytoplasmic granules (< 1 µm) don't stain well with either basophilic dyes or eosinophilic dyes. They are therefore neutral. Neutrophils belong to the nonspecific immune system and phagocytize bacteria (microphages) in particular. Therefore, a large share of their granules are lysosomes in which phagocytized bacteria are broken down. Neutrophils are generated in the bone marrow and are released from there into the peripheral bloodstream when acutely needed (as is the case in bacterial infection). In such cases, a blood smear will reveal increased numbers of neutrophil precursors ("juvenile" cells) with unsegmented or less clearly segmented nuclei. Thus, a reactive increase in neutrophils in a blood smear can suggest a bacterial infection.



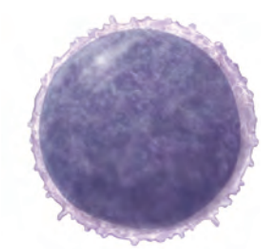
D Eosinophilic granulocytes
Eosinophils (12 µm in diameter) have a bilobed nucleus. They contain eosinophilic granules measuring 1.5 µm which represent modified lysosomes that release their contents to the extracellular matrix in degranulation. The anionic dye eosin binds to the cationic proteins in the granules (such as major basic protein, and eosinophil cationic protein). Eosinophils defend against worms in particular (small eosinophils cannot completely phagocytize large multicellular parasites), which is why their blood count is increased in parasitic diseases. They frequently migrate from the blood into the mucosa of the gastrointestinal tract and lungs. Their numbers are also increased in allergic disorders.



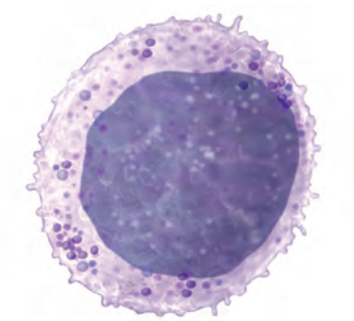
E Basophilic granulocytes
The lobulated nucleus of basophils is often undetectable as it is obscured by granules, which measure 1 µm and stain intensely bluish-violet. The polyanionic heparin contained in the granules takes up cationic dyes (methylene blue, azure). The granules also contain histamine, which is released in an allergic reaction. Although basophils resemble mast cells in their morphology and function, the two are separate types of cells that arise from different stem cells and they do not merge with each other.



F Monocytes
Measuring 20–40 µm in diameter, monocytes are the largest cells in the blood. They exhibit a pale grayish blue cytoplasm and an indented bean-shaped nucleus that also can assume other shapes. This means that monocytes are the most variable type of cell in a blood smear. Small, barely discernible azure granules may be found in the cytoplasm, especially in the indentation of the nucleus. These represent lysosomes. Monocytes leave the bloodstream after about a day and migrate into the connective tissue of the organs, where they differentiate into macrophages. Macrophages are monocytes that have become resident and in which a number of differentiation processes occur. The number of lysosomes in particular increases greatly. The mononuclear phagocytic system (MPS) is a generic term introduced by van Furth which includes all of these cells.

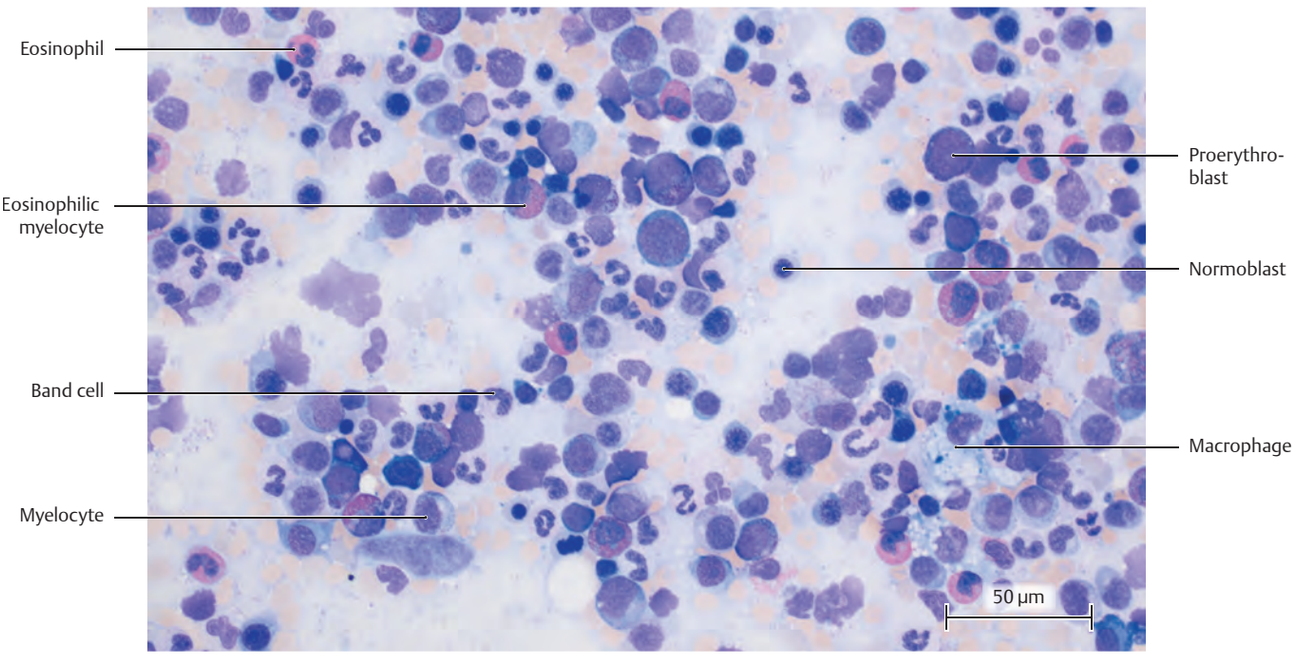


G Lymphocytes
Lymphocytes are characterized by a round nucleus rich in heterochromatin. In small lymphocytes (4–7 µm in diameter), the nucleus is surrounded by a narrow ring of cytoplasm; in medium-sized lymphocytes (up to 15 µm) this ring is wider and can contain granules (see **H**). Lymphocytes are part of the adaptive or specific immune system and occur in two main forms, B lymphocytes and T lymphocytes, which are indistinguishable in a blood smear. They are analyzed with the aid of monoclonal antibodies in flow cytometry (important in AIDS patients). B lymphocytes ultimately differentiate into plasma cells that produce antibodies; T lymphocytes aid in providing specific cell-mediated immunity. Lymphocytes only use the bloodstream for a short time (approximately 1 hour) as a transport medium to enter the lymphatic organs and the interstitium of other organs. Lymphocytes have a similar appearance to monocytes, which is why the two are often grouped together as mononuclear cells. These are distinguished from the granulocytes (polymorphonuclear cells). Reactively increased numbers of lymphocytes in the blood occur often in viral disorders.

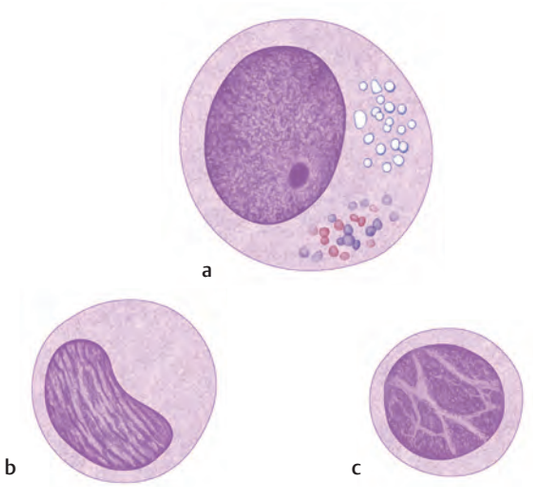


H Azurophilic granulated lymphocytes
Azurophilic granulated lymphocytes are a special form of large lymphocyte distinguishable by their large ring of cytoplasm and their azurophilic granules (large granular lymphocytes or LGL). They represent the natural killer cells (NK cells) that form part of the nonspecific immune system. They react immediately upon contact with virus-infected cells or bloodborne cancer cells and usually destroy these target cells after direct contact.

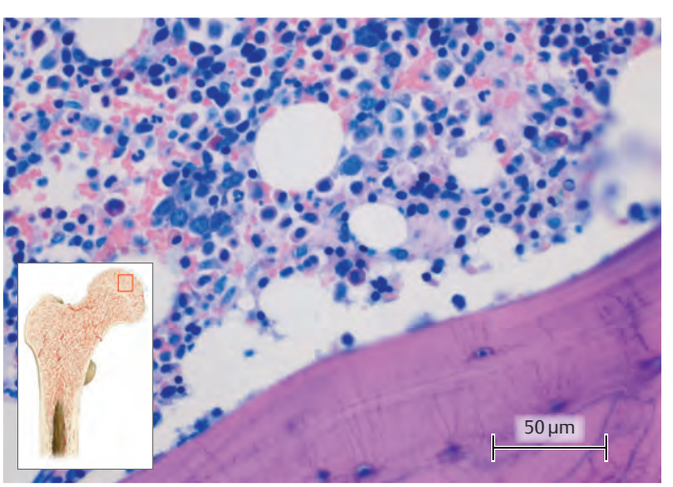
3.3 Blood: Bone Marrow



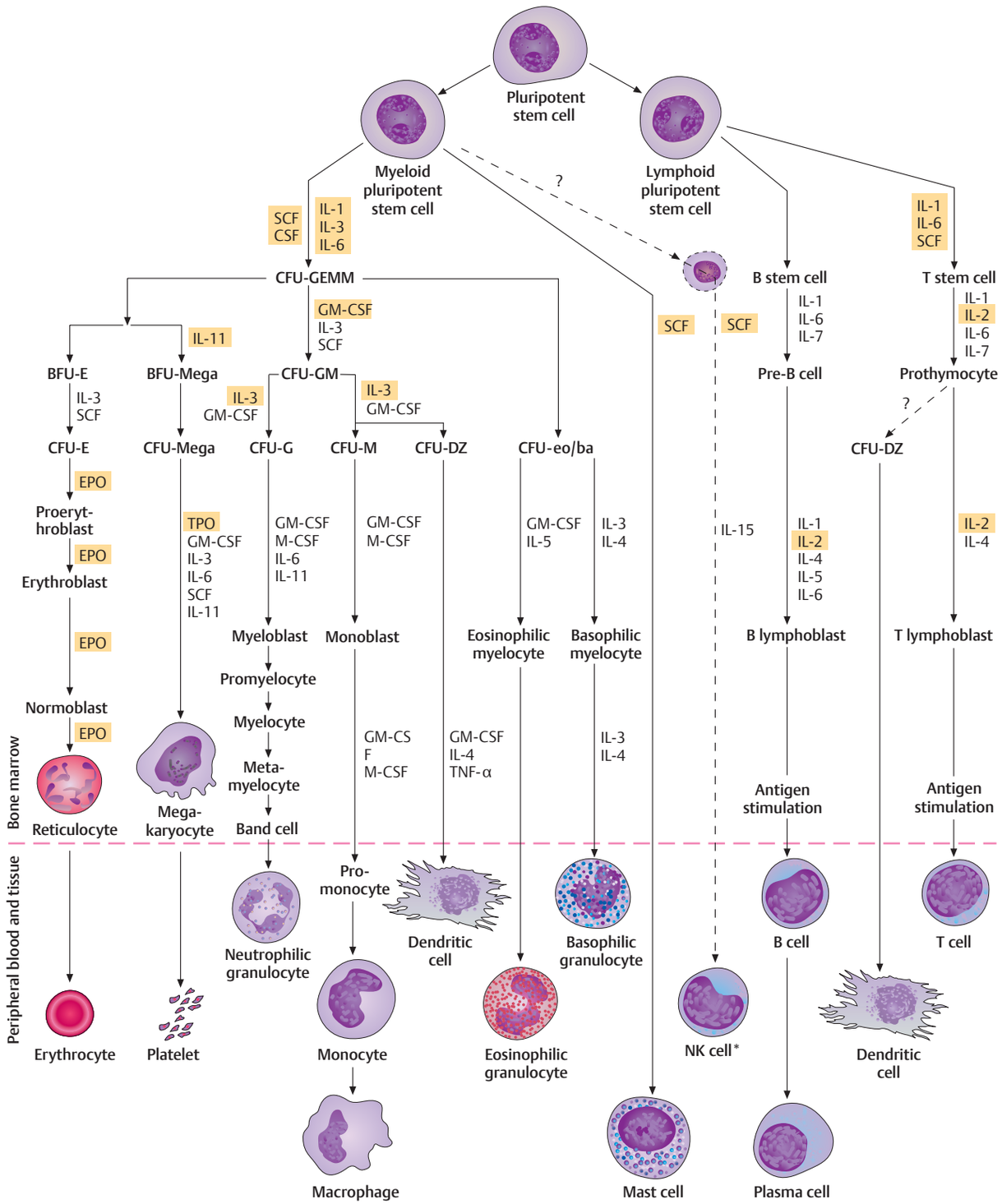
A Bone marrow cytology
Normal medulla ossium contains a bewildering variety of cells. The reason for this is that starting from a single pluripotent stem cell, erythropoiesis, granulopoiesis, and lymphopoiesis all occur simultaneously and produce several different morphologically distinct intermediate stages. A few of the cell types that occur are shown here (see **D** for the classification of cell types in the various lines). In bone marrow cytology, the cells of hematopoiesis from the aspirate are spread out on a slide and are viewed as a single layer of spread out cells. Because the cells are spread out in a single layer in their entirety, cellular details are far more readily discernible than in bone marrow histology where cells may be only partially sectioned because of their size. (Specimen provided by Prof. Hans-Peter Horny, Munich)



B Cytologic evaluation criteria for bone marrow aspirates (after Haferlach et al. Thieme; 2012)
The various different chromatin structures allow us to identify different cell types: **a** myeloblast through promyelocyte; **b** myeloblast through band cell; **c** lymphocyte; clumped chromatin structure. Aside from the structure of the chromatin in the cell nucleus, the structure of the cytoplasm and its granules are evaluated. When granules are present, their affinity for dye allows their classification within a certain series of cells, such neutrophils (granules that do not easily stain) or eosinophils (red stained granules).



C Bone marrow histology
To obtain a histologic specimen, one removes a section of red bone marrow from the femur (in living patients via a biopsy of the posterior superior iliac spine). The cells of the red marrow fill the spaces between the trabeculae. In contrast to bone marrow cytology, histology allows local classification of the cells of hematopoiesis among themselves and with respect to the trabeculae of the bone marrow. This precise classification can be helpful in certain lines of inquiry.
(Specimen provided by Prof. Hans-Peter Horny, Munich)



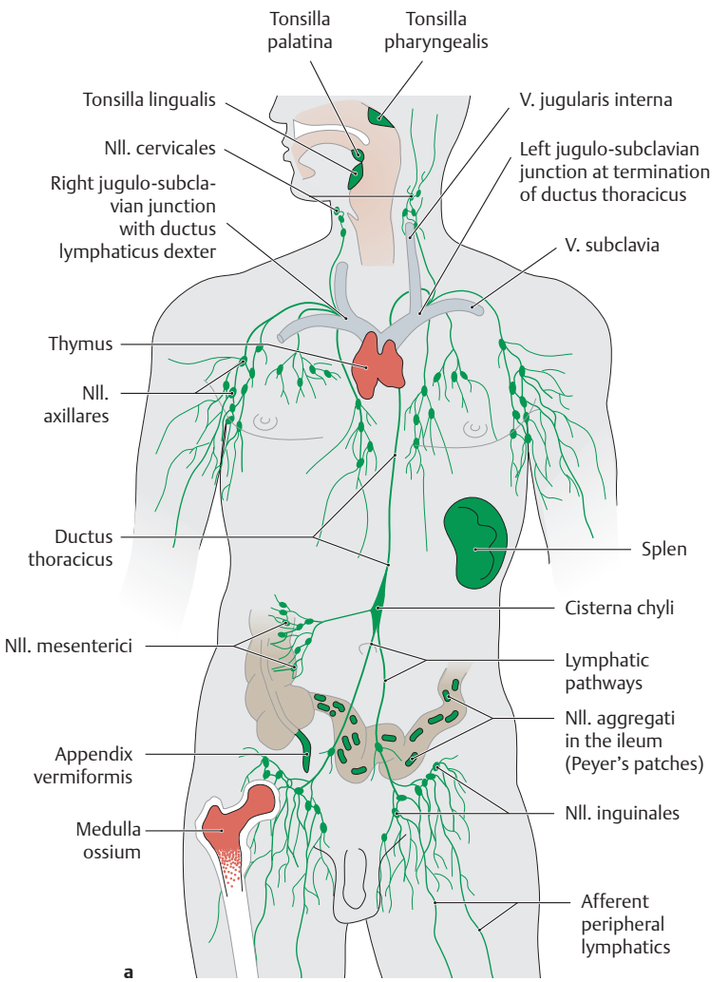
D Hematopoiesis

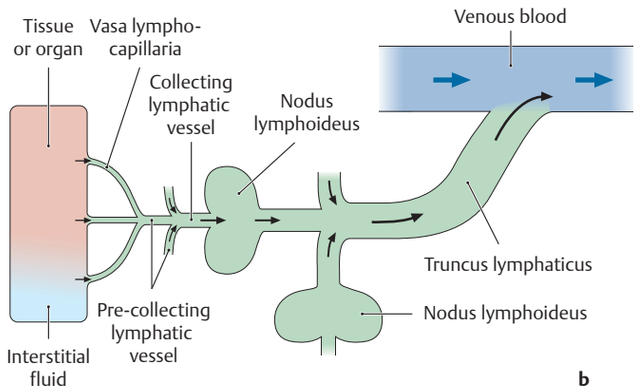
The yellow highlighted growth factors are the most important hematopoietic growth factors for cell differentiation.

All cells in the blood are descended from the pluripotent stem cell. It gives rise to two other cells also referred to as pluripotent stem cells: the lymphoid (right) and the myeloid (left). The various stem cell populations are morphologically indistinguishable from one another. The stem cells that descend from the two pluripotent stem cells are determined; they are stem cells only for the cell populations that follow them. The hematopoietic system requires such a complex hierarchy of stem cells because cells of the most widely varied functions and lifetimes (an erythrocyte that lives 120 days, a neutrophil that lives only a few days) must be constantly produced at a single location (bone marrow). Additionally, increased numbers of erythrocytes must be produced when there has been blood loss, and increased numbers of neutrophils in a bacterial infection. This means the system needs a high degree of flexibility in order to produce cells that function differently and have different lifetimes. The various stem cell populations ensure this flexibility. The morphology of the various normal cells of hematopoiesis is used as the basis for classifying leukemic cells (malignant degenerative cells), for example promyelocytic leukemia or erythroleukemia. This hierarchical scheme of a stem-cell-containing tissue was then applied to other types of tumors, including solid ones (concept of the malignant stem cell).

* The exact classification of the natural killer cells with respect to stem cells has not yet been fully clarified.

4.1 Overview of the Lymphatic System





A Lymphatic organs and vessels
The lymphatic system, which is widely distributed throughout most of the body, consists of lymphatic organs and vessels. It has three main functions:

- Immunological defense (lymphatic organs and vessels). The main function of the immune response is to distinguish "self" from "nonself" (or foreign) substances (such as pathogens, or transplanted tissues) and destroy the "nonself" substances.
- Transport of interstitial fluid to venous blood (vasa lymphatica)
- Removal of lipids from the intestinum tenue while bypassing the hepatic portal system. This allows triglycerides to avoid hepatic metabolism and to be transported directly to organs that can utilize them.

a Lymphatic organs: All lymphatic organs have a stroma that is populated by lymphocytes that originated in medulla ossium (bone marrow). They are directly or indirectly responsible for eliminating antigens (immune response). Antigens are molecules (proteins, carbohydrates, lipids), which the immune system recognizes as foreign and mounts a defense against.

There are two types of *lymphocytes,* which can be further subdivided. (For more details see immunology textbooks.)

- B lymphocytes ("B" stands for bone marrow, where the cells are produced) differentiate into plasma cells, which produce antibodies. Antibodies are essential components of the *humoral immune response*. Humoral immunity refers to antibodies dissolved in blood and interstitial fluid that bind to antigens. Thus, the plasma cells are not directly involved in the immune response.
- T lymphocytes ("T" stands for thymus, where the cells mature) attack and destroy foreign substances (e.g., virus-infected cells) on direct contact (*cellular immune response*).

There are both primary lymphatic organs (*organa lymphoidea primaria,* red organs in **a**) and secondary lymphatic organs *(organa lymphoidea secundaria,* green organs in **a**):

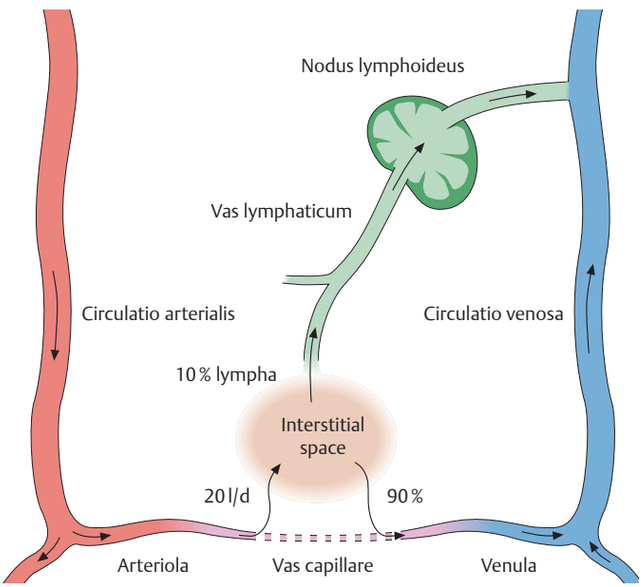
- In the primary lymphatic organs, lymphocytes derived from stem cells mature and become immunocompetent cells (meaning they are capable of distinguishing between self and nonself substances).
- From these primary lymphatic organs, lymphocytes migrate to the secondary lymphatic organs where they continue to proliferate and mature. They are then able to fulfill their specific roles in the immune response. Lymphocytes can leave an organ and enter the bloodstream.

The structure and function of the individual lymphatic organs will be discussed in the respective organ chapters.

b Lymphatic vessels: Lymphatic vessels (green in **a**) are part of a tubular system that is distributed to all parts of the body (except for the CNS and medulla renalis). The vessels are responsible for absorbing fluid from the interstitial spaces (it is now called lymph) and transporting it to the venous blood. Lymphatic vessels start out as tiny, thin-walled capillaries (lymphatic capillaries), which drain into larger pre-collecting and collecting vessels (**b**). These eventually coalesce into trunci lymphatici. These trunks join to form two larger ducts that end at each of the two venous angles (the junction of the v. jugularis interna and v. subclavia) (see p. 30). Nodi lymphoidei are incorporated into the system of peripheral lymphatic vessels. Lymphatic vessels converge in the nodi lymphoidei, where the lymph is filtered and checked for pathogens as it passes through.

B Overview of the lymphatic pathways

Lymphatic pathways play a clinically significant role in the classification of tumors and their cells that metastasize to lymphatic nodes (nodi lymphoidei). Since lymphatic node metastases are sometimes discovered before the primary tumor, the organ where the cancer initiated can be determined from the affected lymph nodes. Thus it is crucial to know the lymphatic pathways of organs and regions. The classification of lymph vessels and the nodi lymphoidei associated with them is illustrated below. If one follows the pathway the lymph travels from the site of origin until it flows into the venous blood stream, the basic classification becomes apparent:

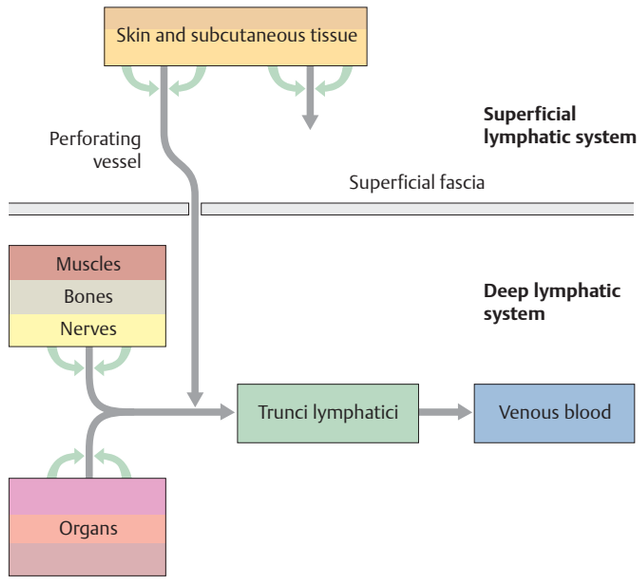


C Lymph formation

Lymph forms as a clear fluid in the capillaries by blood ultrafiltration. Blood passes through capillaries from the arterial to the venous side of the circulatory system. The internal capillary blood pressure is greater than the colloid osmotic pressure in the capillary. As a result, 10% of the fluid from the capillaries remains as interstitial fluid in the interstitial space. This 1.8–2 liters of interstitial fluid (over 24 hours) that is not returned to the blood capillaries is absorbed by lymph capillaries (see **Ab**), and then collected into larger lymphatic vessels and trunks before it drains into venous blood. Eventually all the lymph in the body drains into two trunci lymphatici (ductus thoracicus et ductus lymphaticus dexter, which drain into the anguli venosi sinister et dexter, respectively, at the junction of the neck and thorax [see page 28, Fig. **Aa**]). The lymphatic vessels direct lymph through lymph nodes, and the nodes check the lymph for germs and toxins. In cases of purulent inflammation caused by bacteria, reddened superficial lymphatic pathways are visible, which in layman terms is referred to as "blood poisoning."

Note: After a fat-rich meal, lymph from the small intestine is rich in emulsified lipoprotein particles (chylomicrons) and thus has a milky appearance. Lymph flowing from the small intestine is called chyle and the lymph vessels of the small intestine are sometimes referred to as chyle vessels.

- Lymph is formed by ultrafiltration from capillary vessels (vasa capillaria) in the connective tissue (**C**).
- There is a superficial and deep lymphatic network (**D**).
- 5 major trunci lymphatici drain lymph from all areas of the body (see p. 30).
- The nodi lymphoidei incorporated into the lymphatic system can be classified according to their location (see p. 31).



D Superficial and deep lymphatic systems

There are both superficial and deep lymphatic systems.

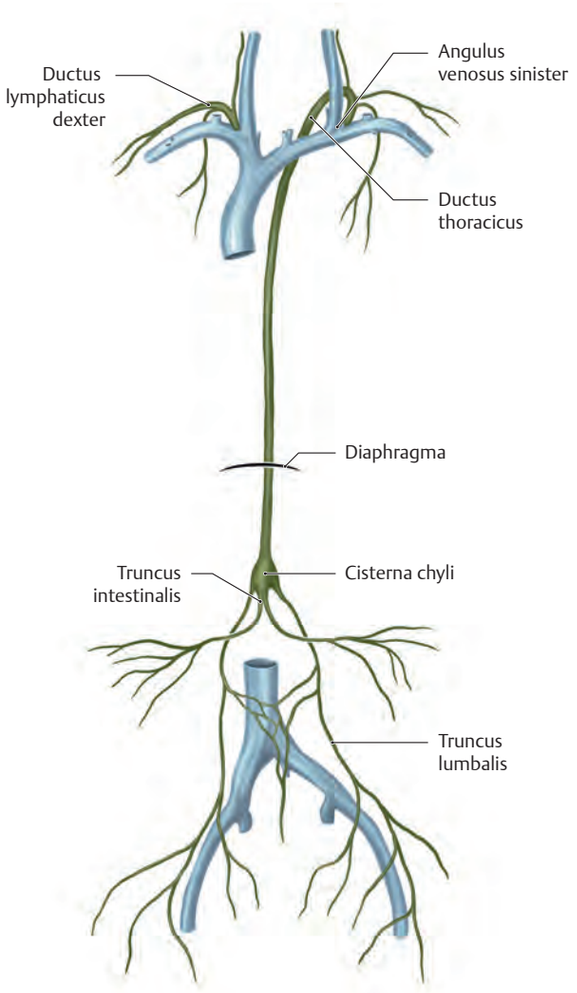
- The superficial lymphatic system is located in and above the superficial fascia and collects lymph from the cutis (skin) and tela subcutanea (subcutaneus tissue).
- The deep lymphatic system lies underneath the superficial fascia and collects lymph from the organs, muscles, bones, and nerves.

Only the deep lymphatic system has direct contact with the major trunci lymphatici (see p. 30). The superficial lymphatic system transports lymph to the deep vasa lymphatica through perforating vessels (which penetrate the superficial fascia). The connection between superficial and deep vasa lymphatica is very pronounced in three spots:

- the sides of the neck
- the armpit
- the groin

Nodi lymphoidei are also particularly numerous in these sites, where they can be readily palpated during clinical examinations.

4.2 Lymphatic Drainage Pathways



A The major trunci lymphatici

There are 5 major trunci lymphatici, most of them paired, which drain lymph from the various regions of the body. Table **B** lists all the trunci and the regions they drain. Generally, all trunci drain into either theductus thoracicus or the *ductus lymphaticus dexter*, both of which empty into the venous system. The 3 major lymphatic trunks for the abdomen, pelvis, and lower limbs (the truncus intestinalis and the two trunci lumbales) merge just beneath the diaphragma into a dilated collecting sac, the *cisterna chyli*. The ductus thoracicus originates from the cisterna chyli, traverses the diaphragma through the hiatus aorticus, ascends through the cavitas thoracica and eventually drains into the left venous angle. On its way it usually receives the left truncus bronchomediastinalis as well as the left truncus jugularis and left truncus subclavius. However, all these trunks may empty separately into the venous system.

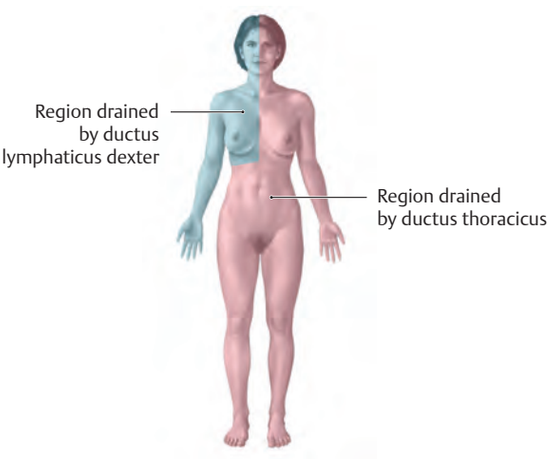
The right truncus bronchomediastinalis, right truncus jugularis, and right truncus subclavius merge to form the very short ductus lymphaticus dexter. The ductus lymphaticus dexter drains into the right venous angle.

Note: Except for the truncus intestinalis, all lymphatic trunks are paired, corresponding with the organization of the body regions they drain. The truncus intestinalis drains the unpaired abdominal viscera (see **B**). Although it is unpaired, it can often be divided into multiple (not individually named) sub-trunks, which in the nomenclature are collectively referred to as trunci intestinales–plural.

B Organization of the trunci lymphatici and the regions they drain

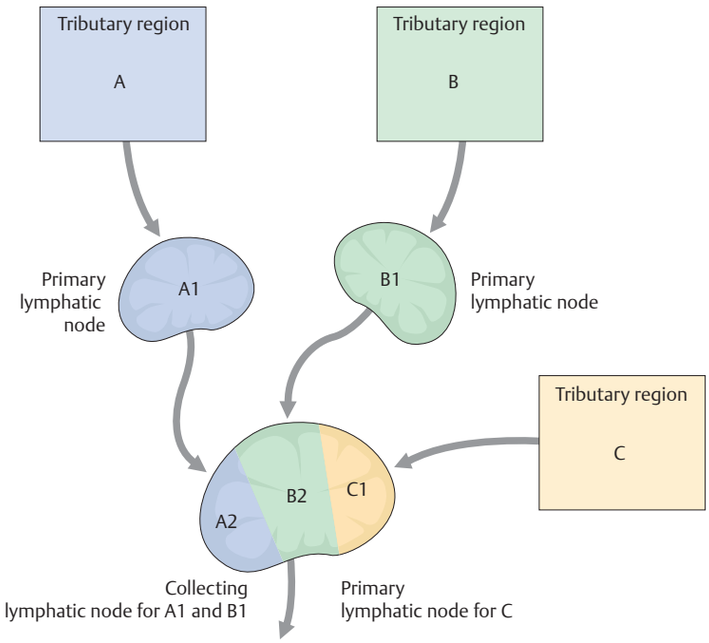
Summary of the lymphatic trunks and the body regions they drain.

Truncus lymphaticus	Drainage area
Head, neck, and upper limbs	
• Left and right trunci jugulares • Left and right trunci subclavii	• Left and right sides of the head and neck • Left and right upper limbs
Thorax	
• Left and right trunci bronchomediastinales	• Organs, internal structures, and walls of the left and right thorax
The trunks located on the right side merge to form the ductus lymphaticus dexter. The trunks located on the left side drain into the ductus thoracicus (see below).	
Abdomen, pelvis, and lower limbs	
The ductus thoracicus collects most of the lymph circulating throughout the body. The duct is formed by the convergence of	
• The truncus intestinalis • The left and right trunci lumbales	• Unpaired abdominal viscera (digestive tract and splen) • Paired abdominal viscera (renes, gll. suprarenales) • All pelvic viscera • Left and right abdominal walls • Left and right pelvic walls • Left and right lower limbs
The ductus thoracicus drains all lymph from areas below the diaphragma and from the left side of the body above the diaphragma. The ductus lymphaticus dexter only drains the lymph from the right side of the body above the diaphragma. Accordingly, it is possible to divide the body into 4 lymphatic drainage quadrants (see **C**).	



C Organization of the body into lymphatic drainage quadrants

The lymphatic drainage of the body is not symmetrical. Rather, it is organized by quadrants. The ductus lymphaticus dexter drains the right upper quadrant, and the ductus thoracicus drains the other three quadrants.



D Classification of lymph nodes (modified after Földi)
Groups of lymph nodes can be classified in different ways. One classification is based on the direction of lymph flow, and another is based on their location relative to the internal organs.

Classification based on direction of lymph flow: If lymph is classified based on the direction it flows (from peripheral tissue to the venous system), it usually passes through several serially connected groups of lymph nodes. These nodes are referred to as primary, secondary, and tertiary lymph nodes:

- Primary lymph nodes (nodi lymphoidei regionales) take up lymph directly from a circumscribed area of the body (organ; limb; part of trunk). The area that passes its lymph to a particular group of primary lymph nodes (blue or green node, A1 or B1) is called the tributary region of the specific group of nodes (in the figure labeled A–C).
- Once the lymph leaves the primary lymph nodes, it can be passed to subsequent (secondary or tertiary) lymph nodes. Since secondary lymph nodes often collect lymph from multiple groups of primary lymph nodes, they are also referred to as collecting lymph nodes (in the figure marked as a multicolored node).

Note: A group of primary lymph nodes for one tributary region can, at the same time, be the secondary or collecting lymph nodes for another region. Thus, the three-colored nodus lymphoideus is a primary node for tributary region C (yellow), while at the same time it is also a collecting node for primary nodes A1 and B1 (blue and green).

Classification based on location relative to the internal organs: Lymph nodes in the abdomen and pelvis are classified as nodi lymphoidei *parietales* or nodi lymphoidei *viscerales* depending on their relationship to major vessels and organs:

- Nodi lymphoidei parietales of the abdomen and pelvis are located either directly adjacent to the major vessels (aorta abdominalis, v. cava inferior cava or iliac vessels) or close to the abdominal wall.
- Nodi lymphoidei viscerales of the abdomen are related to the unpaired abdominal viscera, which are supplied by the three major unpaired arterial trunks. Groups of nodi lymphoidei viscerales are also located next to the organs in the pelvis. These lymph nodes pass their lymph primarily to the (parietal) nodi lymphoidei iliaci, which would then be considered as collecting nodi lymphoidei for the visceral group.

Lymphatic node group	Parietal group	Visceral group
Abdominal	• Nodi lymphoidei lumbales sinistri, dextri, and intermedii • Nodi lymphoidei epigastrici inferiores • Nodi lymphoidei phrenici inferiores	• Named after organ (see p. 222)
Pelvic	• Nodi lymphoidei iliaci interni, externi, and communes	• Named after organ (see p. 223)

E Embryonic development of lymphatic organs and lymphatic vessels
The lymphatic organs and lymphatic vessels (organa lymphoidea and vasa lymphatica) are derived mostly from mesoderma.
Note: Growth and development of the thymus are not complete until after birth. While the other organs develop in the given time frame, they mature in function only around the time of birth (when the immune cells can make the immunologically important distinction between "self" and "nonself").

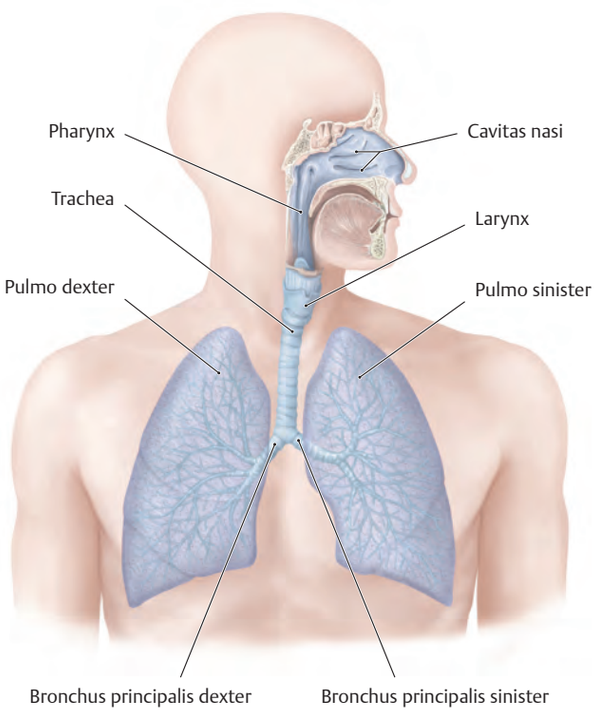
Lymphatic structure	Time frame	Developmental process
Vasa lymphatica	Approx. weeks 5–9	Endothelial buds of the vv. cardinales form sac-like, enlarged vessels, which are connected to a lymphatic plexus close to the dorsal body wall. The major ducts develop from this plexus.
Tonsillae	Approx. weeks 12–16	Epithelial invagination of the 2nd saccus pharyngeus
Splen	Approx. weeks 5–24	Proliferation of mesenchymal cells in the mesogastrium dorsale. As part of gaster rotation, the splen moves to the left upper quadrant.
Thymus	Approx. weeks 4–16	Epithelial invagination of the ventral endoderma and ectoderma in the 3rd saccus pharyngeus

5.1 Overview of the Respiratory System

Introduction and overview

The respiratory organs are the site of gas exchange between the organism and the atmosphere (external respiration vs. internal respiration = cellular respiration). Additionally, respiratory organs contribute to voice production.

Inhaled air reaches the alveoli pulmonales through a network of finely branched tubes (the trachea, bronchi and bronchioli). *Gas exchange* takes place in the alveoli. In the air passages, incoming air is warmed, moistened and filtered. Blood is transported to the lungs (pulmones) through a similarly finely branched network, the aa. pulmonales and their branches. *Carbon dioxide*, an end product of cellular metabolism, is carried with the blood to the lungs. During respiration, *oxygen* is absorbed from the air, and then binds with hemoglobin. At the same time, carbon dioxide is excreted. Carbon dioxide in the blood is a component of the bicarbonate buffering system. Thus, respiration influences the body's acid-base balance by releasing CO_2. The gas exchange between air and blood occurs by diffusion, driven by the differences in partial pressure of the two gases (the difference in the pressure of the gas between the blood and air). Blood does not come into direct contact with the air; they are separated by the blood-air barrier. From the lungs, blood is pumped through the vv. pulmonales back to the heart, and from there it reenters the systemic circulation.

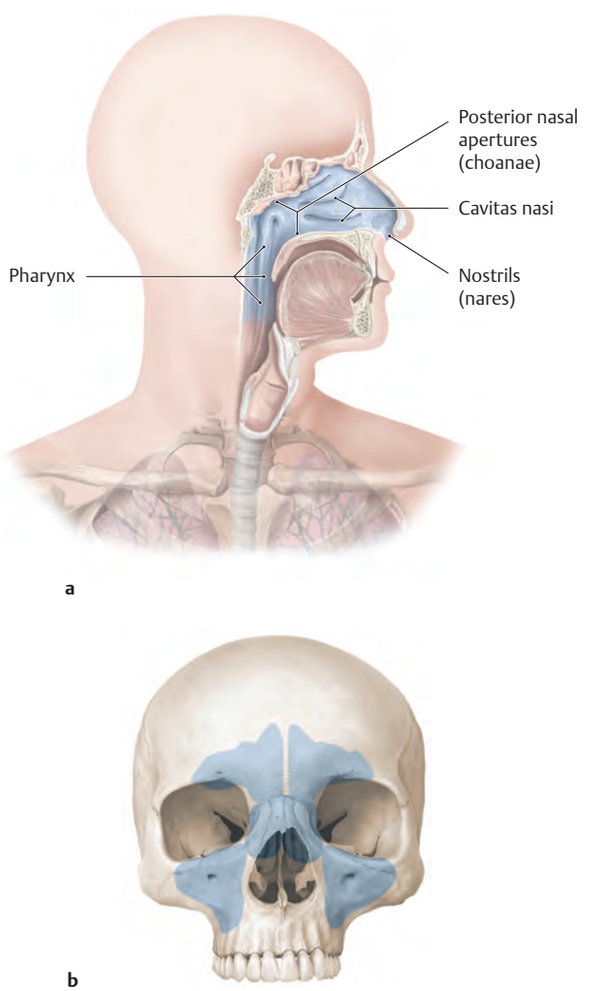


A Structure of the air passages

The respiratory system is divided into an upper and lower respiratory tract:

- **The upper air passages include**
  - the external nose and cavitas nasi,
  - the sinus paranasales,
  - the pharynx (only the upper portion, the pars nasalis pharyngis, is exclusively a part of the respiratory tract; in the middle portion of the pharynx the respiratory and digestive tracts cross each other).
- **The lower air passages include**
  - the larynx, which serves to temporarily close the air passages during swallowing, and also contributes to voice production;
  - the trachea, which divides into the two bronchi principales;
  - the two bronchi principales, which then progressively subdivide;
  - the alveoli, located at the end of the network of progressively narrowing tubes. They are the site of gas exchange.

The histology of the different parts of the respiratory tract will be further discussed in the organ chapters.



B Upper air passages: Nose, cavitas nasi, and pharynx

a Main cavitas nasi and pharynx viewed from the right side with the head turned left; **b** Bony skull, anterior view of the sinus paranasales.

Air is inhaled through the nostrils (nares) into the cavitas nasi. It then passes through the posterior aperture of the nose (choana) into the pharynx, and then to the larynx. Narrow openings connect the sinus paranasales to the main cavitas nasi.

Note: In addition to conducting air, the main cavitas nasi is also involved in odor perception.