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EMBRYOLOGY

Nick Hopwood

"If . . . we say that each human individual develops from an egg, the only answer, even of most so-called educated men, will be an incredulous smile; if we show them the series of embryonic forms developed from this human egg, their doubt will, as a rule, change into disgust. Few . . . have any suspicion," wrote evangelist of evolution Ernst Haeckel in the 1870s, "that these human embryos conceal a greater wealth of important truths, and form a more abundant source of knowledge than is afforded by the whole mass of most other sciences and of all so-called 'revelations.'"[1] Between this extravagant claim and the incredulity and disgust that it invokes lies a contradictory history. In nineteenth-century universities and medical schools embryology was a key science of life; around 1900 modern biology was forged within it; and as developmental biology it buzzes with excitement today. Embryology fired wide publics with Darwinist fervor, sexual knowledge, and the prospect of reproductive control; but it also bored generations of medical students, was molecular biologists' favorite example of scientific decline, and has attracted both feminist and antiabortionist critiques. There are, then, rich histories to be told, and as scholars in various disciplines begin to tell them, existing surveys have come to seem thin. Largely confined to concepts and theories, they tell us little about the daily life of embryology. Written within particular traditions, they do scant justice to the diversity of embryo science and the variety of perspectives on it. In response to these limitations, this highly selective chapter seeks to encourage more adequate attempts at synthesis by following two interlocking transformations: in forms of work and in identity.

Embryology has shared with other sciences two main ways of working: Since the end of the eighteenth century, physicians, professors, and curators,

[1] Ernst Haeckel, *The Evolution of Man: A Popular Exposition of the Principal Points of Human Ontogeny and Phylogeny*, 2 vols. (London: Kegan Paul, 1879), vol. 1, p. xix.

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interested in identifying and classifying, analyzed compound objects into elements; and from the mid-nineteenth century, university researchers claimed experiment as the means to control life.[2] Embryological analysis dealt specifically with development; from collected specimens embryologists derived representations to compare and select, arrange into developmental series and display. Making series of lithographs, wax models, or sonograms may be said to have "produced" development for wide audiences and constructed objects on which to do more work.[3] In the nineteenth century, analysis dealt with germ layers and cells; in the twentieth, it increasingly involved chemicals and macromolecules as well. Early experiments were subordinate to analysis, but in the 1880s some embryologists followed physiology in elevating experimental control above supposedly mere description. Analysis continued, however, and it continued to interact with experiments revealing the potentials of embryonic parts and defining interacting systems. In the mid-twentieth century, biochemical and genetic searches for the molecular agents of these effects intensified. By 2000, deep and subtle interventions went beyond the laboratory, as embryology offered medicine and agriculture to make organisms to order.

Innovations in embryological work have driven and been driven by changes in identity. In the 1960s, "developmental biology" succeeded "experimental embryology" as accounting for most embryological research. The dominant historiography accordingly moves from the "classical descriptive embryology" of the first three quarters of the nineteenth century, through the "classical experimental embryology" that flourished between the 1880s and the 1930s, to its currently prominent successor. It is well known that because embryology rarely acquired its own institutes and professors, most embryologists made their livings wearing physiological, anatomical, zoological, or biological hats. But by taking parts for the whole, historians have seriously underestimated the variety this produced. Treating twentieth-century embryology exclusively as a branch of experimental biology is particularly problematic: The first specifically embryological research institution was founded, during World War I, to describe human embryos; most embryology books were medical texts; and by the 1990s many embryologists worked in fertility clinics. We can best explore the range of embryologies by encompassing a wide spectrum of scientific, technical, and medical activities. More than this, we should begin to look beyond the laboratories and clinics to the encounters of the science with sometimes radically different lay views of generation. For, as this chapter can only hint, it is in the contrasts between the perspectives of professionals

2 John V. Pickstone, "Museological Science? The Place of the Analytical/Comparative in Nineteenth-Century Science, Technology and Medicine," *History of Science*, 32 (1994), 111–38. This usage is close to the opposite of the common identification of embryological analysis with experiment.

3 Nick Hopwood, "Producing Development: The Anatomy of Human Embryos and the Norms of Wilhelm His," *Bulletin of the History of Medicine*, 74 (2000), 29–79.

and laypeople – and not just Haeckel's "educated men" – that we shall find the more general significances of embryological work.

MAKING EMBRYOLOGY

In the 1930s, embryologist-historian Joseph Needham nominated a Hippocratic writer as "the first embryologist" and traced a straight line through Aristotle, William Harvey, and Karl Ernst von Baer (1792–1876) to the premier embryological journal of his own day.[4] Yet even before Needham, embryologists had treated the decades around 1800 as a break in the history of their science when strange debates over generation gave way to a much more familiar world. Historians who trace our natural sciences to the Age of Revolutions find in the late Enlightenment the making not merely of modern embryology but of embryology itself. The science emerged, however, from both new ways of analyzing embryos and the selective restructuring of earlier investigations into generation.

The mechanistic natural philosophers of the late seventeenth century sought to understand the perpetuation of visible order, but the origin of organized beings – How does a soft, fluid hen's egg become a highly ordered chicken? – remained the subject of endless debate. Epigenesis, the ancient view that organization arose progressively from initially unorganized matter, was tainted with atheist materialism. Its preformationist rival taught that, all appearances to the contrary, adult structures were already present in the egg – or, some said, in the "animalcules" of the male semen – waiting to unfold. This positing of a passive nature determined by divine laws was the orthodox account. But though by no means as ridiculous as embryologists would later suppose, preformation gave the epigenesists plenty to mock. If an omnipotent and benevolent God had made all germs at the Creation, why were there ugly and useless monsters? And what about the sensational discovery in the 1740s that a polyp could regenerate from its parts?[5]

These problems contributed during the second half of the eighteenth century to the triumph of epigenesis over preformation. But the shift was more profound than a simple victory for the materialist theories that had attempted to explain the source of embryonic organization. Earlier naturalists had represented external surfaces; anatomists now dissected organisms to reveal the

[4] Joseph Needham with Arthur Hughes, *A History of Embryology*, 2nd ed. (Cambridge: Cambridge University Press, 1959), pp. 31, 36.

[5] Shirley A. Roe, *Matter, Life, and Generation: Eighteenth-Century Embryology and the Haller-Wolff Debate* (Cambridge: Cambridge University Press, 1981); Shirley A. Roe, "The Life Sciences," in *The Cambridge History of Science*, vol. 4: *Eighteenth-Century Science*, ed. Roy Porter (Cambridge: Cambridge University Press, 2003), pp. 397–416; Emma C. Spary, "Political, Natural and Bodily Economies," in *Cultures of Natural History*, ed. Nicholas Jardine, James A. Secord, and Emma C. Spary (Cambridge: Cambridge University Press, 1996), pp. 178–96.

inner structural relations and functional activities of the parts. Because organization defined what it meant to be living, its origin no longer needed to be explained, and comparative anatomists concentrated on seeking the laws relating the various plans.[6] The St. Petersburg academician Caspar Friedrich Wolff and the Göttingen professor Johann Friedrich Blumenbach stabilized epigenesis by turning the once most troublesome beings into instruments of their science. Monstrosities, they argued, were produced when the generative force of a newly active nature deviated into deficiency or excess. Seen in the light of a process of development, monsters even became beautiful.[7]

Embryology was created not only from the philosophy of generation and the natural history of monsters but also by male surgeons moving into midwifery and by enlightened medico-legal interest in the unborn child as a future citizen. At first, the stages of pregnancy were determined within a preformationist framework, and specimens that did not fit the ideal of human proportions were rejected as false conceptions. Whereas even seventeenth-century drawings of chick embryos resemble those produced two hundred years later, pictures and models of human embryos continued to show the increase in size of a miniature child. Then, in 1799, the anatomist Samuel Thomas Soemmerring, extending and revising anatomies of the gravid uterus, had his artist create a space in which human embryos could be seen progressively to change shape (Figure 16.1).[8]

The determinacy of this medical image of development contrasted starkly with, and was used to devalue, women's bodily experiences of the precariousness of pregnancy. This usually took nine months, but occasionally seven or eleven. Several missed periods might mean a child, but could equally signal illness or a false conception – until the only sure sign of pregnancy, "quickening," when a woman felt a child move inside her. In practice, this was taken to correspond to the moment at which, in the long-standing Christian–Aristotelian view, the fetus became animate or ensouled. Abortion was generally tolerated before this point, but the Sicilian Jesuit Francesco Emanuele Cangiamila rejected abortion totally, and his *Sacred Embryology* (1745) was unusually obsessed with baptizing even the earliest embryos. In 1803, abortion

6 Roe, *Matter, Life, and Generation*, pp. 148–56; Michel Foucault, *The Order of Things: An Archaeology of the Human Sciences* (London: Tavistock Press, 1970); François Jacob, *The Logic of Life: A History of Heredity*, trans. Betty E. Spillmann (New York: Pantheon, 1982), pp. 74–129.

7 Georges Canguilhem, "La Monstruosité et le Monstrueux," in *La Connaissance de la Vie*, 2nd ed. (Paris: J. Vrin, 1989), pp. 171–84, at pp. 178–9; Michael Hagner, "Enlightened Monsters," in *The Sciences in Enlightened Europe*, ed. William Clark, Jan Golinski, and Simon Schaffer (Chicago: University of Chicago Press, 1999), pp. 175–217. See also Armand Marie Leroi, *Mutants: On the Form, Varieties and Errors of the Human Body* (London: HarperCollins, 2003).

8 Chapters by Barbara Duden, Nadia Maria Filippini, and Ulrike Enke, in *Geschichte des Ungeborenen: Zur Erfahrungs- und Wissenschaftsgeschichte der Schwangerschaft, 17.–20. Jahrhundert*, ed. Barbara Duden, Jürgen Schlumbohm, and Patrice Veit, Veröffentlichungen des Max-Planck-Instituts für Geschichte, vol. 170 (Göttingen: Vandenhoeck und Ruprecht, 2002). See also Janina Wellmann, "Wie das Formlose Formen schafft. Bilder in der Haller-Wolff-Debatte und die Anfänge der Embryologie um 1800," *Bildwelten des Wissens*, 1, pt. 2 (2003), 105–15.

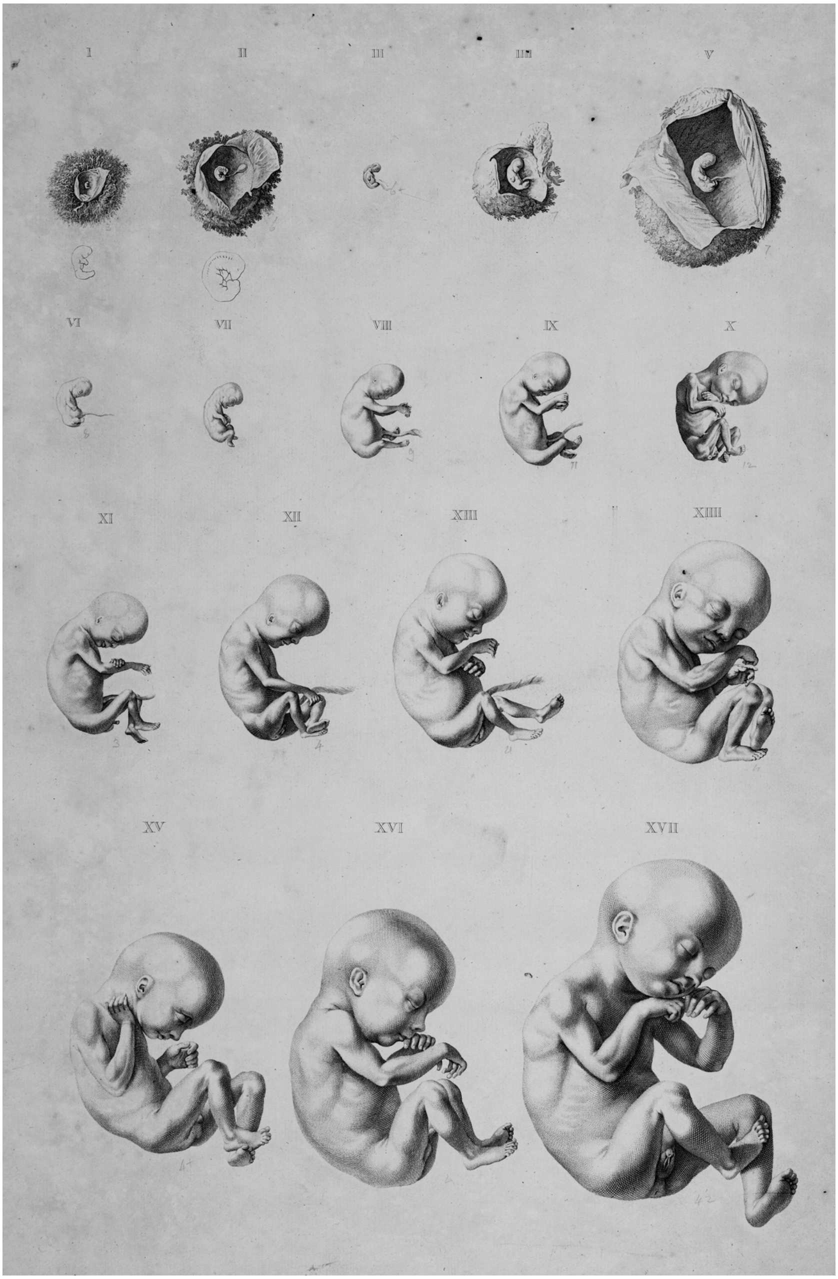

Figure 16.1. Human embryos developing through the first four months of pregnancy. Engraving, after drawings by Christian Koeck, from Samuel Thomas Soemmerring, *Icones embryonum humanorum* (Frankfurt am Main: Varrentrapp und Wenner, 1799), plate I, by permission of the Syndics of Cambridge University Library.

was made a statutory crime in English law, with a lesser penalty if performed before quickening; medical men used embryology to discredit this official recognition of pregnant women's privileged knowledge. More generally, the learned defined the limits of the science by excluding as vulgar superstitions attitudes they had once shared. These included the doctrine that terrible experiences during pregnancy could produce monsters and the conviction that a woman's pleasure during intercourse was a precondition for procreation. Twentieth-century embryologists were nevertheless still confronting similar views.[9]

As a static world gave way to a dynamically changing and historical one, patterns of development came to be seen as the fundamental relation between the different plans of animal organization. Form was to be understood by following its formation, and – especially in the German heartlands of Romanticism – embryology was morphology's guide.[10] Epigenesis offered the Romantics a congenial image of their own becoming: A preformationist fetus, a merely mechanical product of its mother's body that simply inherited its father's power, had been destined for an arranged marriage; the Romantic fetus made itself and would grow up to marry for love.[11] In a universe no longer a machine but a huge animal, generation was the fundamental metaphor and the development of an embryo the model for a nature pregnant with series after ascending series of forms.

The series of adult animals was understood in terms of the parallel development of an individual human being. According to the doctrine of recapitulation, in the course of their development the higher animals passed, in essence, through the adult forms of the lower and a human fetus through the whole animal kingdom. The lower animals, wrote the Romantic nature philosopher Lorenz Oken around 1810, were conversely a series of human abortions. In the systematizations of Halle anatomist Johann Friedrich Meckel the Younger and the Parisians Etienne and Isidore Geoffroy Saint-Hilaire and Etienne Serres, recapitulation gave general significance to a special science of malformations, teratology. But, from the new Muséum d'Histoire Naturelle in Paris, the comparative anatomist Georges Cuvier powerfully opposed this

9 Angus McLaren, *Reproductive Rituals: The Perception of Fertility in England from the Sixteenth Century to the Nineteenth Century* (London: Methuen, 1984); Angus McLaren, "Policing Pregnancies: Changes in Nineteenth-Century Criminal and Canon Law," in *The Human Embryo: Aristotle and the Arabic and European Traditions*, ed. G. R. Dunstan (Exeter: University of Exeter Press, 1990), pp. 187–207. See also Thomas Laqueur, *Making Sex: Body and Gender from the Greeks to Freud* (Cambridge, Mass.: Harvard University Press, 1990), pp. 149–92.

10 E. S. Russell, *Form and Function: A Contribution to the History of Animal Morphology* (London: John Murray, 1916); Owsei Temkin, "German Concepts of Ontogeny and History around 1800," *Bulletin of the History of Medicine*, 24 (1950), 227–46; Timothy Lenoir, *The Strategy of Life: Teleology and Mechanics in Nineteenth-Century German Biology* (Chicago: University of Chicago Press, 1989).

11 Helmut Müller-Sievers, *Self-Generation: Biology, Philosophy, and Literature around 1800* (Stanford, Calif.: Stanford University Press, 1997).

transcendental anatomy by breaking the animal series into four distinct modes of organization.[12]

HISTORIES OF DEVELOPMENT

In the universities of the post-Napoleonic German states, teachers of anatomy and physiology, sympathetic to Romantic nature philosophy but committed to empirical investigations, highlighted the embryological criterion as the key to a true classification. Anatomy without embryology risked artificiality, they taught, but observing developing embryos would show how, from an original internal unity, organisms generated parts in an order corresponding to the natural classification system. By tracing the development of basic structures, one could explain complex morphologies as the elaboration of simple types. Two medical students from the German-speaking Baltic, Christian Pander (1794–1865) and Karl Ernst von Baer, led a host of researchers in creating a new mode of analysis for the science. They showed how organization arose from the transformation of primitive "germ layers," and their followers resolved these into cells.[13]

In 1816, Professor Ignaz Döllinger of Würzburg suggested that his protégés reexamine the classic object of centuries of investigations into generation, the development of the chick in the egg. The noble but impoverished von Baer had to leave the expensive and time-consuming project to Pander, a wealthy banker's son. A custodian ran two incubators so that he could sacrifice several thousand eggs, opening them and probing the embryos with fine needles under a magnifying glass. Extending Wolff's work, Pander expressed his major result in a new vocabulary that replaced earlier circumlocutions: Development began not directly with organ formation but by the organization of sheets of tissue, the germ layers. Pander's greatest expense was paying for engravings that conveyed the complex changes in shape more vividly and in more detail than his words.[14]

Von Baer had followed with interest as Pander proceeded "to wind a laurel wreath of egg-shells around his forehead,"[15] and as soon as he obtained an

[12] Stephen Jay Gould, *Ontogeny and Phylogeny* (Cambridge, Mass.: Harvard University Press/Belknap Press, 1977), pp. 33–68; Toby A. Appel, *The Cuvier-Geoffroy Debate: French Biology in the Decades before Darwin* (New York: Oxford University Press, 1987).

[13] For a survey to about 1880, see Frederick B. Churchill, "The Rise of Classical Descriptive Embryology," in *A Conceptual History of Modern Embryology*, ed. Scott F. Gilbert (Baltimore: Johns Hopkins University Press, 1994), pp. 1–29.

[14] See, most recently, Stéphane Schmitt, "From Eggs to Fossils: Epigenesis and the Transformation of Species in Pander's Biology," *International Journal of Developmental Biology*, 49 (2005), 1–8.

[15] Von Baer to Woldemar von Ditmar, July 10, 1816, quoted in Boris Evgen'evič Raikov, *Karl Ernst von Baer, 1792–1876: Sein Leben und sein Werk*, trans. Heinrich von Knorre, Acta historica Leopoldina, vol. 5 (Leipzig: Barth, 1968), p. 91.

academic position in Königsberg (now Kaliningrad), von Baer embarked on investigations to correct, extend, and generalize his friend's account. These led in 1828 to part of *Über Entwickelungsgeschichte der Thiere* (On the Developmental History of Animals). Like Cuvier, von Baer rejected the linear animal series in favor of four distinct types. During embryogeny, a primary germ common to the whole animal kingdom differentiated into one of four ideal "archetypes," which governed ever more specialized development. An embryo did not pass through the permanent forms of other animals but diverged from shared embryonic forms. In the 1830s, von Baer's work was used in Britain and France to destroy or dilute an often anti-Establishment recapitulationism. Gentlemen of science prayed that the branching view of the animal kingdom would undermine the monad-to-man progressivism of radical lecturers in the London medical schools. In most hands, however, "von Baer's law" did not drive out the "Meckel–Serres law" of parallelism but rather coexisted or was conflated with it.[16]

Von Baer's studies provided a model for a wealth of further research. Between the 1820s and the 1850s, anatomists and physiologists, many of them students of Berlin physiologist Johannes Müller, added cells to the germ layers as a second fundamental unit of embryological analysis and began intensive efforts with the new achromatic microscopes to establish the relations between them. Vesicles surrounding a nucleus were found first as a unifying feature of vertebrate eggs, notably the mammalian ovum, which von Baer, following development to its origins, discovered in 1827. The cell theory of the late 1830s arose from the attempt to generalize the development of these fundamental organs to later structures, and to unify development across the living world. In the 1840s, Robert Remak, an unbaptized Jew forced to work on the margins of the University of Berlin, argued that all cells arise from preexisting cells, from the egg, through the germ layers, to the tissues (Figure 16.2). His doctrine of germ-layer specificity, the most powerful generalization of nineteenth-century embryology, taught that in all vertebrates each layer – endoderm, mesoderm, and ectoderm – gives rise to particular cell types; for example, liver, muscle, and nerve. The argument was expanded as germ layers and cells were investigated in animals with diverse life cycles and modes of reproduction.[17]

None of these men was employed as an embryologist; the science never achieved independent status in the German universities, its most important institutions. In the decades after 1800, it had mainly been the province of

[16] Adrian Desmond, *The Politics of Evolution: Morphology, Medicine, and Reform in Radical London* (Chicago: University of Chicago Press, 1989).

[17] Edwin Clarke and L. S. Jacyna, *Nineteenth-Century Origins of Neuroscientific Concepts* (Berkeley: University of California Press, 1987), pp. 1–100; Jane M. Oppenheimer, "The Non-specificity of the Germ-Layers," in her *Essays in the History of Embryology and Biology* (Cambridge, Mass.: MIT Press, 1967), pp. 256–94; Henry Harris, *The Birth of the Cell* (New Haven, Conn.: Yale University Press, 1999).

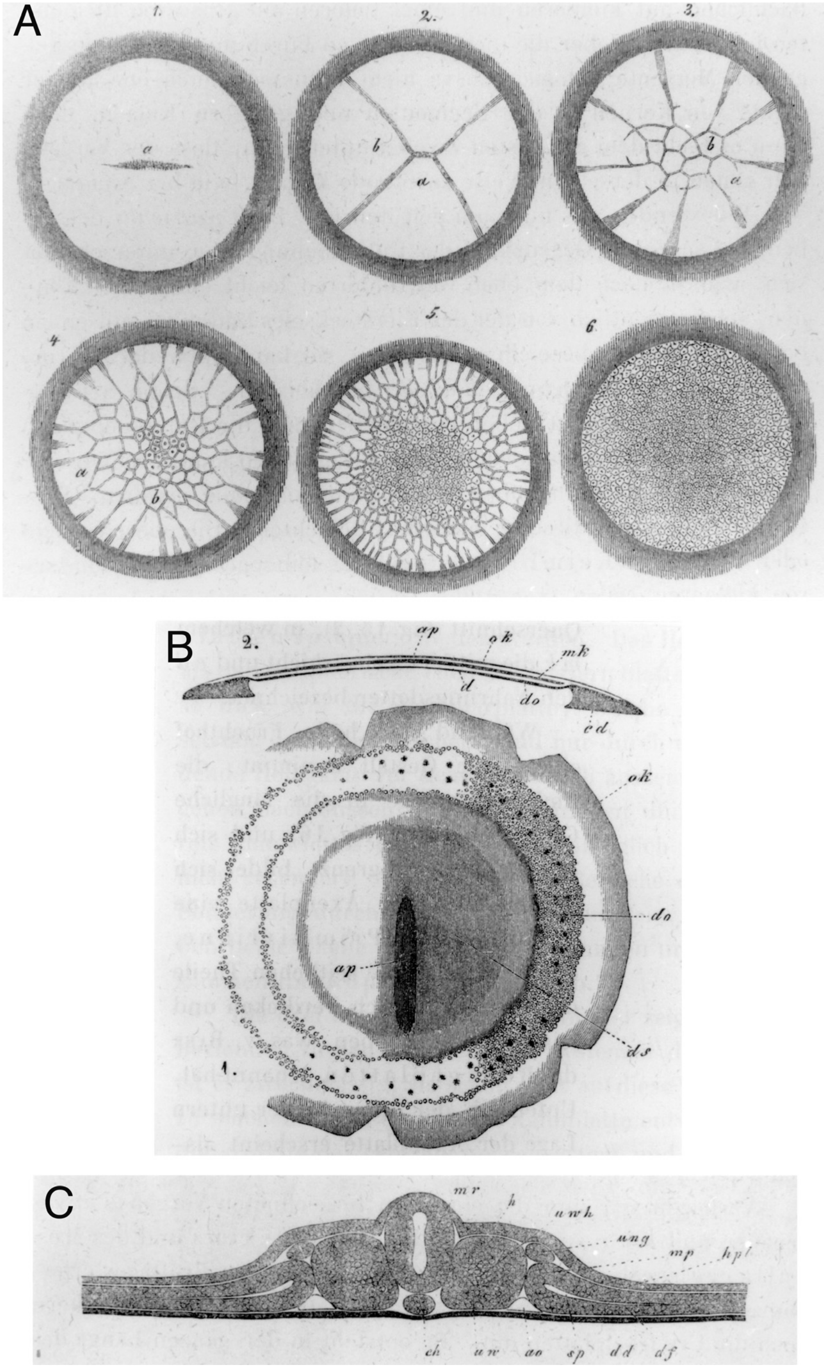

Figure 16.2. Cells and germ layers in chick development. (A) Earliest stages, when cleavage divides the egg's germinal layer into cells. (B) Germinal membrane early in incubation: (1) dorsal view and (2) cross section, showing three germ layers. (C) Cross section through second-day embryo, showing the typical vertebrate structure. Wood-engravings from Würzburg professor Albert Kölliker's successful textbook *Entwicklungsgeschichte des Menschen und der höheren Thiere* (Leipzig: Engelmann, 1861), pp. 41, 43, 48, by permission of the Syndics of Cambridge University Library.

professors of anatomy and physiology, but around mid-century these chairs were divided, and physiology redefined as those topics amenable to experimental manipulation and physico-chemical analysis. Excluded as intractable, development was left to morphologists who were being pushed into independent anatomy institutes and new institutes of zoology. Henceforth embryology was largely split between professors of anatomy in the medical faculties, who tended to specialize in the vertebrates, and professors of zoology in the faculties of philosophy, who made the invertebrates their own.[18] In addition, human embryos were collected and studied in the obstetric clinics; and the discovery of the ovum helped the new discipline of gynecology organize itself around the ovary rather than the uterus.[19] Embryology would form part of fisheries biology, too. The embryology of plants was less clearly demarcated from the rest of botany than human and animal embryology were from general anatomy and zoology.

From the 1830s, enthusiastic teachers arranged special courses in embryology that became the backbone of the science and an important part of anatomical and zoological curricula; some embryology was taught also in obstetrics and gynecology, and to midwives and veterinarians. Medical lectures were oriented toward humans, but embryologists had only limited access to the bodies of pregnant women, and so they concentrated on the chick (Figure 16.2) and domestic mammals. Microscopy practicals were supposed to show students how to recognize in initially unprepossessing specimens the unfamiliar shapes through which bodies gained the structures that in other classes they dissected. Young men interested only in qualifying as doctors disliked these notoriously difficult courses, but embryology provoked great excitement and in the commercial anatomy museums laypeople paid to see preparations and models of the history of development.[20]

EMBRYOS AS ANCESTORS

"Embryology rises greatly in interest, when we . . . look at the embryo as a picture, more or less obscured, of the common parent-form of each great class of animals," Charles Darwin argued in 1859.[21] Evolution made ideal archetypes into real ancestors, and embryonic resemblances into evidence of descent. Ironically, it was not von Baerian embryology that saw the greatest

[18] Lynn K. Nyhart, *Biology Takes Form: Animal Morphology and the German Universities, 1800–1900* (Chicago: University of Chicago Press, 1995), pp. 65–102.

[19] Claudia Honegger, *Die Ordnung der Geschlechter: Die Wissenschaften vom Menschen und das Weib, 1750–1850* (Frankfurt am Main: Campus, 1991), pp. 210–12.

[20] Nick Hopwood, *Embryos in Wax: Models from the Ziegler Studio, with a Reprint of "Embryological Wax Models" by Friedrich Ziegler* (Cambridge: Whipple Museum of the History of Science; Bern: Institute of the History of Medicine, 2002), pp. 12–13, 33–39.

[21] Quoted in Churchill, "Rise of Classical Descriptive Embryology," p. 18.

rise in interest in the age of evolution but the recapitulationist version von Baer had attempted to refute. The extent to which Darwin himself held recapitulationist views is controversial.[22] But it was above all the Jena zoologist Ernst Haeckel (1834–1919) who taught that individuals repeat in the course of embryonic development the most important changes through which their adult ancestors passed during the evolutionary development of the species, or in the pithy formula of his "biogenetic law," "ontogeny recapitulates phylogeny." As a shortcut to otherwise poorly documented relationships, embryology enjoyed a heyday as a key to the history of life on earth and a matter of heated public debate.[23] (See the following chapters in this volume: Hodge, Chapter 14; Di Gregorio, Chapter 12.)

With a premium on investigating the development of a variety of animals, embryologists created new arrangements for collecting embryos that were distant from land-locked European laboratories. The priority was to exploit the sea, the "cradle of life" and home of the richest diversity of animal organization, bringing order to invertebrate embryology and attempting to establish the evolutionary origin of the vertebrates. In 1872, Haeckel's student Anton Dohrn founded the Naples Zoological Station, the most prestigious of a string of new marine laboratories. It played a crucial role as an international trading post for ideas, materials, and techniques.[24] In this age of empire, naturalists also took part in expanding Europe's biological dominion, making expeditions to observe embryos in the wild and bringing them home for collections.[25]

Embryologists revolutionized the analysis of the microscopic specimens they went to so much trouble to find. One line of work enlisted new fixatives and nuclear stains to elucidate the major events of fertilization and cell division. Another made a powerful tool for establishing phylogenies by generalizing the specificity of the germ layers from the vertebrates across the animal kingdom. Through the 1870s, embryologists increasingly used sectioning machines, or microtomes, to convert specimens into series of thin slices that showed more internal structure than a dissection.

Evolutionary hypotheses generally rested on, and inspired, laborious observations, but the bold deductions in Haeckel's semipopular works courted

[22] Robert J. Richards, *The Meaning of Evolution: The Morphological Construction and Ideological Reconstruction of Darwin's Theory* (Chicago: University of Chicago Press, 1992).

[23] Gould, *Ontogeny and Phylogeny*, pp. 69–114; Peter J. Bowler, *Life's Splendid Drama: Evolutionary Biology and the Reconstruction of Life's Ancestry, 1860–1940* (Chicago: University of Chicago Press, 1996).

[24] Christiane Groeben and Irmgard Müller, *The Naples Zoological Station at the Time of Anton Dohrn*, trans. Richard and Christl Ivell (Paris: Goethe-Institut, 1975).

[25] Roy MacLeod, "Embryology and Empire: The Balfour Students and the Quest for Intermediate Forms in the Laboratory of the Pacific," in *Darwin's Laboratory: Evolutionary Theory and Natural History in the Pacific*, ed. Roy MacLeod and Philip F. Rehbock (Honolulu: University of Hawaii Press, 1994), pp. 140–65; Rudolf A. Raff, *The Shape of Life: Genes, Development, and the Evolution of Animal Form* (Chicago: University of Chicago Press, 1996), pp. 1–4; Brian K. Hall, "John Samuel Budgett (1872–1904): In Pursuit of *Polypterus*," *BioScience*, 51 (2001), 399–407.

controversy too. In passing from von Baer to Haeckel, we move from embryologists' patron saint to a man some treat as the evil genius of the science.[26] Although cemented by a revolt around 1900 against a style that to experimental biologists appeared long on speculation and short on substance, this mixed reputation went back to the 1870s. Courageously, cheered Haeckel's supporters, he not only opened up new topics for research but also made the biogenetic law the central principle of an evolutionary worldview. Outrageously, booed his opponents, he inflamed the general public with dogmatic answers to questions his scientific peers had yet to decide.

Within embryology, Haeckel's most effective adversary was the Basel, later Leipzig, anatomist Wilhelm His (1831–1904), who from the late 1860s combined promotion of the microtome and accurate reconstruction of wax models from the sections. He argued for a mechanical approach, joining the reductionist physiologists in claiming that no evolutionary series could explain development. His sought the mechanisms by which one stage transforms itself into the next, and found them in the bending and folding movements generated by unequal growth. For a long time, neither modeling nor this mechanical view of development caught on, but His's charge, that Haeckel's figures (Figure 16.3) tendentiously made the embryos look more similar than they really were, was very widely taken up.[27]

Evolutionary embryology was a much richer enterprise than one might suppose from the polemics directed against Haeckel, as the largest and softest target. Even his admirers, notably the British embryologists Francis Balfour and E. Ray Lankester, applied the biogenetic law more empirically and more flexibly. Comparative embryology also proved extraordinarily productive of lines of work that, like genetics, obscured their origins as they spun off. The notion of active host resistance to infection, for example, was developed out of the idea that phagocytosis characterizes the mesodermal lineage, which itself arose from a study of metazoan ancestry.[28]

It was mainly Haeckel, however, who took embryology out of medical courses, and the titillating world of the popular anatomy museum, and communicated it to the reading public. Recapitulationism was deployed in fields as diverse as anthropology, child study, and psychoanalysis. As European and North American men of science watched their own male offspring climb to the top of the evolutionary tree, it seemed as if everyone else – criminals, "primitives," and women – had arrested at some lower stage of

[26] For a psychopathologizing view, see Oppenheimer, *Essays in the History of Embryology and Biology*, pp. 150–4.

[27] Nick Hopwood, "'Giving Body' to Embryos: Modeling, Mechanism, and the Microtome in Late Nineteenth-Century Anatomy," *Isis*, 90 (1999), 462–96; Nick Hopwood, "Pictures of Evolution and Charges of Fraud: Ernst Haeckel's Embryological Illustrations," *Isis*, 97 (2006), 260–301.

[28] Alfred I. Tauber and Leon Chernyak, *Metchnikoff and the Origins of Immunology: From Metaphor to Theory* (Oxford: Oxford University Press, 1991).

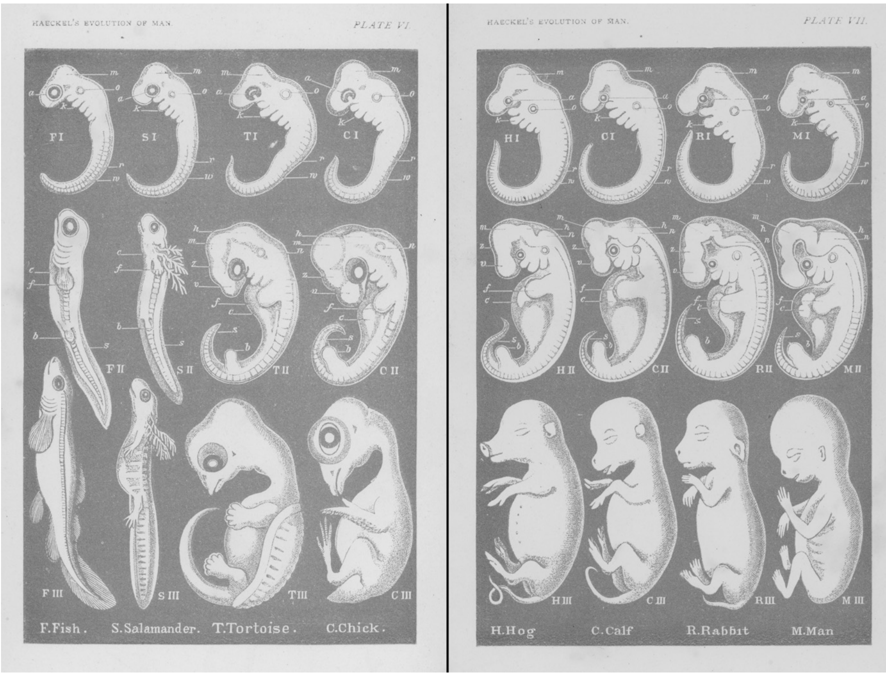

Figure 16.3. Embryology in the age of evolution. Controversial lithographs demonstrating to a wide public the agreement in the relations of form between human and other vertebrate embryos, more or less complete at very early stages (I) and retained longer in more nearly related animals (II, III). From Ernst Haeckel, *The Evolution of Man: A Popular Exposition of the Principal Points of Human Ontogeny and Phylogeny*, 2 vols. (London: Kegan Paul, 1879), vol. 1, plates VI, VII.

development.[29] But what happened to evolutionary embryology beyond the elite? No demonstration of evolution could match the vividness of embryos developing before one's very eyes. But who was encouraged to see the vertebrates' conquest of land in the development of frogspawn collected from a pond? Did Haeckel and his journalist allies persuade pregnant women that they carried first a fish, then a reptile, and only later a human being?

Haeckel reckoned it ridiculous to oppose aborting what he taught began as an animal. But physicians supported, and in the United States campaigned for, laws against abortion – unless performed by themselves. Alarmed at increasing medical intervention in pregnancy, in 1869 Pope Pius IX shifted the Catholic Church from the received distinction between the "inanimate" and the "animate" fetus to a hardline rejection of any abortion at all. Many women meanwhile still held to practices of menstrual regulation that were

[29] Gould, *Ontogeny and Phylogeny*, pp. 115–66. On uses of embryology in literature and art, see especially Evanghélia Stead, *Le monstre, le singe et le foetus: Tératogonie et Décadence dans l'Europe fin-de-siècle* (Geneva: Droz, 2004).

justified by the notion that life was present only from quickening, little knowing or little caring that this had no more authority in an embryology that taught continuity of development than had the Catholic Church's embrace of ensoulment at conception.[30]

EXPERIMENT AND DESCRIPTION

By the 1880s, academic embryology was in turmoil. The inability of teachers to agree, especially on the relative weighting of embryological and comparative anatomical evidence, turned influential students away from evolutionary morphology. They abandoned problems such as the origin of the vertebrates to focus on narrower questions, which they expected to answer using a more limited selection of materials, and many modeled their science on experimental physiology. Indeed, by opposing "experimental" to "descriptive" embryology, the more militant secured an identity as experimental biologists in a science they saw as overly descriptive and rife with unsupported speculation. In the 1970s and 1980s, historians of biology reinvestigated the changes in embryology between 1880 and World War I as exemplifying that wider transformation in the organization, problems, institutions, and methods of the life sciences by which biology as we know it was made. Experimental embryology and genetics were taken as model subdisciplines. Initial efforts to generalize tended to reinforce a one-dimensional view of a "revolt from morphology," but later studies worked to produce a more nuanced and inclusive history.[31] Yet the very agenda of searching for the origins of the new biology has underestimated continuities and excluded significant innovations in human and comparative embryological research.

The most successful iconoclast to emerge from the crisis of evolutionary morphology was Wilhelm Roux (1850–1924), an anatomist working in the 1880s at the University of Breslau (now Wrocław). Founding what he called *Entwicklungsmechanik* ("developmental mechanics"), he established himself over the next two decades as a tireless publicist for the new science and for Wilhelm Roux. By "mechanics" he did not mean the rather crude pressures

[30] McLaren, "Policing Pregnancies." For an opposing interpretation, see David Albert Jones, *The Soul of the Embryo: An Enquiry into the Status of the Human Embryo in the Christian Tradition* (London: Continuum, 2004). On the related debate over embryotomy versus Caesarean section, see Emmanuel Betta, *Animare la vita: Disciplina della nascita tra medicina e morale nell'Ottocento* (Bologna: Il Mulino, 2006).

[31] For surveys, see Jane Maienschein, *Transforming Traditions in American Biology, 1880–1915* (Baltimore: Johns Hopkins University Press, 1991); Nyhart, *Biology Takes Form*, pp. 243–361. See also Paul Julian Weindling, *Darwinism and Social Darwinism in Imperial Germany: The Contribution of the Cell Biologist Oscar Hertwig (1849–1922)* (Stuttgart: Gustav Fischer, 1991); Klaus Sander, "Von der Keimplasmatheorie zur synergetischen Musterbildung – Einhundert Jahre entwicklungsbiologischer Ideengeschichte," *Verhandlungen der Deutschen Zoologischen Gesellschaft*, 83 (1990), 133–77; Reinhard Mocek, *Die werdende Form: Eine Geschichte der Kausalen Morphologie* (Marburg: Basilisken-Presse, 1998).

and pulls by which His had explained the form of the body, but rather signaled a Kantian commitment to causal explanation. Like His, Roux looked to factors in the here and now, but unlike His, he expected conclusive demonstrations of their actions and interactions from experiment alone. In 1888, Roux destroyed with a hot needle one of the two cells formed by cleavage of a fertilized frog egg, a maneuver he likened to throwing a bomb into a textile factory with a view to learning about its internal organization from the change in production. What would the undestroyed cell make? Obtaining a half-embryo (Figure 16.4A), Roux interpreted the result in terms of the "self-differentiation" as opposed to the "dependent differentiation" of the parts.

A year before Roux, Laurent Chabry (1855–1893) had reported a similar experiment on ascidian embryos and with similar results, yet because he worked in the French teratological tradition, these had a different significance. Etienne Geoffroy Saint-Hilaire had varnished hens' eggs in the 1820s, and from the 1850s Camille Dareste, aiming to produce new species by mimicking environmental change, made malformations by the same methods. These naturalists generated new forms to anatomize and taxonomize, or investigated the disturbances for their own sake, rather than using experiment to draw conclusions about normal development. With French zoology on the defensive against Claude Bernard's deterministic physiology, Chabry did not go decisively beyond this tradition, but Roux was oriented toward German physiologists' reductionism and embraced the Bernardian ideal of control.[32]

Roux may have had little to say about evolution, but he was open to phylogenetic questions and included an inherited determination complex among the causal factors of development. In the next generation, Haeckel's student Hans Driesch (1867–1941) accepted his teacher's stark opposition between mechanics and phylogeny, and – cushioned by a private fortune – vehemently rejected evolution. In 1891, shortly after his mathematical-mechanical approach had led Haeckel to recommend a spell in a psychiatric hospital, Driesch carried out a series of landmark experiments. Shaking apart the first two cells of a sea urchin embryo produced not two half-embryos, as Roux's frog results predicted, but two half-sized normal larvae (Figure 16.4B). This discovery of "regulation" set the agenda for a great deal of later work: How could an embryo possibly overcome such massive intervention and still develop into a harmonious whole? Although he had initially worked within a mechanistic framework, by 1900 Driesch had come to doubt that any machine could mimic the regulative ability of the embryo. He became

[32] Frederick B. Churchill, "Chabry, Roux, and the Experimental Method in Nineteenth-Century Embryology," in *Foundations of Scientific Method: The Nineteenth Century*, ed. Ronald N. Giere and Richard S. Westfall (Bloomington: Indiana University Press, 1973), pp. 161–205; Jean-Louis Fischer, *Leben und Werk von Camille Dareste, 1822–1899: Schöpfer der experimentellen Teratologie*, trans. Johannes Klapperstück, Acta historica Leopoldina, vol. 21 (Leipzig: Barth, 1994); Jean-Louis Fischer, "Laurent Chabry and the Beginnings of Experimental Embryology in France," in Gilbert, *Conceptual History of Modern Embryology*, pp. 31–41.

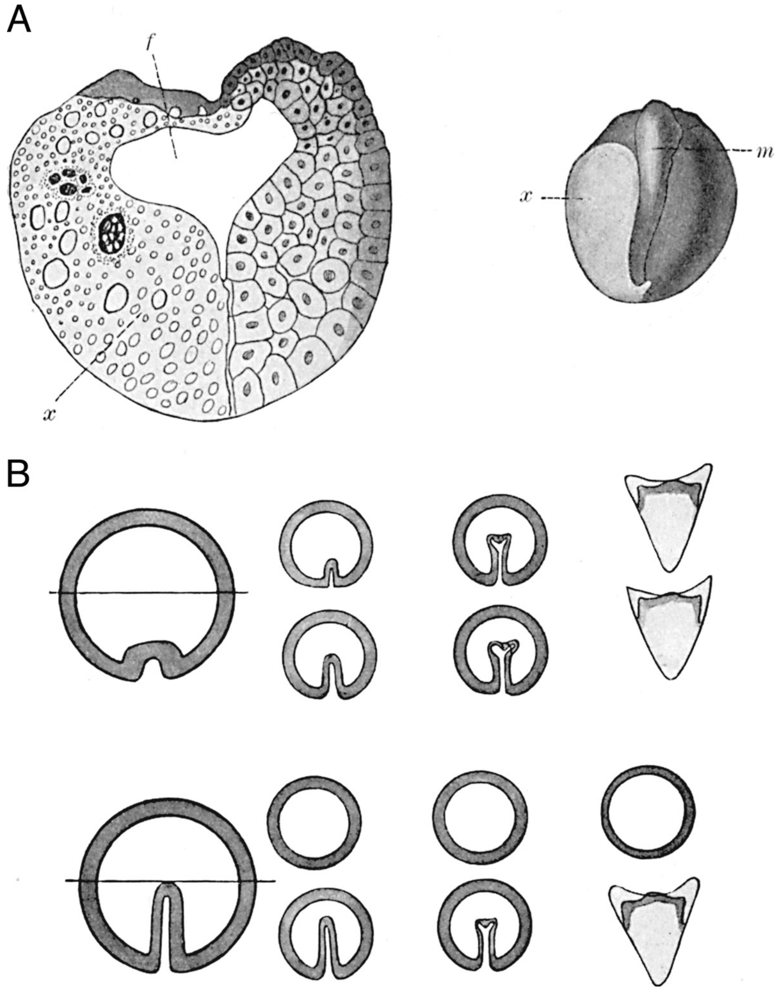

Figure 16.4. Classics of *Entwicklungsmechanik*. (A) Results of Wilhelm Roux's hot-needle experiment: section of frog embryo at blastula stage and dorsal view at neurula stage; "x" marks the damaged half. (B) Schematics of Hans Driesch–style experiments by Thomas H. Morgan showing which divisions of sea urchin embryos during and after gastrulation (upper and lower panels, respectively) regulate to produce whole larvae. From the early textbook by Otto Maas *Einführung in die experimentelle Entwickelungsgeschichte (Entwickelungsmechanik)* (Wiesbaden: Bergmann, 1903), pp. 33, 88.

a philosophy professor and espoused a vitalism that reached very wide audiences but was unpopular among biologists (and philosophers).

Roux found it difficult to establish his new science in the stagnating German university system that militated against specialization; experiments tended merely to embellish rather stable medical courses. So marine stations and independent research institutes became the key European sites of *Entwicklungsmechanik*. In the United States, the field flourished at the Marine Biological Laboratory at Woods Hole on Cape Cod and was also more readily integrated into departments of biology. German emigré Jacques Loeb's artificial parthenogenesis of sea urchin eggs, performed at Woods Hole in 1899, was interpreted in the newspapers as "a long step towards . . . creat[ing] life in a test tube"; feminists were intrigued by the prospect of male redundancy. But *Entwicklungsmechanik* was far from the only game in town: Cell lineage work on invertebrates was neither primarily experimental nor modeled on physiology; painstaking morphological investigations followed cell divisions and colored plasms through the generations.[33]

More generally, descriptive work not only persisted but also changed. Indeed, as the field against which experimentalists demarcated their own endeavors, "descriptive embryology" was arguably only created around 1900. The term "descriptive" had long been used in embryology, but in the early nineteenth century it meant anatomical as opposed to comparative studies, whereas Haeckel used it to disparage work not informed by phylogenetic concerns. Now, as the worthy but dull counterpart of experimental embryology, "descriptive embryology" was reframed to include both comparative and phylogenetic work. Yet though increasingly thrown onto the defensive, and in crisis at the grand theoretical level, "descriptive embryology," especially of the vertebrates, was being transformed technically and institutionally in ways that lastingly shaped embryo science.[34]

The technical transformation was modeled on the monumental study with which in the early 1880s Wilhelm His reformed research on human embryos; though experimentally inaccessible these were the prime medical and anthropological concern. He disciplined physicians to collect rare aborted material, rendered this into embryological drawings, arranged the pictures in developmental order, and selected those most likely to represent normal development for inclusion in a "normal plate" depicting a series of standard images from the end of the first two weeks through the first two months of pregnancy. This was far from trivial: Modern human embryology was founded on the exclusion, after a seven-year controversy, of an embryo described as human – and supporting Haeckel's views – that His eventually persuaded anatomists was in fact that of a bird. The normal plate provided a framework for a wealth of research on human embryos and was used as a model for formalizing developmental sequences in other species.[35]

33 Philip J. Pauly, *Controlling Life: Jacques Loeb and the Engineering Ideal in Biology* (Berkeley: University of California Press, 1987), fig. 10 and pp. 100–1; Jane Maienschein, *100 Years Exploring Life, 1888–1988: The Marine Biological Laboratory at Woods Hole* (Boston: Jones and Bartlett, 1989).

34 Nick Hopwood, "Visual Standards and Disciplinary Change: Normal Plates, Tables and Stages in Embryology," *History of Science*, 43 (2005), 239–303, especially p. 244.

35 Hopwood, "Producing Development"; Hopwood, "Visual Standards and Disciplinary Change."


A


B
Macaca irus. ?


C
FRIEDRICH ZIEGLER in FREIBURG in BADEN.
1 Meter.
AUSSTELLUNG IN CHICAGO 1893.

His also insisted that to grasp complex microscopic structures it was necessary to reconstruct wax models from serial sections. As modeling became a crucial method of research, monographs and articles described models, which Adolf and Friedrich Ziegler of Freiburg in Baden "published" in parallel and sold to institutes all over the world (Figure 16.5C).[36] Scientists who published with the Ziegler studio did not abandon evolutionary interests; they rather used normal plates and plastic reconstruction to reinvestigate Haeckel's questions in exquisitely detailed analyses, especially of scarce and complex mammalian embryos. But embryology's independence was promoted by the perceived need to gain a much stronger empirical basis if the science was to continue to contribute to a phylogeny increasingly dominated by comparative anatomy and paleontology.

This "descriptive" vertebrate embryology was not simply entrenched in old institutes; it took three major institutional initiatives. First, from 1897, the German anatomist Franz Keibel edited an international series of normal plates to provide a basis for reinvestigating the relations of ontogeny and phylogeny. The subsidiary goal, in a science that is often said to have been mired in "typological" thinking, was to study variation between individual embryos.[37] Second, the International Institute of Embryology was founded in 1911 as a club devoted to comparative vertebrate embryology and specifically to promoting the collection and study of the embryos of endangered colonial mammals. Its monument is the Central Embryological Collection of the Hubrecht Laboratory; Figure 16.5A shows jars of whole embryos in alcohol and Figure 16.5B cabinets of sectioned embryos on slides.[38] Third, in 1914, His's student Franklin Paine Mall obtained funds from the Carnegie Institution of Washington for a Department of Embryology at the Johns Hopkins

[36] Hopwood, *Embryos in Wax*.

[37] Hopwood, "Visual Standards and Disciplinary Change."

[38] P. D. Nieuwkoop, "'L'Institut International d'Embryologie' (1911–1961)," *General Embryological Information Service*, 9 (1961), 265–9; Patricia Faasse, Job Faber, and Jenny Narraway, "A Brief History of the Hubrecht Laboratory," *International Journal of Developmental Biology*, 43 (1999), 583–90; Michael K. Richardson and Jennifer Narraway, "A Treasure House of Comparative Embryology," *International Journal of Developmental Biology*, 43 (1999), 591–602.

Figure 16.5 (opposite). Collections of embryos. (A) Whole embryos of the macaque monkey *Macaca irus*, and (B) sections of the embryos on microscope slides at the Central Embryological Collection, Hubrecht Laboratory, Utrecht, in the 1990s. (In 2004, the collection was moved to the Museum für Naturkunde, Berlin.) (C) Friedrich Ziegler's prizewinning display of embryological wax models, many reproduced from plastic reconstructions of serial sections, at the 1893 World's Columbian Exposition in Chicago. From *Prospectus über die zu Unterrichtszwecken hergestellten Embryologischen Wachsmodelle von Friedrich Ziegler (vormals Dr. Adolph Ziegler)* (Freiburg in Baden: Atelier für wissenschaftliche Plastik, 1893). (A–B) courtesy of the Hubrecht Laboratory and (C) Cornell University Library, Rare and Manuscript Collections.

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University in Baltimore; it became a "bureau of standards" for human embryos.[39] The explorers of the gravid uterus compared ever-younger human specimens – increasingly obtained during gynecological operations – with the embryos of "out-of-the-way species" that they "ransacked" from the "jungles and hillsides of the world" or took from colonies, including of primates, at home. Moderating Haeckel's evolutionary zeal, they concluded that the human embryo is an archive in which is written evidence of descent, but it is also a germ, which must live and so is "open for business during construction."[40]

Experiment, we can conclude, worked in two ways: as a practice and as a rhetoric, even an ideology.[41] As a practice, experiment became the method of highest status. As a rhetoric, experimentalism associated its practitioners with modern rigor and control and simultaneously created "descriptive embryology" as its unglamorous other, ideally relegated to a "classical" past. Experiment did not in fact replace analysis but was added to it. Experimentalists sought to reveal the potentialities of parts and analyzed operated embryos for the presence or absence of tissues, cells, or molecules; they also invested time in making standards, "normal stages" adapted from Keibel's plates and "fate maps," against which to assess the effects of their interventions. Nor did "descriptive embryology" just fade slowly into the background; in the years before World War I, when most histories have experimenters making all the running, "descriptive" embryologists founded both the first specifically embryological society and the first research institution dedicated to the science. And though the war seriously disrupted the European initiatives, comparative work continued.

ORGANIZERS, GRADIENTS, AND FIELDS

Building new experimental sciences onto the dilapidated but still inhabited evolutionist mansion threatened its very foundations. And, as debates over mechanism and vitalism engaged wide audiences, it was hard to contain fundamental metaphysical and methodological disputes – especially during war, revolution, and slump. Some biologists and clinicians were more interested

39 Ronan O'Rahilly, "One Hundred Years of Human Embryology," *Issues and Reviews in Teratology*, 4 (1988), 81–128, at p. 93; Lynn Morgan, "Embryo Tales," in *Remaking Life and Death: Toward an Anthropology of the Biosciences*, ed. Sarah Franklin and Margaret Lock (Santa Fe, N.M.: School of American Research Press, 2003), pp. 261–91; Jane Maienschein, Marie Glitz, and Garland Allen, eds., *Centennial History of the Carnegie Institution of Washington*, vol. 5: *The Department of Embryology* (Cambridge: Cambridge University Press, 2004); Hopwood, "Visual Standards and Disciplinary Change," pp. 281–4.

40 Quotations from George W. Corner, *Ourselves Unborn: An Embryologist's Essay on Man* (New Haven, Conn.: Yale University Press, 1944), p. 28; O'Rahilly, "One Hundred Years of Human Embryology," p. 99.

41 Oppenheimer, *Essays in the History of Embryology and Biology*, pp. 4–10; Maienschein, *Transforming Traditions in American Biology*; Pickstone, "Museological Science?"

in what, from organ transplantation to limb regeneration, they might make Roux's science do. Others, seeking to unify the life sciences, warned of a crisis and searched for a synthesis. Those working in "*Entwicklungsmechanik*," "developmental physiology," or "experimental morphology," as it was variously called, adopted two strategies for bringing order. In 1919, Haeckel's last student, Julius Schaxel, argued that only wholesale theoretical clarification could overcome fragmentation, discipline speculation, and guide experiment, and he founded the first journal of "theoretical biology."[42] Others pursued experimental programs using highly productive systems to define "organizers," "gradients," and "fields," organicist entities designed to avoid both the mechanist Scylla and the vitalist Charybdis.[43]

Early twentieth-century experimentalists refined the tools for answering the questions raised by Roux and Driesch. Under low-power stereomicroscopes, they exploited especially the remarkable healing powers of amphibian embryos, transplanting tissue from one embryo to another or removing it for culture in isolation. Some manipulations focused on cells. In 1907, American zoologist Ross Harrison (1870–1959) explanted parts of the larval neural tube into clotted lymph; by watching living neuroblasts send out fibers, he decisively supported the neuron doctrine and pioneered modern cell culture. Other experiments asked whether a graft would develop according to its origin or its new location, or whether an explant had become self-sufficient or still needed further interactions. In this way, Harrison defined the mesodermal cells of the limb rudiment as what would be called a "field," a physically bounded area of interaction within which state of determination is a function of position.[44]

Chicago biologist Charles Manning Child (1869–1954) cut a piece out of the middle of a flatworm and found that anterior structures regenerated anteriorly and posterior structures at its posterior end. Each cell could form any structure; what it made appeared to be determined by an original polarity. Some saw here gradients of a formative substance, but shortly before World War I, Child articulated a dynamic view of a polarity of activity. Flatworms placed in a cyanide solution died from the head backward, indicating an anteroposterior gradient in metabolic rate, which, he argued, was expressed in the structure of the worm. Developmental plasticity supported an antihereditarian social philosophy but also a disciplinary politics: As carriers of developmental memory, gradients competed with the genes to explain inheritance.[45]

[42] Nick Hopwood, "Biology between University and Proletariat: The Making of a Red Professor," *History of Science*, 35 (1997), 367–424.

[43] Donna Jeanne Haraway, *Crystals, Fabrics, and Fields: Metaphors of Organicism in Twentieth-Century Developmental Biology* (New Haven, Conn.: Yale University Press, 1976).

[44] Maienschein, *Transforming Traditions in American Biology*, pp. 261–89; Klaus Sander, "An American in Paris and the Origins of the Stereomicroscope," *Roux's Archives of Developmental Biology*, 203 (1994), 235–42.

[45] Gregg Mitman and Anne Fausto-Sterling, "Whatever Happened to *Planaria*? C. M. Child and the Physiology of Inheritance," in *The Right Tools for the Job: At Work in Twentieth-Century Life Sciences*,

Just as axial gradients originated in ideas of polarity and postulated a privileged region, so did the "organizers" of German zoologist Hans Spemann (1869–1941). He led the dominant school of interwar embryologists in microsurgery with fine glass instruments on cultures of amphibian spawn (Figure 16.6A). At Freiburg in the early 1920s, Spemann's student Hilde Pröscholdt (later Mangold) carried out the most exciting biological experiment of the age. She transplanted the "dorsal lip" of a newt gastrula into the belly of a host embryo of a more darkly pigmented species and found that it induced the host tissues to participate in the formation of a secondary axis, including a central nervous system (Figure 16.6B). Spemann called the dorsal lip the "organizer," which in Germany on the brink of civil war was a metaphor for the restoration of social order. He envisaged development as a sequence of inductive interactions following this "primary" induction and in 1936 won a Nobel Prize.[46]

The productivity of these experimental systems stimulated even such polymaths as Julian Huxley to concentrate their laboratory work in embryology and fueled his and his brother Aldous's science fiction. Julian's "amazing story" of 1927 had a British researcher become religious adviser to an African king and mass-produce "living fetishes," including double-headed toads and three-headed snakes, by applying the "methods of Mr. Ford" to some of Spemann's and Harrison's artisanal experiments. Excitement reached fever pitch with the discovery in 1932, mainly by Spemann's student Johannes Holtfreter (1901–1992), that fixed, boiled, or otherwise mistreated organizers induced normal structures. The suggestion that the active principle could be isolated chemically captivated a group of Cambridge radicals who had started to meet in an informal "Theoretical Biology Club." Joseph Needham (1900–1995) and comrades took from Germany both Schaxel's vision of a theoretical biology and Holtfreter's embryological techniques, and combined them with the local biochemistry. The team prepared cell-free inducing extracts, but their organicist molecular models respected different hierarchical levels in the whole embryo.[47]

In practice, the organizer proved biochemically intractable, and attempts to marry organizers and gradients or gradients and fields were short-lived. Instead of leading a grand embryological synthesis, by the mid-1940s

ed. Adele E. Clarke and Joan H. Fujimura (Princeton, N.J.: Princeton University Press, 1992), pp. 172–97.

46 Peter E. Fäßler, *Hans Spemann, 1869–1941: Experimentelle Forschung im Spannungsfeld von Empirie und Theorie. Ein Beitrag zur Geschichte der Entwicklungsphysiologie zu Beginn des 20. Jahrhunderts* (Berlin: Springer, 1997).

47 C. Kenneth Waters and Albert Van Helden, *Julian Huxley: Biologist and Statesman of Science* (Houston, Tex.: Rice University Press, 1992); Julian Huxley, "The Tissue-Culture King," *Yale Review*, 15 (1926), 479–504; Susan Merrill Squier, *Babies in Bottles: Twentieth-Century Visions of Reproductive Technology* (New Brunswick, N.J.: Rutgers University Press, 1994), pp. 24–62; P. G. Abir-Am, "The Philosophical Background of Joseph Needham's Work in Chemical Embryology," in Gilbert, *Conceptual History of Modern Embryology*, pp. 159–80.

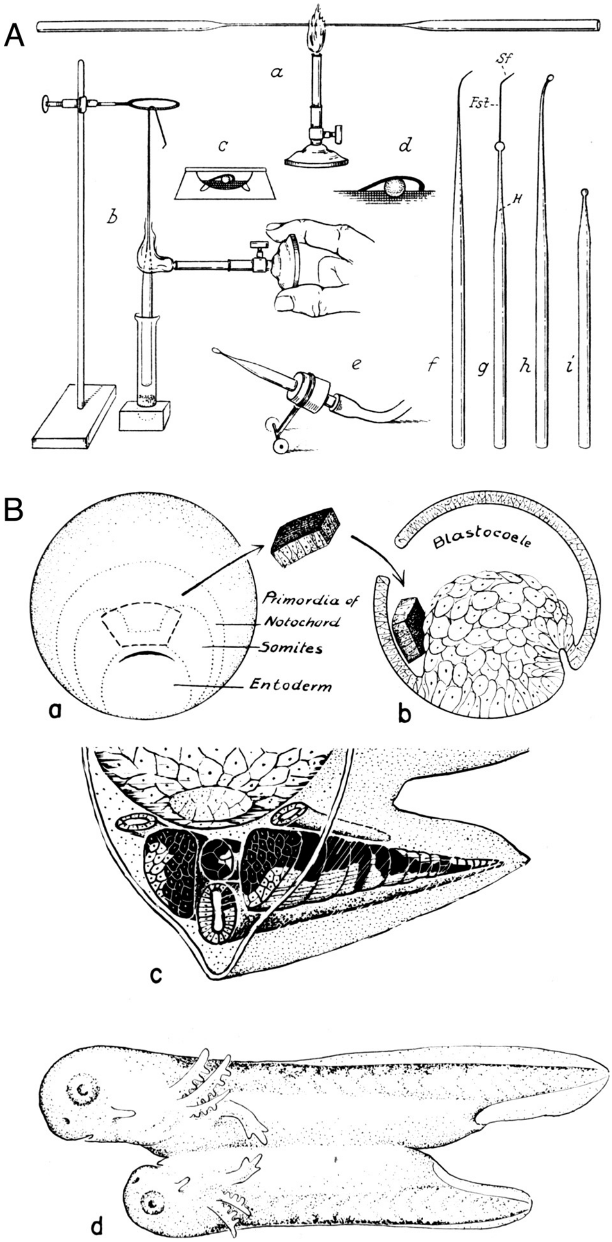

Figure 16.6. Hans Spemann's developmental physiology. (A) How to make the microsurgical instruments; from Otto Mangold, *Hans Spemann, ein Meister der Entwicklungsphysiologie: Sein Leben und sein Werk* (Stuttgart: Wissenschaftliche Verlagsgesellschaft, 1953), p. 111. (B) Simplified design of the organizer graft, in which (a) the dorsal lip from a darkly pigmented donor is (b) inserted into the blastocoelic cavity of a lightly pigmented host, where it (c, d) induces host tissues to participate in forming a secondary axis. From J. Holtfreter and V. Hamburger, "Amphibians," in *Analysis of Development*, ed. Benjamin H. Willier, Paul A. Weiss, and Viktor Hamburger (Philadelphia: Saunders, 1955), pp. 230–96, at p. 244.

embryologists found themselves on the sidelines of the distinctly nonembryological Modern Evolutionary Synthesis. Anachronistically, "chemical embryology" is often reckoned to have run into the sands because the problem needed the molecular biological techniques that were not applied to it until the 1980s. Historically, we can understand the fate of embryology only in relation to other sciences with alternative programs. We should also remember that in many departments embryology remained a comparative science well into the postwar era.

EMBRYOS, CELLS, GENES, AND MOLECULES

A major drive in twentieth-century biology was to gain access to, and perhaps to explain, mechanisms of development through the properties of cells, molecules, and genes. But other sciences – especially biochemistry, molecular biology, and genetics – claimed embryonic components for themselves. What were their relations to embryology, and what was their relative status and success? Embryology appears in the decades around 1900 as the powerhouse of the new biology, generating such key innovations as cell culture and the gene. After World War II, by contrast, it struck biochemists, geneticists, and the new molecular biologists as a field of great problems but no progress. Recast by the 1960s as "developmental biology," in the last quarter of the twentieth century it was a very active area of research.

The first geneticists drove a wedge between genetic transmission and embryonic development, between nucleus and cytoplasm. Genetics has been better funded, of higher status, and, until recently, more successful; developmental biology has been championed as a more holistic, feminine, embodied, and European alternative to the dominantly reductionist, masculine, abstract, and American style of genetics.[48] American genetics in part came out of an embryological debate in the early 1900s about the relative importance of the nucleus and cytoplasm in development; Thomas H. Morgan's work on the fruit fly *Drosophila* convinced him of the importance of the nucleus and the chromosomes on which he began to localize genes. Interwar embryologists, conversely, came to regard the cytoplasm as the more interesting part of the cell; genes that affected only eye color struck them as too trivial to explain how the eye itself formed. Greater pragmatism, and funding by agricultural and eugenic interests, allowed geneticists to claim pride of place in an evolutionary synthesis organized around quantitative change in gene frequencies. Whereas in the late nineteenth century the mechanism of evolution was development, by shunning evolutionary questions, experimental

[48] Evelyn Fox Keller, *Refiguring Life: Metaphors of Twentieth-Century Biology* (New York: Columbia University Press, 1995), pp. 3–42.

embryology had left a vacuum for genetics to fill.[49] (See Burian and Zallen, Chapter 23, this volume.)

After World War II, massive investment in other biomedical sciences pushed embryology to the margins. Research continued, however, on a series of levels, from the whole embryo through cells to molecules, until in the 1960s the science was reformed. In the United States, from 1939, the Society for the Study of Growth, later the Society for Developmental Biology, brought embryologists and other scientists together. In the early 1930s, the International Institute of Embryology had made a modest overture to experiment, and in 1968 it was renamed the International Society of Developmental Biologists. Developmental biology was a joint initiative of self-consciously "modern" embryologists and geneticists, biochemists, cell biologists, and molecular biologists who saw a field ripe for their skills. It took over the problems and practices of experimental embryology but drew on other resources to claim a universal role in explaining development and differentiation throughout the living world.[50]

The new field's key generalization was development as differential gene expression. From the late 1930s, when several influential embryologists and geneticists converted to "developmental genetics," it became clear that mutations could have embryologically interesting effects. Transplantations of nuclei from differentiated frog cells into enucleated eggs suggested from the late 1950s that they still had all the genes to make at least a tadpole, perhaps a frog – and sparked a public debate about cloning. At the Pasteur Institute in Paris, molecular biologists presented bacterial genes turning on and off in response to environmental stimuli as a model for multicellular differentiation. Did the ensuing drive to investigate "gene activity in early development" represent a long takeover of embryology by genetics and molecular biology or is it better seen as an updated version of (bio)chemical embryology? Tools were increasingly imported from outside, but the traffic was not all one way. There remained among embryologists a powerful impetus toward molecular analysis: Around 1960, Jean Brachet's nucleic acid cytochemistry had a hand in the notion of mRNA, and in the 1970s frog oocytes became a favored system for testing the expression of eukaryotic genes.[51]

[49] Reviewed in Scott F. Gilbert, John M. Opitz, and Rudolf A. Raff, "Resynthesizing Evolutionary and Developmental Biology," *Developmental Biology*, 173 (1996), 357–72.

[50] Jane M. Oppenheimer, "The Growth and Development of Developmental Biology," in *Major Problems in Developmental Biology*, ed. Michael Locke, Symposia of the Society for Developmental Biology, vol. 25 (New York: Academic Press, 1966), pp. 1–27; Oppenheimer, *Essays in the History of Embryology and Biology*, pp. 1–61; Keller, *Refiguring Life*.

[51] Scott F. Gilbert, "Induction and the Origins of Developmental Genetics," in Gilbert, *Conceptual History of Modern Embryology*, pp. 181–206; Richard M. Burian, "Underappreciated Pathways toward Molecular Genetics as Illustrated by Jean Brachet's Chemical Embryology"; Scott F. Gilbert, "Enzymatic Adaptation and the Entrance of Molecular Biology into Embryology," in *The Philosophy and History of Molecular Biology: New Perspectives*, ed. Sahotra Sarkar, Boston Studies in the Philosophy of Science, vol. 183 (Dordrecht: Kluwer, 1996), pp. 67–85, 101–23. For contrasting views, see

As studies of cell differentiation continued, some developmental biologists insisted that there was more to development than that. How did the embryo make not just skin, muscle, and bone – but a hand? One answer was morphogenesis, a term used in this period to refer specifically to changes in embryonic form in early development, notably gastrulation and neurulation. In the mid-1950s, attention was focused on the cell surface by experiments showing that if cells from different germ layers were disaggregated, mixed, and reaggregated, they could re-sort. Scientists in the borderlands of embryology and cell biology explored cell adhesion and locomotion, attempting to understand their coordination and searching for the subcellular components responsible for their specificity. But from the late 1960s, "pattern formation" was promoted as deeper than either differentiation or morphogenesis. The concept of "positional information" sought to specify how cells "know" their relative positions in a field and regulate by recognizing discontinuities. With experiments on insect embryos, this boosted gradients back into the mainstream – but now of "morphogens" activating batteries of genes in patterns.[52]

Developmental biology was made in part by reinventing experimental embryology, in part by biochemists and molecular biologists who despised the embryological tradition but saw in its failure a challenge. Embryology appeared to one biochemist as "a field so primitive that no modern research was being done in it. And yet it had this huge, incredible problem – how an egg develops into a multicelled organism."[53] In the mid-1970s, Christiane Nüsslein-Volhard (b. 1942) went from molecular biology to learn methods for working with mutations that affected early *Drosophila* embryos – and then increased their productivity a hundredfold. At the European Molecular Biology Laboratory in Heidelberg, she and Eric Wieschaus screened not for a couple of genes but for all those controlling segmentation.[54] This was not "molecular" work but classical developmental genetics pursued in an unusually aggressive style; combining it with experimental embryology and new technology for cloning the genes won them a Nobel Prize. Nüsslein-Volhard's colleagues did not just represent the progressive specification of the axes in terms of a hierarchy of interacting genes, mRNAs, and proteins (Figure 16.7); they visualized a gradient of the anterior morphogen and watched how changing its concentration altered the body plan. In the 1980s, some

J. B. Gurdon, "Introductory Comments," and G. M. Rubin, "Summary," in "Molecular Biology of Development," *Cold Spring Harbor Symposia on Quantitative Biology*, 50 (1985), 1–10 and 905–8, respectively.

52 Sander, "Von der Keimplasmatheorie zur synergetischen Musterbildung," pp. 162–72; L. Wolpert, "Gradients, Position and Pattern: A History," in *A History of Embryology*, ed. T. J. Horder, J. A. Witkowski, and C. C. Wylie (Cambridge: Cambridge University Press, 1985), pp. 347–62.

53 Donald D. Brown, quoted in Patricia Parratt, *One Scientist's Story*, Perspectives in Science, vol. 4 (Washington, D.C.: Carnegie Institution, 1988), p. 6.

54 Evelyn Fox Keller, "*Drosophila* Embryos as Transitional Objects: The Work of Donald Poulson and Christiane Nüsslein-Volhard," *Historical Studies in the Physical and Biological Sciences*, 26 (1996), 313–46.

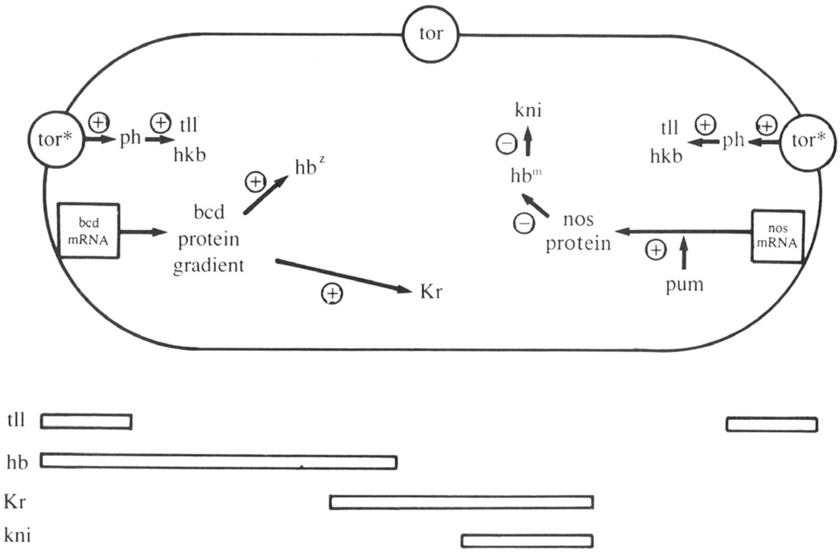

Figure 16.7. Roles of the maternal genes that control the anteroposterior pattern in *Drosophila* in activating (+) or repressing (−) expression of the first zygotic developmental genes (bars below). From J. M. W. Slack, *From Egg to Embryo: Regional Specification in Early Development*, 2nd ed. (Cambridge: Cambridge University Press, 1991), p. 238.

embryologists saw molecular cloning as finally reducing development to gene expression and developmental biology to an anonymous grind in the sweatshops of molecular cell biology. By the 1990s, however, they were analyzing complex phenomena, including Spemann's organizer and flower formation, with techniques of unprecedented sophistication and depth, displaying and manipulating embryos as never before.

Developmental biology focused on principles it claimed would be universal and so could be studied in whatever species was most convenient. By the late 1980s, most work used one of only a half dozen "model organisms": *Drosophila*, the frog *Xenopus*, mouse, chick, a nematode worm, and zebrafish, plus the mustard *Arabidopsis* as a model flowering plant.[55] Frog embryologists transplanted, microinjected, and did biochemistry but almost no classical genetics; drosophilists mutated and crossed but struggled to manipulate the embryo directly. As the field expanded, they formed distinct communities specializing in different phenomena and techniques and attending organism-specific meetings. Textbooks had long presented a composite view,

[55] Jessica A. Bolker, "Model Systems in Developmental Biology," *BioEssays*, 17 (1995), 451–5; Soraya de Chadarevian, "Of Worms and Programmes: *Caenorhabditis elegans* and the Study of Development," *Studies in History and Philosophy of Biological and Biomedical Sciences*, 29 (1998), 81–105; John B. Gurdon and Nick Hopwood, "The Introduction of *Xenopus laevis* into Developmental Biology: Of Empire, Pregnancy Testing and Ribosomal Genes," *International Journal of Developmental Biology*, 44 (2000), 43–50.

exemplifying different developmental mechanisms in whatever systems had been engineered for a particular job. The investment necessary to make a species accessible to genetics and/or molecular biology reinforced a paradoxical ghettoization. But searches for homologous DNA sequences across the animal kingdom showed, for example, that flies and mice have a similar set of genes, arranged in the same chromosomal order, which they use to identify the same relative positions along the anteroposterior axis. This breathed new life into once-scorned evolutionary studies; it again appeared rewarding to work not just on fruit flies but on bugs, spiders, and lobsters as well. Promoters of "evo-devo" hold out the prospect of a new synthesis organized around macroevolution, homology, and embryology, the very problems that the Modern Synthesis excluded.[56]

EMBRYOLOGY AND REPRODUCTION

Although many experimental embryologists and developmental biologists took biomedical funding but valued independence from medical service roles, much embryology in the twentieth century was oriented primarily toward medicine and agriculture. Those studying mammals especially have been engaged not only in academic biology but also in rationalizing human and animal reproduction. Promoting its scientific representation, planning, and control has begun to achieve long-term goals but also galvanized a wide range of critics, from antiabortionists to feminists, from conservative defenders of "traditional" families to red-green opponents of commodifying life.

Anatomist-embryologists continued to be responsible for teaching human development to medical students from textbooks that Carnegie Institution scientists revised with ever more complete embryonic series. In Boston, between 1938 and 1953, gynecologist John Rock and pathologist Arthur T. Hertig recovered fertilized eggs in the first two weeks of development from women scheduled for hysterectomies. The doctors increased the chances and value of a successful "egg hunt," as they called it, by asking their patients to keep rhythm charts in the months before surgery and to note if and when they had sex during their last fertile period. The operation was set for shortly after ovulation, and Hertig took embryos to the Carnegie Department for sectioning.[57]

In the early twentieth century, human embryology's association with sex and evolution still tended to keep it out of the schools. So it was adult educators and sex reformers who first made series of human embryos part

[56] Gilbert, Opitz, and Raff, "Resynthesizing Evolutionary and Developmental Biology"; Walter J. Gehring, *Master Control Genes in Development and Evolution: The Homeobox Story* (New Haven, Conn.: Yale University Press, 1998).

[57] O'Rahilly, "One Hundred Years"; Loretta McLaughlin, *The Pill, John Rock, and the Church: The Biography of a Revolution* (Boston: Little, Brown, 1982), pp. 58–92.

Figure 16.8. Communicating the embryological vision of pregnancy with a Schick anatomical chart at a maternity welfare center in Paddington, London, around 1950 (London Metropolitan Archives, photograph 80/7364).

of the scientific facts of life (Figure 16.8). Having encountered social worlds in which eggs, sperm, and developing embryos were by no means taken for granted, they deplored what they presented as women's "ignorance" of their own bodies. Working-class women who sought abortions because a missed period indicated that "clotted blood" needed "tipping out" were ignorant by the standards of the relatively new medical knowledge, but their practical understandings of how babies were (not) made often worked.[58]

Embryologists' claims to provide physicians and midwives with knowledge relevant to obstetrics and gynecology had always been strained. But as pregnancy became hospitalized after World War II, obstetric technologies – as x-rays gave way to ultrasound – increasingly visualized inside the womb what embryologists had described only postmortem. Obstetricians, whose primary charge had been the pregnant woman, became advocates for a "fetal patient" that physiologists represented as active and in control. But the unborn may be constructed in diametrically opposed ways. While a fetus is the subject of surgical intervention inside the body of a pregnant woman, in the same hospital, aborted material may be used as a tool for transplantation or research. Embryos and fetuses are now supercharged with controversy. Since the early 1980s, antiabortion activists have deployed embryonic and

[58] Cornelie Usborne, "Rhetoric and Resistance: Rationalization of Reproduction in Weimar Germany," *Social Politics*, 4 (1997), 65–89, at pp. 80–1.

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fetal images as weapons against the reforms of the late 1960s and early 1970s. Feminists critiqued icons of the "unborn child" for blurring the distinction between embryo and baby, and – like much human embryology – for constructing an illusion of autonomous fetal development only by effacing pregnant women.[59]

In the early twentieth century, reproductive scientists carved out from embryology a new field of research on sex, but attempts to control reproduction by manipulating gametes and early embryos continued to overlap with embryology. After World War II, in vitro fertilization and embryo transfer were presented as offering the potential for livestock to be bred more intensively from valuable females and for women to overcome infertility caused by blocked Fallopian tubes. During the 1950s, earlier reports of in vitro fertilization became so mistrusted that it was very hard to make claims stick. The 1969 announcement that Robert Edwards, a physiologist at the University of Cambridge, had managed it for humans was universally accepted only a decade later, when he collaborated with Oldham gynecologist Patrick Steptoe and technical assistant Jean Purdy to help Lesley Brown have a baby by laparoscopically removing a mature oocyte, fertilizing it in vitro, and replacing the embryo in her uterus. Meanwhile, culture techniques had begun to overcome the obstacles to experimental analysis of the small and inaccessible mammalian embryos, and in the 1970s cattle embryo transfer was made a major international business. The 1997 report of the cloning of a sheep by nuclear transplantation from an adult udder realized developmental biologists' long-standing ambition to show that the nucleus of a differentiated mammalian cell is totipotent. This technique, combined with advances in stem-cell culture, is also opening up new markets in agriculture, pharmaceuticals, and "regenerative medicine."[60]

The second wave of feminism brought radical broadsides against embryology's complicity in a male takeover of female procreative powers. Feminists in and around developmental biology – where women were by the 1980s and 1990s unusually well represented – led a more conciliatory and more successful campaign against, for example, mapping stereotypes of active male

[59] Ann Oakley, *The Captured Womb: A History of the Medical Care of Pregnant Women* (Oxford: Blackwell, 1984); Monica J. Casper, *The Making of the Unborn Patient: A Social Anatomy of Fetal Surgery* (New Brunswick, N.J.: Rutgers University Press, 1998); Lynn M. Morgan and Meredith W. Michaels, eds., *Fetal Subjects, Feminist Positions* (Philadelphia: University of Pennsylvania Press, 1999).

[60] Adele E. Clarke, *Disciplining Reproduction: American Life Sciences and "The Problems of Sex"* (Berkeley: University of California Press, 1998); Robert Edwards and Patrick Steptoe, *A Matter of Life: The Story of a Medical Breakthrough* (London: Hutchinson, 1980); C. E. Adams, "Egg Transfer: Historical Aspects," in *Mammalian Egg Transfer*, ed. C. E. Adams (Boca Raton, Fla.: CRC Press, 1982), pp. 1–17; John D. Biggers, "*In vitro* Fertilization and Embryo Transfer in Historical Perspective," in *In vitro Fertilization and Embryo Transfer*, ed. Alan Trounson and Carl Wood (London: Churchill Livingstone, 1984), pp. 3–15; Gina Kolata, *Clone: The Road to Dolly and the Path Ahead* (London: Allen Lane, 1997); Sarah Franklin, "Ethical Biocapital," in Franklin and Lock, *Remaking Life and Death*, pp. 97–127.

and passive female onto sperm/nucleus and egg/cytoplasm.[61] Since the birth of Louise Brown, many have been assisted to have much-wanted children. In spite of criticism of the heavy emotional, physical, and financial costs to women of a procedure that usually failed, the discussion quickly moved on to the legal regulation of the market in reproductive services and the ethics of experimentation on surplus embryos. In response to a backlash from antiabortion groups, British scientists lobbied to be allowed to continue embryo research. Although in clinics eggs may be represented as children as little as an hour after fertilization, scientists argued that research should be permitted until the appearance of the primitive streak, an early sign of gastrulation. Whereas in the United States a ban on federal funding pushed the work into an unregulated private sector, in 1990 the U.K. Parliament recognized it as legitimate up to fourteen days but as requiring strict regulation by a Human Fertilization and Embryology Authority.[62]

At the start of the twenty-first century, embryology is again a high-profile science, as it was at the beginnings of the nineteenth and twentieth. But embryologists no longer just analyze embryos or even intervene experimentally in development; cloning companies and fertility clinics are creating new organisms. The identities and relations of embryology have also been transformed. Most dramatically and controversially, embryological practices and products have been powerfully extended into medicine, agriculture, and everyday life.

[61] Gena Corea, *The Mother Machine: Reproductive Technologies from Artificial Insemination to Artificial Wombs* (London: Women's Press, 1985); Scott F. Gilbert and Karen A. Rader, "Revisiting Women, Gender, and Feminism in Developmental Biology," in *Feminism in Twentieth-Century Science, Technology, and Medicine*, ed. Angela N. H. Creager, Elizabeth Lunbeck, and Londa Schiebinger (Chicago: University of Chicago Press, 2001), pp. 73–97.

[62] Sarah Franklin, *Embodied Progress: A Cultural Account of Assisted Conception* (London: Routledge, 1997); Michael Mulkay, *The Embryo Research Debate: Science and the Politics of Reproduction* (Cambridge: Cambridge University Press, 1997).