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Evolution of human gametes–oocytes

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Evolution in outline

Remarkably enough, fossil relics of pre-metazoan unicellular life are recognizable as far back as the period between 3900 and 3400 Myr (million years ago) (Strother, 1989). Though their systematic status is unknown, the spheres and filaments that are visible in the rocks are thought to be the remains of prokaryotes, which would have required the support of firm cell walls, and in some instances these organisms could have been cyanobacteria. Undoubted stomatolite remains date from about 3000 Myr, and many more instances of presumed early organisms, including eukaryotes, are evidenced from about 1500 Myr onwards. Consistently with this estimate, de Duve (1991) maintains that the transition from prokaryote to eukaryote must have taken about 2000 Myr. Representatives of most invertebrate phyla were already established by the start of the Cambrian era 1600 Myr, and pre-Cambrian rocks were subjected to such temperatures and pressures that useful fossil evidence of complex organisms there is scarce (Table 1).

Modern blue-green algae, similar to those responsible for stromatolite formations, reproduce asexually by means of spores, as well as sexually with ciliated gametes, but there does not appear to be evidence relating to gametes of any kind in the fossil record; of course, it is quite possible that multiplication in the early forms took place without the involvement of gametes. Consequently (as with 'Evolution of human gametes – spermatozoa' in 'The Spermatozoon'), the course of evolution of eggs or macrogametes of man and other species must be inferred from the taxonomic relationships of whole organisms, as revealed in fossil relics or by the detailed study of existing forms.

Valentine & Erwin (1987) proposed that the impressive Cambrian 'explosion' in animal forms was possible because the genetic programme of animals was then more flexible. As evolution proceeded, successful genetic sequences became 'locked in', so that the possibilities of change progressively diminished. However,

Table 1. *Evolution in outline* (approximate dates for the first appearance of many living forms)

(Earth began	4500 Myr)
Prokaryotes	3900–3400
Invertebrates	3400–1500
Stromatolites	3000
Plant life	2500
Eukaryotes	1500
First vertebrates	500–600
Tetrapods	425
Amphibians	370
Reptiles	320
Mammals (primitive)	220
Mammals (modern groups)	150
Primates	65
(Extinction of dinosaurs and radiation of mammals)	64
Primitive apes (*Propliopithecus*)	38–24
Primate radiation	26–7
Hominidae	15–5
Australopithecus afarensis	4
Homo erectus	3–1.5
'African Eve'	0.2

this situation could be changed dramatically by major catastrophies, and the mass extinction which terminated the era of the dinosaurs about 64 Myr allowed reptiles, birds and mammals to radiate. Ohno (1985) has argued much along the same lines, namely that evolution is, in effect, 'a continuous series of irrevocable commitments', the first of which was the adoption of three base triplets as codons for protein synthesis. Each new commitment reduced the range of future possibilities, and so variation became increasingly restricted, and progressively each apparent innovation is in fact attributable to a modified gene. With something of the order of 150 000 genes in mammals, and the prospects of interactions between genes and between their induced characters, the possible range of responses would be sufficient to account for the remarkable diversity of animal and plant life.

As to the origins of man himself, the evidence is really quite abundant (see, for example, Campbell, 1979). The first identifiable primates (admittedly recognizable from evidence of continuity rather than morphology) are represented by fossils found in strata dating back to the start of the Tertiary period, about 65 Myr. More abundant relics occur in the Paleocene (65–54 Myr), some 60

genera being recognized, grouped in eight families (the three most primitive genera were rodent-like and later became extinct). Approaching 38 Myr, the fossils represent more advanced forms, resembling contemporary lemurs and tarsiers. During the Oligocene (38–26 Myr), primitive monkey forms are recognizable and some very primitive apes, labelled *Parapithecus*. More distinctive forerunners of apes were *Aelopithecus*, an ancestral gibbon, and *Aegyptopithecus* phyletic to modern great apes. There was also *Propliopithecus* which was possibly ancestral to the hominids. During the Miocene (26 Myr to as recently as 7 Myr), the fossil record reveals 50 species in 20 genera of large primates, including *Dryopithecus fontani*, a species of large ape that was notably numerous. Also relatively abundant among the Miocene relics are entities classed as *Hominidae*, which separated from the ape stock between 15 and 5 Myr. Notable members of this group were *Ramapithecus* and *Kenyapithecus*. Then, about 4 Myr, the Australopithecine series began, exhibiting the highly significant innovation of erect stance and bipedal progression; the earliest representative was *A. afarensis*, of which an unusually complete collection of bones has been made. Finally, the apparent forerunner of modern man emerged in the form of *Homo erectus*, between 3 and 1.5 Myr, the bones being accompanied by crude stone tools.

Modern biochemical technology has produced a large body of evidence that is broadly confirmatory of the archaeological data. Thus the indications from amino acid sequencing, restriction mapping of mitochondrial DNA, sequencing of mitochondrial and genomic DNA and analysis of the globin gene complex all put the period of separation of human and chimpanzee stocks at between 5 and 10 Myr.

The most recent advancement for the human race could have resulted from the acquisition of the power of speech, and there are reasons to believe that this occurred in a group of Australopithecines in Africa about 200 000 years ago. The evidence rests on analyses that have been made of mitochondrial DNA in 147 living individuals from five geographic populations, the results being interpreted to show this time and place of the probable common origin (Cann, Stoneking & Wilson, 1987).

Diverse ways of multiplying

Quite an impressive variety of methods is employed by living organisms to multiply their kind (or by man to multiply other creatures) and a number of these is set out in Table 2. The first four systems listed do not involve gametes, but are included here as they could well represent procedures that were preliminary to the evolution of gametes. In many instances, species depend on more than one method (as, for example, both sexual reproduction and 'identical' twinning

Table 2. *Reproductive strategies*

	Description	Species
Binary fission	Whole-body division into two parts	Protozoa to identical twinning in mammals
Multiple fission	Whole-body division into many parts	Protozoa to identical twinning in mammals
Autogamy	Twin daughter cells unite	Protozoa, e.g., *Actinophrys sol*
Endogamy	Union of descendants of one cell after several divisions	Protozoa, e.g. *Paramecium aurelia*
Syngamy	Union of specialized sex cells after meiosis	
	(a) Union in the same individual	*Dicyema* and other hermaphrodites, e.g. *Serranus, Sagus*
	(b) Union in different individuals	Mammals and others
Parthenogenesis		
Cyclical	Parthenogenesis and sexual reproduction alternating	Rotifers, aphids, *Daphnia*
Arrhenotoky	Production of haploid males (ameiotic)	*Hymenoptera,* turkeys
Thelytoky		
Apomictic	Production of haploid females (ameiotic)	Cockroaches, *Pyknocelis*
Automictic	Ditto but with meiosis and fusion of nuclei	*Lacerta* and *Cnemidophorus* spp.
Deuterotoky (or amphitoky)	Production of both sexes without mating but with meiosis	
Gynogenesis	Females produce young after mating but without syngamy	*Poecilia* (Amazon molly) and *Poeciliopsis*
Androgenesis	*Development with only paternal chromosomes*	
	Experimental:	Various animals
	Natural:	Human hydatidiform mole
Paedogenesis	Reproduction by larvae within mother	Gall flies, midges
Artificial	Development from eggs stimulated by heat, cold, acid, needle prick, etc.	Frogs, fish etc.

by man), but for conciseness not all of the possible combinations are shown in the Table.

Multiplication by whole-body fission

The simplest way organisms can multiply is by whole-body subdivision, i.e. 'binary' or 'multiple fission', most evident in the Protista. Binary fission involves cleavage into two parts immediately after mitosis, whereas in multiple fission the nucleus commonly divides several times within the cell body, and the cytoplasm fragments terminally. Many Protozoa maintain continuity and increase for long periods by means of a series of mitotic cell divisions; the method is highly efficient, with every member involved directly in multiplication, but it perpetuates uniformity, unless mutations occur, and the resulting population is deficient in the genetic diversity that allows selection and adaptation to changing circumstances. Multiple fission in Protozoa is well illustrated in the life cycle of the malarial parasite *Plasmodium vivax*, which displays 'sporogony' on the gut wall in the mosquito and 'schizogony' in the liver of the human host; this is in addition to sexual reproduction involving meiosis, with the formation of micro- and macrogametes, within the gut of the mosquito.

Multiplication by fission also occurs in the 'vegetative reproduction' of Metazoa, well illustrated by sea anemones which may detatch small portions of the body while moving across rock surfaces, these portions then developing into new adult forms, or the anemones may simply divide themselves into two individuals. Not only coelenterates but also some echinoderms employ this method. Alternatively, multiplication in the Metazoa may take place by budding, as seen in bryozoans, coelenterates, polychaets, cestodes and ascidians; groups of cells assemble and grow rather like a neoplasm in the body of the host, and then become separated to found a new individual. An allied process is that of *Polyembryony*, in which an embryo arising from a single fertilized egg can subdivide, giving rise to two or more embryos. The process is exploited by the liver fluke, *Fasciola hepatica*: fertilized eggs hatch into miracidia which metamorphose into sporocysts in the pond snail. Within the sporocysts develop many rediae by polyembryony and these produce further rediae over several generations, finally becoming cercariae which leave the pond snail and reinfect the sheep. Polyembryony is also to be seen in certain parasitic hymenoptera, where a fertilized egg may divide to produce 100+ progeny. Finally, the process identified as 'identical twinning' is well known in the human subject, where the Dionne quins could still hold the record for the number surviving to adulthood, and also in armadillos: *Dasypus novemcinctus* regularly produces litters of identical quadruplets, while *Dasypus hybridus* can achieve litters of eight to twelve identical young.

A system allowing much greater variation and adaptation than multiple fission is sexual reproduction, in which organisms produce gametes, small aliquots of their genetic information, and new organisms arise from the union of these.

The emergence of gametes in evolution

Gametes are essentially packets of chromosomes, and a basic tenet in the theory of evolution is that chromosomes play the primary role in this process, since they carry the great majority of the genes and these, in turn, specify virtually all somatic characters. Chromosomes, though commonly depicted as stable structures, are in fact moderately fragile, being prone to breakage and random repair, so that genes can become displaced on the same chromosome or exchanged for genes on other chromosomes or lost altogether. Genes have specific molecular configurations but they too are liable to undergo structural changes ('mutations'), with resultant alterations to the specified characters. The great majority of such mutations are deleterious ('non-adaptive') and generally fail to be conserved in the population, their removal depending on the process of natural selection.

A regular feature of populations is genetic polymorphism, the predominant characteristics shown being dependent upon the frequency with which the genes appear. In small populations, gene frequency may change through 'genetic drift', seen as a progressive change in expressed characters throughout the group (Bodmer & Cavalli-Sforza, 1976). The transfer of genes between individuals can occur in several ways, including autogamy, endogamy, transduction, transformation, and syngamy.

Autogamy

Autogamy is seen, for example, in the protozoan *Actinophrys sol*, when after a succession of mitotic cell divisions, it builds a wall around itself thus forming a cyst. In this, it divides into two, and each new cell undergoes *meiotic* divisions, whereby half the chromosomes in each cell are discarded. The two cells then reunite and their nuclei fuse into a single nucleus; the organism emerges from the cyst, apparently refreshed by its experience, and resumes its multiplication by mitosis. The manoeuvre is thought to involve a 'shuffling' of the genes, the new relationships conferring some benefit. Autogamy has also an intriguing feature, namely that when the two *Actinophrys* cells reunite they do not simply fuse, but one cell *actively invades* the other in a manner vaguely prophetic of sperm–egg union. Certain other protozoa have the same suggestive pattern of behaviour, and the participating cells could be regarded as actual forerunners of the gametes, from the evolutionary point of view; the phenomenon is similar to 'hologamy' (discussed later under 'Sexual reproduction').

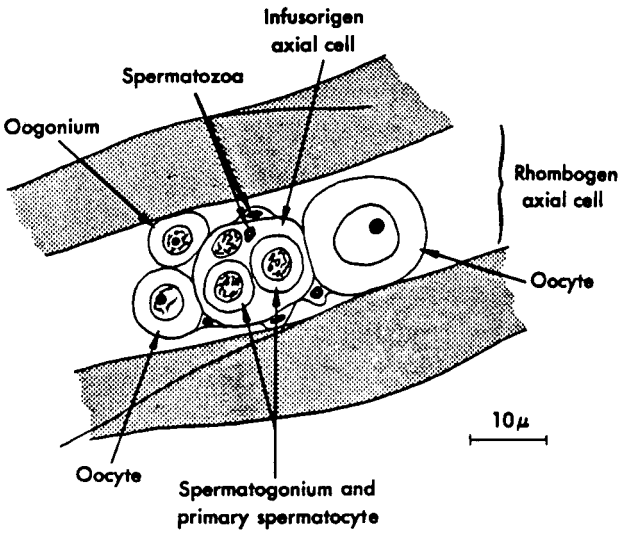

Fig. 1. Gametogenesis and fertilization in the mesozoan *Dicyaema*, which is a self-fertilizing hermaphrodite. (From Austin, 1965.)

Endogamy

Endogamy is exhibited by, for example, another protozoan *Paramecium aurelia*. After only a few mitotic divisions, pairs of cells among the descendants of a single cell may conjugate, undergo meiosis and then take part once more in a series of mitotic divisions. As with autogamy, the benefit is thought to arise from the reassortment of genes. Much the same process is seen in the self-fertilization of higher plants and of mesozoan and metazoan hermaphrodites.

The mesozoan *Dicyaema* (Fig. 1), which is a parasite of cephalopod kidneys, is made up of several cells but has no body cavity; its core consists of a long 'rhombogen axial cell' and this is surrounded by a single layer of ciliated surface cells. Within the rhombogen axial cell is an 'infusorigen axial cell', and within this again a spermatogonium cell produces spermatocytes, which in due course become amoeboid spermatozoa. When mature, these escape from the infusorigen axial cell and fertilize oocytes that have been produced by an oogonium cell resident in the rhombogen axial cell. After the resulting zygote has undergone several divisions, it makes its way out of the mother organism to proceed with independent existence.

Many metazoan species have a bar to self-fertilization, but it does occur in certain cestodes, nematodes and molluscs. Self-fertilization can presumably happen even in some vertebrates, notably teleost fish in the genera *Serranus* and *Sagus*, which shed male and female gametes simultaneously.

Transduction

Transduction takes place through the carriage of genomic DNA by bacterium, virus or plasmid. This is best known as an experimental procedure in genetic engineering, but viruses (bacteriophages) can certainly pass fragments of DNA between their bacterial victims; should the new victim survive, the foreign DNA becomes lodged in the new genome and expressed in the owner. The effect can be produced artificially by adding to cultures of bacteria cell-free extracts of other bacteria possessing distinguishable characteristics, when the recipients come to express heritable features of the donor. This variation is identified as *transformation*, and there is evidence that it can occur naturally, the death and lysis of a bacterium freesing fragments of DNA that are taken up and expressed by other bacteria.

Syngamy (fertilization)

This is distinguished from the other processes just described chiefly by the fact that it involves the orderly union of balanced quanta of DNA from two separate individuals, but otherwise there is no hard and fast line of demarcation.

Gametogenesis in animals

Weismall (1887; see Wilson, 1928) first established that, for gamete production, there would need to be a specific mechanism inducing a reduction in chromosome number, and the reduction had, of course, to be exactly half the original number, a state to be compensated for by union of the gametes. In addition, it came to be appreciated that the chromosomes must exist in homologous pairs, so that union of gametes would restore the chromosome complement appropriately.

In relatively simple organisms like *Parascaris equorum*, the origin of the gametes is demonstrable through a difference in chromosomal material: one of the four cells formed by the second cleavage division of the fertilized egg retains its chromosome complement intact, while in the other three cells a large part of each chromosome passes into the cytoplasm and breaks up (e.g. Wilson, 1928). At the third cleavage division, the first cell divides and one of its daughter cells shows the distinctive 'chromatin diminution' but not the other, nor do the remaining cells; the process is repeated at the fourth cleavage division. Thus one cell stands out alone as having an intact chromosome complement: it is from this cell that the *primordial germ cells* will eventually develop. The factor responsible for preserving the integrity of this cell is identified as the 'germ-cell determinant', and in many eggs its presence can be inferred from the existence

of certain deeply-staining granules in the vegetal cytoplasm. Similar events have been described in the eggs of scyphozoans, chaetognaths, rotifers, insects, crustaceans and amphibians. The behaviour of the germ-cell determinant gives support to the 'germ-plasm' theory, which was put forward towards the end of the last century. This held that the germ cells are not really the products of the parent body but share an origin with it from a preceding germ cell, and because a clear distinction between germ cells and somatic cells is generally difficult to draw, emphasis was placed rather on a specifically organized 'germ-plasm' which is transmitted from generation to generation (Wilson, 1928).

In mammals, primordial germ cells first become recognizable in an extra-embryonic location, namely the posterior yolk-sac endoderm of the early embryo (at about the 24th day in the human subject), and they migrate in amoeboid fashion from here through the connective tissue of the hind gut into the gut mesentery, and then, passing close to the developing kidneys, congregate in the genital ridges which represent the gonadal primordia (Byskov, 1982). Observations of germ cells *in vitro* suggest that their migration is guided chemotactically. When first recognizable, the germ cells number rather less than 100, but they multiply rapidly during transit, and after final congregation. (In birds, many more germ cells reach the left gonad than the right, consistently with the left ovary normally being the sole functional entity throughout the life of the bird.) Anomalies too can arise: for some germ cells, migration is faulty and small regions of accessory gonadal tissue may later be found; in certain chromosomal disorders the germ cells may all degenerate, the loss underlying states of sterility. The cells may also migrate into blood vessels and so be carried to anomalous regions, or in the cases where fusion has occurred between the placental blood vessels of non-identical twins, such migration may underlie cases of germ-cell chimaerism.

During fetal life, the germ cells in the embryonic ovaries, now called oogonia, multiply dramatically, reaching a peak in the human subject of around 7 million at about the fifth month of pregnancy (Baker, 1982). Thereafter, the number falls equally dramatically, so that by the time of birth there are generally rather less than 2 million. During the latter part of prenatal life, the oogonia enter upon the prophase of the first meiotic division (thus becoming primary oocytes) and this change ends their capacity for division. After birth, and especially after puberty, the primary oocytes grow in size. In some species (dog, fox), ovulation takes place at this stage and sperm penetration may occur; in others (most mammals), the first meiotic division precedes ovulation, and sperm penetration is thus into the secondary oocyte; fertilization follows with the egg emitting the second polar body and becoming an ootid. Cleavage of the egg at the end of fertilization marks the start of embryonic life. In the first meiotic division, chromosome pairs are

formed (maternal and paternal) and portions of some chromosomes are exchanged between pairs; with separation of the two sets of chromosomes, the total number is halved (diploid to haploid), hence the first meiotic division is known as the reduction division. One group of now modified chromosomes passes into the first polar body leaving the egg in a haploid condition, and the other group proceeds to undergo the second meiotic division. This is 'equational', so the ploidy of the egg is unaffected. With fertilization by a similarly haploidized sperm, the normal diploid state is restored. Meiosis like fertilization is a process of great antiquity, and may have been employed by blue-green algae which are thought to have originated about 3000 Myr.

Throughout post-natal life, the number of oocytes steadily decreases through atresia and, after the menarche, through ovulation as well. Their final disappearance marks the time of menopause.

Parthenogenesis

A serious drawback to multiplication by an unbroken series of ameiotic cell divisions (i.e. involving only mitosis and so without gene-shuffling) is the resulting genetic uniformity which is highly prejudicial to the prospects of change by natural selection, and species practising such a method live in serious risk of extinction. This problem is partially remedied by the inclusion of meiosis with its gene-shuffling feature of 'crossing-over' and this addition is seen in diploid parthenogenesis, which has the virtue that all members of the population can take part in maintaining the race (this and other features of parthenogenesis are discussed helpfully by Maynard Smith, 1978). Parthenogenesis is found in rudimentary or fully developed form in many groups of animals, including coelenterates, rotifers, platyhelminths, nematodes, annelids, molluscs, crustaceans, myriapods, insects, arachnids, fishes, amphibians, birds, and mammals. In rotifers, water fleas, aphids and gall wasps, cyclic parthenogenesis is common, a sexual generation being included in a series of parthenogenetic generations. Among the vertebrates, there are about 30 races of lizards that reproduce parthenogenetically (Maslin 1971), also the bony fish *Poecilia* and *Poeciliopsis* and the salamander *Ambystoma* (Cuellar, 1974).

Parthenogenesis is manifest in angiosperms, such as *Alchemilla, Thalictrum, Taraxacum* and *Hieracium*; almost always, it occurs in the 'egg-cells' which differ from the female gamete by being diploid. The process is known as 'apogamy', another form of which involves development from various other cells of the megaspore. Parthenogenesis also occurs in algae that exhibit isogamy or anisogamy.

Development by parthenogenesis may lead to the production of males