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Embryology and Teratology in the Curricula of Healthcare Courses

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SUMMARY

Significant changes are occurring worldwide in courses for healthcare studies, including medicine and dentistry. Critical evaluation of the place, timing, and content of components that can be collectively grouped as the anatomical sciences has however yet to be adequately undertaken. Surveys of teaching hours for embryology in US and UK medical courses clearly demonstrate that a dramatic decline in the importance of the subject is in progress, in terms of both a decrease in the number of hours allocated within the medical course and in relation to changes in pedagogic methodologies. In this article, we draw attention to the need to provide within medical and dental curricula a universally accepted terminology for embryology and teratology, to develop core syllabuses and, in addition to providing professional training, to follow the practice of university education in taking students to the frontiers of knowledge. We also discuss different ways of teaching and assessing embryology and teratology, preferring to see the employment of practical methodologies, and we highlight problems related to the poor attitudes of students towards the perceived clinical relevance of embryology and teratology.

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INTRODUCTION

Embryology is a sub-discipline of developmental biology that relates to life before birth. Teratology (τέρατος (teratos) meaning 'monster' or 'marvel') relates to abnormal development and congenital abnormalities (i.e. morphofunctional impairments). Embryological studies are concerned essentially with the laws and mechanisms associated with normal development (ontogenesis) from the stage of the ovum until parturition and the end of intrauterine life. Complementary studies relate to the formation and maturation of the gametes (gametogenesis), fertilization and fecundity, and such phenomena as parthenogenesis, cloning, superfecundity, superfoetation (i.e. reproductive anatomy). The term 'general embryology' can be employed to indicate the early development of the embryo from the ovum until the formation of the primordia of systems and organs (early organogenesis). The term 'special embryology' may be used to follow the development of the foetus after organogenesis has begun. Comparative embryology compares development across species. However, other than to demonstrate consistent aspects of mammalian development, comparative embryology is rarely taught nowadays to students in healthcare courses.

Embryology and teratology should play a

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significant part in healthcare education, in terms of understanding prenatal life, of grasping how the organization of the mature human body has developed, and of providing essential information for general medical practice, obstetrics and pediatrics. Students should also have an appreciation of the genetic and environmental factors that produce congenital malformations in order to be able to understand differences between inherited, acquired, and so-called multifactorial malformations. Early development also has an influence on age-related diseases, not least because donor tissues might have to be screened for genetic and congenital abnormalities. Furthermore, there is now the possibility of investigating, and treating, foetuses by drugs, genetic engineering or intra-uterine surgery. Indeed, such developments are leading to a new specialty in medicine, prenatal medicine, which is devoted to embryonic and foetal diseases (including abnormal development)[1].

Embryological research is probably one of the most productive areas for investigation within the anatomical sciences[2], contributing significantly to the practical and theoretical backgrounds in life sciences and medicine. Much research these days is at the molecular level but we are of the opinion that healthcare disciplines must not be overly reductive and should not lose sight of 'the whole body'. Indeed, morphology is increasingly relevant to the development of molecular science, by placing the manifestations of gene expression, cell signalling and the processes of cell physiology in context, in real time, in cells and tissues[3]. To provide an example, integration of molecular and genomic processes within embryology is a key element for fertility treatments and also for developing *in vitro* fertilisation therapies.

Despite the importance of embryology both clinically and scientifically, it often seems that, although many universities have within their faculty a significant number of embryologists, such academics are generally developmental biologists who have little interest in system-based, descriptive human embryology. Nevertheless, it would be expected that developmental biologists wish fervently for their students to understand the finer points of their research, and indeed a university education requires that students are taken to the frontiers of knowledge[4]. However, it cannot be expected that undergraduate students from healthcare disciplines requiring tuition in embryology and teratology can deal effectively with material that is beyond 'core knowledge'.

Remarkably, while there is a vast literature concerning the teaching of gross anatomy to students within the healthcare professions[5], to date there has been little discussion concerning the teaching of embryology and teratology. In this article, we intend to provoke debate as a contribution to ensuring that undergraduate students have appropriate education and training in embryology and teratology. We will concentrate on issues that centre around four areas:

- establishing a terminology for embryology and teratology;
- defining relevance and core knowledge in embryology and teratology;
- understanding the importance of university education as well as professional training;
- putting the teaching of embryology and teratology in the correct context for the healthcare professions.

TERMINOLOGY FOR EMBRYOLOGY AND TERATOLOGY

Without an internationally-accepted terminology we are not able to agree on important issues of communication across the world and between science and the clinic. At present, responsibility on a worldwide basis for the reviewing of terminologies in the anatomical sciences resides with the International Federation of Associations of Anatomists (IFAA) and this organisation has set up several terminological groups under the auspices of the IFAA's Federative International Programme for Anatomical Terminology (FIPAT)[6]. FIPAT has made rapid progress across a wide front and one of its groups is concerned specifically with embryological terminology, the *Terminologia Embryologica* being published in 2013[7]. This group was headed by John Fraher (Ireland) with 4 advisors: Bruce Carlsen (USA), Darrell Evans (United Kingdom and Australia), Hans ten Donkelaar (Netherlands), and Christoff Viebahn (Germany).

Terminologia Embryologica deals with the entire human intra-uterine period up until birth and presently excludes postnatal development. The first part of the terminology is a 'naming of parts' (the early stages of embryogenesis being followed by terms related to the development of the systems). The second part of the terminology arranges the events chronologically and employs the Carnegie Stages for the embryonic period. *Terminologia Embryologica* was formulated according to the principles set out for the development of the terminologies for gross anatomy, histology, neuroanatomy, anthropology, and oral anatomy. In particular, Latin is central to FIPAT's way of working – "The Latin term is the formal, official version. It enables translation into any vernacular and provides an exact point of intersection for communication across disciplines, languages, countries, regions and associations"[7]. Some have criticized this principle, since they argue that the use of Anglicized terms offers a better basis for translation, for publication of research papers and books, and for discussions at international meetings. However, FIPAT holds to the view that, for terminologies to remain universal, prominence should not be given to a language currently in use since other linguistic communities might reject a terminology if it is construed as furthering 'linguistic imperialism'.

Controversially, *Terminologia Embryologica*, as for the other FIPAT terminologies, eschews eponyms, despite this practice being at variance with usage in the clinic. There is an obvious need to bring together the embryological terminology with clinical usage since, without the congruence of scientific and clinical terminologies, there will remain problems for educators within the field of embryology and teratology. Indeed, a 'Tower of Babel' should not be built yet higher as a result of the various biomedical, scientific, and clinical disciplines using different terminologies. And yet, recognition of some ancestors and giants of embryology is regarded by some as a sign of respect for their achievements and an exciting detail for the student who wants, or needs, an explanation for the evolution of a concept. Furthermore, wolffian, müllerian and fallopian remain standard elements in both anatomical and clinical embryological terms.

The reader is referred to the FIPAT website for further information and guidance[6].

EMBRYOLOGY AND TERATOLOGY FOR MEDICAL STUDENTS

As stated by Carson[8]: "Embryology as a field is in a period of unprecedented change in its knowledge base. Similarly, this is a period of great change in medical curricular planning." Drake *et al.* (2002, 2009, 2014)[9] have published a series of papers showing how the time allocated to the anatomical sciences in medical courses in the U.S.A. has declined. For embryology, there being no data for teratology, contact hours has suffered the greatest decline of all the anatomical sciences. They reported that the hours devoted to embryology fell by over 70% between 1955 and 2014 (from approximately 60 hours to 16 hours on average). Some medical courses reported that they devoted zero hours to embryology. Within the U.K., it has been reported that some medical schools adopt a perfunctory approach to the teaching of embryology while other schools refer only occasionally to the subject or even not at all[10]. Although data of this kind do not appear to have been collected elsewhere in the world, anecdotally it seems that similar decreases in the time allocated to embryology have occurred. Such changes have been the result of medical schools' shift of emphasis away from a firm grounding in the biomedical sciences and towards basic medical training that deals primarily with what is perceived as being of 'clinical relevance'[11]. The drivers for emphasising 'clinical relevance' seem to arise partly from social and political needs, partly from students increasingly wishing to engage with clinical matters at the outset of their studies, and partly from trends in medical education. Consequently, it can appear to medical course organisers that embryology and teratology are specialities and are not of core clinical relevance. Furthermore, our impression is that, even where embryology continues to be taught in the medical course, little information is provided about teratology. This seems to us to be an unfortunate situation since there is now a great understanding of embryology within the population at large, as evidenced by the frequency of Down's syndrome in society and an understanding by laypersons of trisomy, and maternal and age considerations about its aetiology. In addition, if a student does not have a clear understanding of the main stages of normal development, (s)he will not be able to understand how malformations occur or appreciate the possible association/relationship of multiple malformations, which might be found either independently or linked. We will follow up these matters by a discussion as to how core embryological and teratological knowledge can be defined, whether medical courses are now instrumentalist and have moved away from the ethos of university education, and the context of teaching the disciplines in terms of methodologies that have been, or could be, adopted within medical curricula.

Defining Clinical Relevance and Core Embryological and Teratological Knowledge

The amount of available knowledge relating to embryology and teratology is beyond the requirements to learn of the medical undergraduate. Indeed, including too much in the curriculum can lead to factual overload[12]. Consequently, course organisers and medical educational authorities often talk about the need to teach and examine core knowledge, supposedly meaning that which is deemed to be most clinically relevant. However, there is as yet no internationally accepted set of core syllabuses available for the anatomical sciences, embryology included.

Several attempts have been made to provide core syllabuses, particularly for gross anatomy. For example, the Anatomical Society within Great Britain and Ireland has provided a core syllabus for gross anatomy[13] and others have been developed by anatomical societies in America and in the Netherlands[14]. Nevertheless, these syllabuses have been developed by national bodies and are not internationally-agreed syllabuses. Furthermore, there is no syllabus that specifically deals with embryology and teratology. The IFAA, together with the Trans-European Pedagogic Anatomical Research Group (TEPARG) that is supported by the European Federation for Experimental Morphology (EFEM), is in the process of formulating core syllabuses using Delphi Panels to initiate the process[15]. To date, core syllabuses in the first stages of development have been published for the gross anatomy of the head and neck[16] and for neuroanatomy[17]. These have also been announced on the IFAA website so that they become available for comment and amendment by interested parties (anatomical, scientific and clinical). At the time of writing, a core syllabus relating to embryology and teratology for the medical course is being developed by the IFAA/EFEM, and it is envisaged that this will become available early in 2017 within an anatomical journal and on the IFAA website.

Even when a core syllabus is arrived at, it cannot be definitive and set 'in tablets of stone' and it is important to emphasise that core syllabuses should not dictate what *cannot* be taught within the medical curriculum. Consequently, the core syllabus must be regularly, and frequently, reviewed since the importance of embryology and teratology is increasing with clinical progress and scientific advancement. Indeed, it is recognised that the input of clinicians into the development of an IFAA/ EFEM core syllabus is essential so that they guide both the scientific and clinical aspects of medical training. In addition, a core syllabus does not dictate how to teach the syllabus nor when in the curriculum the subject has to be taught. Nevertheless, without an internationally-recognised syllabus to hand, it is not easy to combat politically the continuing decline of embryology and teratology in the medical course[9].

Core syllabuses are there to help ensure consistency, reliability and transparency of medical training wherever it is undertaken. They also help with the drive to ensure clinical relevance. However, there are consequences to this essentially 'instrumentalist' approach to medical education that will be touched upon when considering the need to maintain medicinal training within a university setting. There are also conceptual problems relating to defining core elements within a medical course[18]. Presently, it seems that each medical school has its own version of what is a core sylla-

Table 1a.

THE PRE-EMBRYONIC AND EMBRYONIC PERIODS
Gametogenesis, mitotic and meiotic divisions, hormones, normal /defective development of gametes, meiotic disturbance is resulting in chromosomal aberrations; genetic regulation of germ cell formation;
Maternal advanced age: nondisjunction of chromosomes, presence of chromosomal abnormalities; paternal old age: occurrence of new mutations;
Fertilization (natural, strategies of IVF, ART); Contraceptive techniques / risks;
Principles of morphogenesis / dysmorphogenesis, signalling pathways, cell-cell interactions; cascades of signals determine cells fate;
Zygote, cleavage-mitotic division, morula, early blastocyst formation, epiblast, primordial germ cells, genetic regulation of PGC formation, proliferation, migration and development, complex regulator gene cascade, apoptosis, normal / defective development as a starting point of teratogenic changes, teratoma, mutations of genes cause many tumour development/ groups of cells as a basis for future tumour;
Hatching, normal / pathological, assisted hatching;
Chromosomal abnormalities result in spontaneous abortion or abnormal development, 60-80% of early blastocysts are lost, only 5% of implanted embryos survive – natural screening;
Dating of pregnancy; Carnegie embryo stages generally used pattern of development by weeks, months and by trimesters, periodicity of prenatal development;
Cell differentiation from totipotent cells present in the inner cell mass, to the pluripotent cells present in the three basic embryonic layers, stem cell sources (also cell lineage, cell migration, cell transformation);
Influence of signal molecules activity on endodermal, mesodermal and ectodermal layers differentiation;
Process of establishing of the body plan and fate map of the systems and organs; primitive streak, epiblast cells forming embryonic mesodermal layer, establishment of the cranio-caudal axis, lateralization (left-right asymmetry), dorsalization-ventralization; primitive node, notochordal process, basic role of signals, production of signal molecules, induction, all determinative for the formation of small groups of cells, basic „for the beginning of future organ development";
Formation of neural plate, neural tube, development of brain vesicles, spinal cord and neural crest, formation of cardiogenic zone, primary and secondary heart plate, development and positioning of heart tube, cardiac loop; folding; coeloma differentiation, development of bases of organs of abdominal cavity and lungs; streams of cell, migration, (PGC,mesoderm , neural crest cells etc.), vasculogenesis, angiogenesis, primitive blood circulation; period in which differentiation of cells under the effect of failed signalling / induction results in defective development;
Foetal membranes development: amnion, chorion buffer the embryo in the interim before the placenta has been formed, uteroplacental circulatory system development, normal development / defects of placental development and functioning;
Histology of developing embryonic tissue;
Environmental influences: mother´s inadequate nutrition, (women living in poor conditions / lack of proteins, folic acid, vitamins), chemical pollutions, exposure to hypoxia (low level of pO2 in blood) because of mother´s lung and heart chronic diseases, smoking, defects of placenta; mother´s diabetes; mother abusing alcohol (foetal alcohol syndrome) or smoking, (or both), mother abusing drugs, medicaments, infection diseases in mother viral, bacterial, parasitic, i.e. rubella, HIV / AIDS, Zika viral infection, tuberculosis, syphilis, toxoplasmosis etc.; mental stress; physical teratogens: radiation, noise / vibrations, hyperthermia, etc.;

bus and this certainly applies to embryology and teratology. Unfortunately, it seems that the core syllabus often changes merely as a result of changes in personnel (the medical dean, head of department or course organiser)! This matter is taken up when later we discuss the context of teaching and learning the topics. What is important to state now is that unwarranted diversity of clinical training should not be accepted educationally. To do so ultimately disadvantages both the student/ prospective medical practitioner and the patients by not having more universally agreed standards and syllabuses. Should governmental agencies perceive that there is not consistency, reliability and transparency across the sector, then they might impose state-wide examinations that inevitably would lead to teaching that would be examination-focused, and to learning that would be strategic according to what was assessed. This therefore would result in medicine moving further away from the established university education model.

Inevitably, a core syllabus in embryology and teratology concentrates on descriptive topics. Descriptive embryology, while remaining as a basis of the subject matter, has been enriched by findings in genetics, molecular biology, and electron and scanning microscope research. Since the time when genes such as *HOX*, *SHH*, *PAX* were discovered, and their influence on the origin of embryonic structures was recognized, our knowledge in this field has been deepened. However, Carlson[19] has highlighted a dilemma in this respect, writing: "One of the most significant questions in embryology education for medical students is how much of the 'new' molecular embryology to mix with the 'old' developmental anatomy approach". Nevertheless, a new era of embryology was opened up. For example, recent developments include matters relating to fertilization and assisted reproduction beginning from gametogenesis, selection and differentiation of stem cells that raises the hope for successful treatments of up-to-now incurable diseases or post-traumatic lesions, ways of preventing stem cells producing tumours, recognition and understanding of the influence of teratogens (often multifactorial), and study of tumour development in relation to the differentiation of embryonic and foetal structures. Such developments require careful consideration as to whether or not they are core topics at this time, but Table 1 provides a list of topics that, even if they cannot be made available in an embryological course early during medical education, should be part of the medical curriculum by the end of the medical course.

The Importance of a University Education

Consumerist societies are inevitably instrumentalist. The Oxford Dictionary defines instrumentalism as: "a pragmatic philosophical approach which regards an activity (such as science, law, or education) chiefly as an instrument or tool for some practical purpose, rather than in more absolute or

Table 1b.

THE FOETAL PERIOD
Maturation and growth of foetal organ systems; crown-rump length; processes of intensive growth, influence of biological molecules and hormones on differentiation of tissues and organs; cell proliferation; formation of extracellular matrix;
Differentiation of definitive body topography; understanding that, although all organ systems are present by 8 weeks, few are functional; organs established in the embryonic period are developed to definitive positions, prepared for their function in postnatal life, a number of organs do not finish maturing until after birth; foetal movements start: differentiation of muscle proteins, muscle groups, eye movements, diurnal rhythm of movement originates;
Microscopic anatomy and functional development of different tissues and organs; differentiation of special groups of cells important for the function of given organ; differentiation of nervous system, CNS, brain, spinal cord and PNS, ganglions and peripheral nerves, normal and defective; sensations; cardiovascular system: this is a period of frequent development of heart defects, heart beats from forth week of pregnancy, (100 beats increasing to 150 beats per min.); endocrine glands produce small amount of hormones involved in foetal development: anterior pituitary stimulates peripheral endocrine glands (i.e. activity of thyroid hormone, corticoids) ; digestive system: maturation of gastric mucosa cells that differentiate for secretory function, development of enzymes, mucosa of small intestine differentiates for process of absorption in craniocaudal direction, formation of villi followed by development of crypts 1 -2 weeks later, development of gland cells, meconium; kidney differentiation producing small amounts of urine; lungs: alveolar lining differentiation with development of type IIpneumocytes (producer of pulmonary surfactant), note that the premature new-born lacks surfactant, giving rise to distress syndrome; placental function: hormone production continues (HCG, GRH) steroid and protein hormones and prostaglandins; differentiation of liver, spleen, temporary hematopoietic organs; development of bone marrow tissue: hematopoietic cells are present;
Critical period is when there is intensive differentiation of an organ - influence of failed signalling / failed induction or infection and toxic agents activity, and other factors causing cell modifications or mutations; teratogens reach foetus by crossing the placenta; cell changes: source of teratoma or tumour formation (tumour might be developed either in foetal period or survive perhaps for years as a 'sleeping group of cells' that might in future be activated to produce tumour growth;
Therapy of defective organs; therapeutic manipulation on the foetus, wide range of foetal anomalies could be corrected operatively, by open foetal surgery,(e.g. hydrocephalus correction by ventriculoamniotic shunt, correction of obstructive uropathy); foetal blood transfusions; gene therapy of foetus, correction of defects of development now being investigated;
Delivery normal /pathological, establishing of date of delivery (usually 38th week of pregnancy); process consists of three distinct phases of labour; role of prostaglandins F_{20}; adaptation in perinatal period: changes in lungs, new-born first inspiration with opening of the alveolar sacs, role of pulmonary surfactant; conversion of blood circulation from foetal to air- breathing pattern so that there are two circuits (pulmonary and systemic);

ideal terms". In other words, the 'truth' of a concept or the cultural value or history of a topic is regarded as of little value in the face of the need to show practical worth. Instrumentalism, a relativistic notion, emanated from the philosopher John Dewey, who supposed that "thought is an instrument for solving practical problems, and that truth is not fixed but changes as the problems change"[20]. In terms of medical education, this comes down to teaching clinical relevance and core topics. However, clinical relevance is often narrowly defined as being disease-orientated, and this impoverishes medicine by a failure to accept the functionality model of medicine that recognises the importance of normality and health[21]. Medicine might be further impoverished by becoming disengaged from the standard university educational experience of taking students to the frontiers of knowledge[4].

A problem here relates to the medical course being developed by a 'top down' approach – through government agencies, the medical profession, medical deans and/or medical educationalists. Little consideration is given to the needs and opinions of patients/potential patients by introducing 'bottom up' elements to course organisation and content. This is seemingly a paradox within an increasingly consumerist society. A recent survey of laypersons' attitudes towards the importance of gross anatomy within the medical course shows that they have a reasonable knowledge of human anatomy and that they strongly express the view that their confidence in the medical profession would be greatly diminished should anatomy be downgraded[22]. There is consequently a need to develop these studies further to assess the extent to which laypersons have knowledge of embryology and teratology and how they view the importance of these disciplines.

No one presently is suggesting that medical schools should become separate from university institutions, but the instrumentalist philosophy puts a strain on the relationship. In the past, medical students received some form of university education in the biomedical sciences prior to clinical training, with the student having a 2- or 3-year preclinical part of the medical course[5]. However, this model is becoming less and less recognised by medical educationalists.

Perhaps this situation is related to how students are recruited to the medical school. In the main, worldwide, students are recruited straight from secondary school and is an undergraduate course. In some universities that recruit medical students straight from school, for example Oxford and Cambridge in the United Kingdom, medical students are required to complete three years of scientific training leading to a scientific degree before being fully enrolled within medical schools. Furthermore, throughout the U.S.A., medicine is a postgraduate course and the students are usually required to have undertaken a Bachelor's Degree prior to admission into the medical course. However, these examples aside, we remain concerned that instrumentalism in medical education could mean that our medical students will be less well versed in the scientific basis of medicine and that the trend that we see in cutting scientific courses will continue to the detriment of the medical profession. The previously stated decrease in the amount of time devoted to embryology in the medical course is indicative of this trend[9]. Within the United Kingdom and Ireland, it has become commonplace for many medical students to opt out of the medical course for a year or two to obtain an 'intercalating' Bachelor's Degree, often in the biomedical sciences and including a research project. Indeed, options are available for students to study aspects of embryology and teratology in this way, although we are aware that their studies are more likely to be focused upon signal molecules and genetic considerations and upon experiments performed on *Drosophila*, zebrafish (*Danio rerio*), quail, and chick, the only popular experimental mammal being the mouse.

Assuming that we persist in the notion that doctors of medicine are learned and aware of the frontiers of knowledge so that they are prepared for future scientific and medical developments, we are of the opinion that, if the medical course is to continue to decrease the amount of time devoted to the biomedical sciences (including embryology and teratology), we would encourage the medical establishment to think positively of maintaining (or introducing) intercalating medical degrees in the basic medical sciences and to include embryology and teratology in such programmes.

The Context of Teaching Embryology and Teratology

Traditionally, before being placed in front of patients, it was considered that students needed 2 to 3 years when they were informed of the scientific basis of medicine. The model was thus established that the healthy body was the first object of study, to be subsequently followed by interpretation of this knowledge to appreciate how disease produced abnormalities. This model is exemplified by the findings in the Flexner Report in the USA (1910)[23]. Within this model, embryology (rarely teratology) would be taught as a stand-alone course. This would occur most often later in the 'preclinical' course and after the students had learned a substantial amount of gross anatomy. In some medical schools, embryology would be integrated with gross anatomy, so that each discipline would benefit from each other to the extent that the complexities of the anatomy of the human body could be explained by recourse to understanding development.

It is also evident that teaching about malformations and about teratology at an early stage of the medical course provides the student with early contact with pathology and with clinical cases. It offers a good basis for problem-based study. There is also the issue of age-related diseases, which, for the moment, lies in a sort of 'no man's land' and is not included in any textbook of (medical) embryology. In this regard, a basic question is: where does one stop the taught domain? Ontogenesis takes place throughout our lives, from fertilization until death. Other interesting, and useful, concepts deal with the embryonic vestiges, rudimentary organs, homologous and analogous organs or parts of the organs. Above all, we believe that one of the important functions of an embryology and teratology course is to teach general principles that extend beyond the detailed descriptive embryology present in textbooks. Indeed, we hold that three basic concepts need to be imbedded in the embryology curriculum:

1. The relationship between genotype and phenotype;
2. The concept of 'normal' needs to be discussed. It can imply the most common, the most functional, or even the most healthy, but students need to appreciate that 'normal anatomy' is not present in ALL individuals and this understanding leads to the third point;
3. The continuum that exists between the 'normal', anatomic variant, malformation, and disability needs to be understood. It is thus important for medical students to understand the concepts of normotype, anatomical variation, heterotype, morphologic versus functional disability, and malformation[24], as well as the relationship and equilibrium between general ontogenesis, organogenesis, histogenesis and cell transformation[25].

It is clear from the surveys of Drake *et al.*[9] that increasingly in the U.S.A. (and indeed it seems elsewhere in the world) the whole medical course is being integrated both horizontally (across a year) and vertically (across the whole course). The 2014 survey by Drake *et al.* reported that the anatomical sciences were now part of an integrated curriculum in 45% of US medical courses. In relation to integrated courses, there could be difficulties relating to positioning scientific topics within the overall medical curriculum. While there are advantages in having scientific topics taught at a discreet time in the overall medical curriculum, increasingly medical educationalists are thinking about such courses being a theme that 'snakes' its way throughout the entire medical course. The belief is that the biomedical sciences should appear throughout the medical course so that material is delivered, not for integration within the scientific discipline, but for providing foundation material for the clinical course as and when a clinical topic is taught or delivered (another aspect of instrumentalism). At the most extreme end of the spectrum, embryology and teratology is not taught in the medical curriculum at all[9].

As part of a survey of the attitudes of European medical students towards the clinical relevance of embryology[26], cognisance was taken of the different arrangements for the teaching of embryology in the medical schools participating. This ranged from stand-alone courses to integrated teaching, from separate departments of embryology to teaching being conducted in anatomical or clinical departments, and from the topics being taught by specialist embryologists who are involved in developmental research to anatomists with other research or pedagogic interests. To provide examples:

At a UK medical school there is not a distinct department of embryology and the teaching of the discipline involves staff who are neither recognised experts with research experience in normal embryogenesis and organogenesis nor clinically qualified. Furthermore, the teaching is scattered over the 5 years of the medical curriculum. Indeed, there is no longer a department of anatomy, since this has been incorporated within a school of biology. On the other hand, at a Greek university, there is a recognized department of histology, embryology and anthropology that is distinct from a department of gross anatomy. It has stand-alone courses and clinically qualified staff. Both universities, however, emphasise clinical cases that reflect on the teaching of embryology. At a Czech university, there is also a separation between the institutes of embryology (with histology) and gross anatomy, while at a medical school in Romania there is a Laboratory of Embryology within the department of Anatomy, with dedicated full-time teaching staff who are all medically qualified. They teach embryology for three semesters during the 1st and 2nd year of the medical course. In addition, there is an optional course on Molecular Biology of Human Development for the 2nd year medical students. At a medical school in Portugal, general and special embryology were taught until 2010, together with histology, in the second year of the medical curriculum, but embryology is now only taught within the 5th year of the medical course and in association with paediatrics. In Malta, a short series of introductory lectures on human development, potency, determination, differentiation, blastogenic birth defects and stem cells is given at the start of Year 1 of the course. In addition, an introductory lecture on the embryology of each organ system is included at the start of each of a series of systemic modules with the topics being assessed at the end of Years 1 and 2. At a medical school in Paris, there is also a separation between the departments of gross anatomy and embryology, and embryology is taught during the three first years of medical school. At a medical school in Austria, there is a common department of anatomy, histology and embryology but with a distinct 'division' for histology and embryology with dedicated full-time staff.

General embryology is taught within the 2nd term and further embryological and teratological aspects in the clinical context of pregnancy are taught in the 7th term.

These examples demonstrate the extent of diversity of practice and organisation and suggest that, because of lack of appropriate pedagogic research, there are not firm foundations upon which to build notions of how best to teach embryology and teratology.

Methods of teaching embryology and teratology

Teaching methods appear to be as various as those employed to teach gross anatomy. It can be envisaged that the topics could be taught simply didactically (by lectures, tutorials, or e-learning), or more practically (by laboratory classes with specimens, dissection and histology slides), or by means of the use of models. Furthermore, in a more integrated model, the topics can be part of problem-based learning or problem-based teaching incorporating clinical scenarios. Presently, the efficacies of these methods have not been adequately assessed. Taking the case of problem-based learning in general, Hattie[27] has shown, from a synthesis of 8 meta-analyses involving over 38,000 subjects, that there are no beneficial educational effects. On the other hand, for problem-based teaching, he showed, from 6 meta-analyses involving over 15,000 persons, that there are desirable effects. Looking at attitudes of professional anatomists and medical students to the perceived value of different methodologies for teaching gross anatomy[28], practical methods of teaching the subject were preferred and theoretical methods (including e-learning) were not well regarded. The authors would hypothesise that similar findings from medical students and professional embryologists would also apply to the teaching of embryology and teratology.

However, didactic teaching approaches for studying normal embryological/foetal development remain fundamental in many courses worldwide. Nevertheless, they are not enough to successfully inculcate to the contemporary student all the exciting and new knowledge concerning normal and abnormal embryological development, nor to teach them about the clinical problems that arise when a malformation is seen in a new-born who will survive despite the health problems that arise as a consequence. We would argue that new knowledge in embryology requires a new attitude to embryology teaching. For students, it is often hard to imagine the developmental processes occurring within the embryo. Indeed, a great number of documents often have to be prepared for lectures to help students visualize human development. 3-D reconstructions, scanning microscope pictures, slides with embryological tissue sections, articles outlining recent results of embryological research, and setting self-study tasks with 'wash-up' seminars can also be employed. In particular, many aspects of embryogenesis and of organogenesis are better understood practically by means of 3D reconstructions. However, animations and other virtual imaging techniques (such as Digitally Reproduced Embryonic Morphology (DREM)[29]) are likely to be useful in enabling the student to better appreciate the complex folding and 3D aspects of embryology. It can therefore be argued that didactic teaching and student learning can benefit from both practical experience and from the use of computer imaging technologies that improve visualization of difficult topics and embryological processes. Indeed, this is particularly necessary to explain the multifactorial relationships occurring in embryology and teratology in order to build embryonic/foetal ontologies and to correlate these with clinical malformations. Furthermore, the use of computer imaging technologies helps the understanding of genome studies where regulatory variation in the embryonic/foetal human genome is mapped. This is increasingly becoming important as we are employing knowledge of the genetic factors to study epigenetics and diseases such as malignant tumours that are sustained by rare stem cells that originate from embryonic stem cells, and that have been affected by teratogens during gestation. In addition to new computer imaging technologies, there should be access to ultrasound techniques (if only by recourse to having access to ultrasound reports), and all teaching materials (e.g. EM (transmission and scanning) pictures, PPT demonstrations, LM slides scans, hand drawn schemes) should be available online to students. Furthermore, clinical histories and case scenarios describing malformation development should be presented in classes or during practicums.

A moot point concerns the extent to which students nowadays should be taught behavioural aspects in relating to, for example, alcohol abuse and congenital abnormalities. Although some might argue that this is best left to the clinic, some acknowledgement of the issues involved should appear in an embryology and teratology course. Whatever pedagogic methods are used to teach embryology and teratology, we plead for embryologists throughout the world to collaborate through an open exchange of knowledge, using useful educational and research materials, and to work together on pedagogic research projects to evaluate what is best for teaching and for student learning and ultimately for the betterment of patients.

It can be argued that the teaching of embryology requires knowledge of the longitudinal sequence of events in the development of systems, organs and tissues and also appreciation of the transversal correspondence between developmental aspects of systems, organs and tissues in order to understand the level of structural organisation step by step, or stage by stage. This leads us on to the thorny issue of the extent to which the learning of embryonic stages is important within the medical course[30]. Many would argue that this is not ‘core’ knowledge but, if it is to be taught/learned, then perhaps the use of the ‘Carnegie standard stages’ is best[31]. Indeed, as mentioned earlier, this is the system employed within the *Terminologia Embryologica*. This system allows a better understanding of the correspondence between organs and tissues in normal development, and offers a reference for understanding the potential risks of malformations in teratology and tumour transformation. Indeed, students should appreciate that each stage of development is a collection of linked events seen as a snapshot on a 4D map. If all events belonging to a specific stage happen synchronously, it means that the general development of the body is proceeding normally, whereas, if some developmental events are happening earlier or later, it means that the normal scheme is disrupted and a malformation occurs.

Embryologists would hold to the opinion that standard timing, measuring, featuring / defining typical changes are essential for a correct use of embryology information. Of course, medical students would not be expected to know what events are happening day by day or hour by hour, but should understand the succession of events in their natural order and should appreciate that they run in parallel within different systems, organs and tissues. Furthermore, they should appreciate that such parallel events must proceed in harmony during normal development, and could be unsettled by teratogenic factors.

The most significant weeks in human ontogeny are weeks 3 to 6/7, corresponding to stages 6 to 19. We note however that contemporary embryology handbooks, as well as research articles, do not provide consistent accounts of stages and the timing of events. To provide a specific example from the research of one of the authors (Chirculescu et al., 2010)[32], stages 12 and 23 are key developmental moments for the pituitary, and studies on the development of the human and rat pituitary suggest that there is discordance of timing such that, from an assessment of when hormone positive immunostaining and their co-localisation in the same cells commences (in cells presumed to be already differentiated), pituitary development defined by weeks or by stages do not match.

It may be regarded as unfortunate that many ‘facts’ in embryology, for both normal development and for the action of teratogenic agents, come from attempts to correlate information obtained from human, mouse, rat, rabbit and chick. Perhaps we should not be surprised, since attempting to provide equivalence between a 9 month and 3 week gestation period is unsupportable. Nevertheless, drawing equivalence by considering stages offers better scientific support (see Table 2).

Table 2. Comparisons of the chronology of events during the first 23 stages of embryonic development for the rat and human

EMBRYONIC STAGE	Rat Chronology	Human Chronology
1-5	Day 1 - 7	Week 1
5-6	Day 7	Week 2
6-9	Day 7 - 9	Week 3
10-13	Day 9 - 11	Week 4
13-15	Day 11 - 12	Week 5
15-17	Day 12/13	Week 6
17-19	Day 14	Week 7
19-23	Day 14 - 20/21	Week 8

It goes without saying that learning ALL 23 stages would make embryology almost impossible within a course for healthcare professions, but a rational selection of the main stages that define significant organogenetic and histogenetic steps would make it more acceptable. We advocate therefore that the use of simplified Carnegie stages should be considered in the design of lectures and student handbooks. Whether or not students are expected to learn the stages, it is always instructive for the student to be made aware of the mismatch in the timing of an event between two different books and research articles. At the very least, students should be made aware that using stages improves precision and avoids acquiring contradictory data. The obverse is that, if students merely stumble upon mistakes and contradictions, they might come to the conclusion that reported information is not safe and that the scientific rigour of the data supplied is questionable.

It should be mentioned here that the teaching of teratology is regrettably too often regarded as a ‘Cinderella topic’, seeming to be taught perfunctorily or not at all. This is regrettable because of teratology’s importance scientifically, clinically and socio-politically. At present, however, although there are studies on the amount of teaching of embryology taking place in medical courses[9], there have yet to be surveys undertaken on the amount of time devoted in the curriculum to teratology. We look forward to this anomalous situation being rectified.

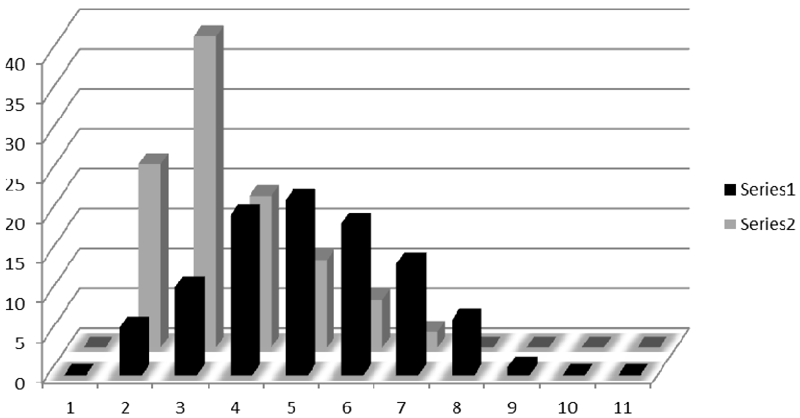
There is much talk these days of introducing optionality within the medical curriculum, often as elective modules. The implication is that students have a choice of courses beyond what is considered to be core. Agarwal *et al*.[33] have recently provided a systematic evaluation of preclinical elective courses in the medical curriculum and have reported that “the range of electives available and their impact upon medical student education are not well described in the literature”. It is recognised that the prime purpose of such courses is to introduce flexibility in the medical course, and to allow the students to follow their own individual pathways by pursuing their own personal interests. This seems to us to be a fine concept where the topics covered are not core. Indeed, having already argued that many topics in embryology and teratology should be regarded as core, we would be dismissive of attempts to incorporate the subjects into optional courses or electives. Moxham and Pais[34] have argued that, until core material is defined (and generally agreed), then optionality has conceptually no real foundation. Furthermore, it is worrying that the diversity of elective courses (including content, teaching methodologies, assessment, admissions, and outcomes) detracts from the important educational principles of consistency, reliability and transparency. Indeed, medical education worldwide is already fractured by a high degree of diversity such that there is difficulty in appreciating the standards set (and thus the quality of future medical practitioners). Most concerning, however, is the lack of understanding of how important embryology and teratology is to the clinic, to patient welfare and to the concerns of society (particularly the detrimental effects of environmental factors and infections (viz. the Zika virus that according to teratologists will be the second most harmful teratogen after thalidomide[35])). Thus, the subjects are clearly important for obstetrics, paediatrics, community medicine and general practice but to provide core embryology and teratology topics in an optional module before a student has considered their future career pathway is nonsensical, especially if the elective is early in the medical course (as it usually is).

In terms of who teaches embryology and teratology, it can be argued that there is a need to ensure that the teachers of embryology are clinically qualified, persons with whom the students can empathise and who can provide appropriate clinical examples. Clearly, clinical scenarios for both gross anatomy and embryology are more powerful when they are constructed together and preferably taught simultaneously by embryologists and clinicians. It would of course be expected that the clinician would be appreciated by the students as being a specialist who has clinical cases involving health problems associated with development of organs and systems. However, we are concerned that there is a lack of medical embryologists available to satisfy this requirement. Moreover, in order to plead for the necessity of the survival of embryology, directors of medical education these days frequently are looking to see not only the clinical relevance of disciplines and topics, but also the research relevance. Accordingly, the development of courses in human genetics and developmental biology can lead to a better appreciation of the importance of embryology in medical education, and this can only be appreciated if the teaching is research-led and the teachers are research-active. So the dilemma is finding medically-qualified, research-active, developmental biologists who are interested and capable of teaching! Perhaps this is a tall order!

The attitudes of medical students in Europe to the perceived importance of embryology to the clinic

Regardless of the methods of teaching employed, successful tuition in any subject depends primarily upon the enthusiasm of the teacher and the motivation of the students. In terms of motivation, there have been many studies assessing the attitudes of medical students towards the perceived clinical relevance of the anatomical sciences using Thurstone and Chave's (1951) attitude analyses. However, most studies have been concerned with reporting the attitudes towards the clinical importance of gross anatomy[28]. For embryology, attitudes in the early stages of their training of nearly 1,600 medical students studying across Europe have been assessed[26]. It was reported that, regardless of the university and country surveyed and also regardless of the teaching meth-

Fig. 1. Histograms comparing medical students' attitudes toward the clinical importance of gross anatomy (series 2) and for embryology (series 1) obtained using attitude analyses of Thurstone and Chave (1951). The attitude scales are from 1 (extremely positive) to 11 (extremely negative). x axis is % frequency; y axis is attitude scale. The data for embryology is a composite for all the countries surveyed by Moxham et al. (2016)[26] and the data for gross anatomy are taken from the paper by Moxham and Plaisant (2007)[28]



ods employed, there is significantly less understanding of the importance of embryology compared with gross anatomy. Figure 1 provides a comparison graphically, where the mode for gross anatomy is 3 on the attitude scale compared with a mode of 5 for embryology. It was suggested that students' attitudes towards embryology are influenced predominantly by their pre-university education, mainly in biology classes. The assumption was made that at pre-university there is almost no embryological content within the school curriculum; whereas (gross) anatomy is taught at least to some extend in secondary school. Furthermore, gross anatomy is often anchored in the minds of the general population by such different means as permanent anatomical museums or temporary exhibitions, broadcasted documentaries, etc. This is not the case for embryology. The conclusion was reached that teachers, medical educationalists, and devisors of medical curricula need to pay special attention to informing students of the significant role played by embryology in attaining clinical competence and achieving the knowledge and understanding of the biomedical sciences that underpin such clinical areas as obstetrics, paediatrics and teratology. Consequently, the importance of embryology must be stated explicitly at the start of their course and must be often reinforced, including by having embryological topics reintroduced at various stages of medical education. Perhaps one way of gaining the attention of the students towards the importance of embryology and teratology is to highlight some of the ethical issues that relate to the discipline. In this regard, we would advocate that the students should be encouraged to debate ethical issues such as embryonic tissue sampling and collection, legal limitations, the use of experimental animal models, the use of embryonic stem cells, cloning and genetic engineering, and eugenics.

EMBRYOLOGY AND TERATOLOGY FOR DENTAL STUDENTS

Many of the issues that we have raised for the medical curriculum also apply to the dental curriculum, but dental students clearly require much less understanding or knowledge of embryology and teratology than medical students (except for topics that relate to the head and neck). There are however specialisations that require greater understanding and knowledge because of clinical necessity. In particular, the dental student should have a good education relating to craniofacial development. This however requires that some elements and principles of general embryology are taught to enable a full understanding of the craniofacial specialisations. We advocate therefore that the dental student is taught such topics as gastrulation, somites, neurulation and the neural crest. Presently, a core syllabus for embryology and teratology for the dental course has yet to be devised. However, in Table 3 we conjecture what such a core syllabus might comprise and would urge the IFAA/EFEM to progress swiftly to the development of a core syllabus.

EMBRYOLOGY AND TERATOLOGY FOR SCIENCE STUDENTS

Developmental biology features strongly in many biomedical science degree schemes. Indeed, some universities nowadays have distinct bachelor degree schemes in the discipline and their appearance signals the major research endeavours being undertaken. Clearly, students studying embryology as part of a science degree require core knowledge in excess of that needed for students on healthcare schemes. More importantly, since many science students would be expected to consider careers in research (either as researchers or technicians), practical training in embryological experimental techniques is core and goes beyond just knowledge and understanding of embryological facts. A further important consideration is the necessity of going beyond core material and to take the students to the frontiers of knowledge. This is best accomplished by allowing their teachers to expand upon the core syllabus by a more detailed, discursive and critical appraisal of their own areas of interest and expertise in embryology. Finally, it is important for a science student to appreciate the cultural, historical and philosophical/ethical approaches relating to the discipline.

CONCLUSIONS AND RECOMMENDATIONS

The following points relate to the need to teach embryology and teratology and how to teach the subjects:

1. Medical students require embryology and teratology to understand clinical situations that traditionally relate to obstetrics and paediatrics, but also to appreciate new therapeutic approaches (e.g., intra-uterine therapy; stem cell therapies). Other healthcare professions (such as dentistry) require specialist courses tailored to their clinical requirements;
2. Students are better able to understand gross anatomy if they have knowledge of normal embryology. Accordingly, gross anatomy and embryology should ideally be taught together;
3. Environmentally, and increasingly in a consumerist, information-rich, politicised society, teratology plays a significant role in improving the health and well-being of the developing foetus, the new born and the developing child;
4. The best methods for teaching embryology are not simply didactic methods but are practical methods that also use animations to aid the students' 3D appreciation of the complexi-

ties underpinning embryogenesis and organogenesis;
5. Enthusiastic teachers, who are preferably clinically qualified, are needed. Furthermore, the teachers require motivated students, and evidence suggest that presently the less than positive attitudes toward the clinical relevance of embryology needs to be addressed before the students study embryology and teratology;
6. It is important that clinicians and embryologists use similar terminologies that are recognised internationally;
7. There is an urgent need to develop flexible, core syllabuses for embryology and teratology that, having international acceptance, are seen to be educationally and politically important;

The next points reinforce our belief that the scientific basis of embryology and teratology should exist as well as its clinical context:

1. Following developments throughout the world (e.g. The Flexner Report in the US[36]), there is a strong view that medicine should be a university-based course. This was proposed to ensure the delivery of professional, scientifically based courses that resulted in medical practitioners being well-rounded and learned persons respected as such in society. Biomedical courses such as embryology and teratology help to deliver this, particularly if the student receives research-led teaching;
2. Medicine, as for other healthcare disciplines, is not just a disease-based discipline, but is also concerned with functionality and health. In terms of embryology, it is important that the student should understand normal development in advance of being introduced to clinical cases;
3. All students should be exposed to scientifically- and clinically-relevant courses in embryology and teratology that take them to the frontiers of knowledge. This may be delivered in several ways, e.g. by healthcare courses that have graduate entry, by having 3 years of scientific training before clinical training, or by a programme of students opting out to pursue intercalating science degrees.

ENDNOTES

[1]As well as the numerous journals concerned with obstetrics and gynecology in general, there is an academic journal that deals specifically with this aspect of medicine - *Journal of Prenatal Medicine* published by CIC Edizioni Internazionali. In addition, there are journals of teratology (e.g. *Teratology* published By Wiley and *Neurotoxicology and Teratology* published by Elsevier).
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Table 3. A Suggested Core Embryology Syllabus for the Dental Course

PRINCIPLES OF EMBRYOLOGY AND PURPOSE OF STUDY IN DENTISTRY
The meaning and importance of embryology and teratology
Embryology in the context of human development and growth
Outline of the early aspects of implantation and embryonic development
Formation of the inner cell mass, blastomere and blastocyst
The bilaminar disc – epiblast and hypoblast
Formation of the amniotic and yolk cavities
GASTRULATION
Purpose of gastrulation
The primitive streak, the primitive node and the notochord
The appearance of the buccopharyngeal and cloacal membranes
Migration of epiblast cells at the primitive streak
Formation of the germ layers and the trilaminar disc
Formation of paraxial mesoderm, intermediate mesoderm, lateral plate mesoderm
Lateral plate mesoderm development into splanchnopleuric and somatopleuric mesoderm
Concept of the role of signalling molecules during gastrulation
DEVELOPMENT OF THE NERVOUS SYSTEM
Role of the notochord
Development of the neural plate and hinges
Development of the neural tube
The neuropores
Spina bifida
Neural; tube landmarks – prosencephalon, mesencephalon, rhombencephalon
The appearance of the cranial nerves
Brain flexures
Development of the neural crest and the characteristics of neural crest cells
General derivatives of the neural crest
The role of the neural crest in craniofacial and dental development
Early sense organ development – the ectodermal placodes
Development of the nasal pit
Early eye development
Inner ear development
EMBRYONIC FOLDING
Head, tail and lateral folds
Appearance of the foregut, midgut and hindgut and the outcome of development of the yolk sac
PARAXIAL MESODERM AND THE SOMITES
Formation from paraxial mesoderm that shows a segmented pattern but not in the developing head region where the paraxial mesoderm remains unsegmented
Definition of a somite and the division into a ventral sclerotome that forms ribs and vertebrae and a dorsal dermomyotome that forms dermis and skeletal muscle

DEVELOPMENT OF THE PHARYNGEAL ARCHES
Alternative names
Appearance on either side of pharyngeal foregut as mesenchymal thickenings
Origin of the mesenchyme of the pharyngeal arches and the role of the neural crest
5 pairs and their numbering
Ist arch forming maxillary and mandibular processes
Derivations of the pharyngeal arch cartilages
Derivations of the pharyngeal arch skeletal muscle primordia
Derivations of the pharyngeal arch nerves
Derivations of the pharyngeal arch aortic arch arteries
The pharyngeal pouches and their derivatives
The branchial clefts and membranes and their derivatives
Branchial cysts
Treacher Collins sequences
Pierre Robin syndrome
CRANIOFACIAL DEVELOPMENT
Formation of the stomodeum and the fate of the buccopharyngeal membrane
Development of the tongue (including innervation and musculature) and the thyroid gland
Thyroglossal duct cysts, ectopic thyroid tissue (incl. lingual thyroid)
Formation of the facial processes and the upper lip
Clefts of the lips
Formation of the nasal cavity
Formation of the nasolacimal duct
The head skeleton – formation of the neurocranium and the sensory capsule
Fates of the prechordal, hypophyseal and parachordal cartilages
The head skeleton – formation of the viscerocranium
Development of the palate from the common oronasal chamber
Primary and secondary palates
Mechanisms responsible for palatal shelf elevation
Cellular events associated with fusion of the palatal shelves post-elevation
Palatal clefts
The aetiology of clefts of the lips and palate and teratogenic influences
PRINCIPLES OF TERATOLOGY
Common congenital malformations in the craniofacial region and the roles of genetic and environmental factors
Folic acid and its beneficial effects
EMBRYONIC STEM CELLS
Therapeutic value of stem cells
Origins of stem cells
Role of ‘embryonic’ stem cells derived from the periodontal and pulpal connectives tissues in a around the tooth