

Doctor Honoris Causa

ASIM KURJAK



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PRESENTACIÓ
D'ASIM KURJAK
PER
LLUÍS CABERO

Excel·lentíssim i Magnífic Senyor Rector,
Digníssimes Autoritats,
Benvolguts Col·legues
Senyores i Senyors,

La Universitat Autònoma de Barcelona ha proposat que ens reuníssim avui aquí per donar testimoni públic dels mèrits acadèmics d'Asim Kurjak i de la col·laboració científica establerta entre el Departament de Pediatria, d'Obstetrícia i Ginecologia i de Medicina Preventiva d'aquesta universitat, i el Departament d'Obstetrícia i Ginecologia de la Universitat de Zagreb. Per això, se li ofereix aquest homenatge i se l'acull a la nostra comunitat en qualitat de doctor *honoris causa*.

El professor Asim Kurjak ha vingut més de quinze vegades a Barcelona i ha participat en la majoria de reunions científiques que tractaven diversos aspectes de la medicina perinatal. Fruit d'aquesta interrelació, ha publicat diversos llibres amb membres de la nostra comunitat científica que han representat els nostres punts de referència. Tanmateix, gràcies al seu ajut, vam poder organitzar el Congrés Mundial de Medicina Perinatal, que vaig tenir l'honor de copresidir amb el doctor Josep M. Carrera, i que va ser el lloc de reunió de més de 4.500 especialistes vinguts de més de setanta països de tot el món.

Ha estat un dels pares del concepte de la medicina perinatal, i ja en la introducció d'un gran llibre titulat *Tractat de medicina perinatal* deia que era un concepte en el qual hi havia una estreta interrelació entre obstetres i neonatòlegs, i la investigació clínica i bàsica, tal com ja havia somiat el professor E. Saling. Continuava dient que els perinatòlegs europeus podem mirar enrere amb satisfacció, ja que el progrés que hem fet en aquest tema ha estat molt important i superior al d'altres col·legues internacionals, i jo afegeixo que ha estat gràcies a l'activa participació de grans prohoms de la medicina perinatal, com el professor Asim Kurjak.

El professor Asim Kurjak va néixer el 13 de setembre de 1942, és a dir, ara té seixanta-un anys. És casat i té dos fills. Es va llicenciar en Medicina i Cirurgia a la Universitat de Zagreb l'any 1966 i va completar la seva formació com a ajudant d'investigació a l'Institut d'Obstetrícia i Ginecologia de Londres. L'any 1974 va especialitzar-se en Obstetrícia i Ginecologia, i l'any 1977 va rebre el grau de doctor en Medicina.

Actualment és el catedràtic d'Obstetrícia i Ginecologia de la Facultat de Medicina de Zagreb. Ha publicat més de 300 articles en revistes d'impacte i ha escrit o participat en 79 llibres de l'especialitat. Ha estat professor invitat en més de 400 reunions internacionals i els seus treballs s'han citat més de 2.600 vegades en el *Science Citation Index*.

S'ha de dir que des de molt aviat es va reconèixer la seva trajectòria professional i investigadora. Així, l'any 1971 va rebre el Premi Nacional de Joves Investigadors de Croàcia. L'any 1985 va ser distingit amb el Premi Nacional Croata Ruder Boskovic per la seva trajectòria científica. Aquest premi és un dels més importants del seu país i es dona cada any. L'any 1990 va rebre el Premi Josip Juraj Strossmayer de l'Acadèmia de les Ciències de la República de Croàcia.

L'any 1994 li van atorgar el Premi de l'Acadèmia de les Ciències i l'Art de la República de Croàcia per les seves investigacions en ciències mèdiques. L'any 1996 va rebre el Premi del Moviment Europeu. L'any 1998 li van concedir el Premi William Lileys pel millor treball científic sobre diagnòstic i tractament fetal. L'any 2000 li van donar el Premi Maternitat de la Societat Europea de Medicina Perinatal. L'any 2001 va rebre la condecoració presidencial de l'orde de la Croatia Starr amb l'efígie de Ruder Boskovic. El mateix any l'Ajuntament de Zagreb li va concedir la placa de la Ciutat de Zagreb en agraïment pel seu treball científic sobre ultrasons i medicina perinatal reconegut a tot el món.

En l'actualitat és el president de l'Associació Mundial de Medicina Perinatal i de l'Acadèmia de Ciències Mèdiques de Croàcia.

Tanmateix, ha rebut el grau de doctor *honoris causa* de les universitats de Banja Luka i Budapest.

El seu perfil investigador s'ha centrat en el desenvolupament de les tècniques d'estudi ultrasonogràfic del fetus, tant en la vessant fisiològica com fisiopatològica. Per això sabem el que succeeix tant de forma estructural com funcional en el fetus des dels primers moments de la seva existència. Són rellevants els seus estudis sobre l'angiogènesi en la placentació i els primers moments del desenvolupament. Aquest coneixement ens ha permès poder saber el grau de possibilitat d'avortament en la fase embrionària. Alhora, els estudis morfològics dels embrions de tan sols vuit o nou setmanes fan possible la sospita que sigui portador d'una cromosomopatia. En la primera meitat de l'embaràs, gràcies a la introducció de les metodologies tridimensionals, també es poden identificar malformacions fetals molt subtils que en la metodologia bidimensional podrien passar desapercibudes.

El coneixement del fetus, en els seus atributs de normalitat, ha facilitat l'estudi d'anomalies, no tan sols estructurals sinó també funcionals. El control del creixement o els estudis hemodinàmics han estat dels avenços més significatius dels últims deu anys, i en aquest camp el professor Kurjak hi ha tingut molt a veure. Les variacions hemodinàmiques d'alguns vasos, com les artèries cerebrals mitjanes o els grans troncs venosos, ens han posat en situació d'alerta sobre el grau de benestar del fetus i ens han ofert la possibilitat de tractar el fetus, sigui dins del ventre matern o bé a fora. D'aquesta manera, s'han evitat lesions de molts fetus que haurien malmès la seva història posterior. En tots aquests estudis científics, el professor Kurjak també ha estat capdavanter i mestre de molts grups investigadors.

Un altre camp, innovador però alhora molt important, és l'estudi, mitjançant l'efecte Doppler, dels patrons d'angiogènesi tumoral com a factor indicador de pronòstic de certes tumoracions malignes, especialment ovàriques. Ja fa més de deu anys que Asim Kurjak va definir els patrons de vascularització de les tumoracions malignes ovàriques, fet que ha permès fins i tot fer un seguiment molt acurat de diagnòstic precoç d'aquesta tumoració maligna, mentre que les altres tècniques d'estudi no donen cap signe ni avís. Per això actualment en les malalties de risc, especialment pels seus antecedents familiars o senzillament per la seva edat, es fa un estudi anual de la vascularització ovàrica com a marcador de les tumoracions malignes d'aquest òrgan femení.

En el camp de les organitzacions professionals, el seu període com a president de l'Associació Mundial de Medicina Perinatal s'ha centrat bàsicament a orientar els coneixements cap als països del tercer món. Fins i tot va organitzar un congrés mundial per tractar les temàtiques pròpies d'aquestes àrees malmeses per la pobresa, on la mortalitat materna és cinc-cents vegades superior a la nostra. Perquè tinguin un exemple esfereïdor, mentre he llegit aquestes paraules de presentació del professor Kurjak, al món s'han mort més de quaranta dones, el 99% d'elles al tercer món. Si ens centrem en els nadons, la mortalitat perinatal és unes 100-400 vegades més gran, i si comptem les conseqüències negatives dels parts, és a dir discapacitats i altres defectes, les xifres encara són més colpidores. Doncs bé, durant el seu període de mandat, s'han posat en marxa molts programes d'ajut i de divulgació en aquests països, fet que li ha valgut la fama de ser una de les persones amb més sensibilitat pels desfavorits. Aquesta forma de pensar i de veure les coses ha fet que hagi entrat de ple en el terreny de la bioètica i la medicina perinatal, i és avui dia un dels defensors dels drets del fetus com a pacient, és a dir com a persona malalta. El concepte del fetus com a pacient, introduït fa molt pocs anys (no arriben a set), ha marcat una nova forma d'investigar i d'exercir de metge i ha provocat canvis estructurals i organitzatius en els centres assistencials més capdavanters.

Des del punt de vista universitari, ha estat reconegut professor visitant de moltes universitats d'arreu del món (Yonago, Jakarta, el Caire, Nova York, etc.).

Per les seves aules han passat una gran part dels investigadors perinatals més importants d'Europa, i al seu centre de Zagreb hi té un equip d'investigadors i becaris dedicats exclusivament a la medicina perinatal.

És membre del consell de redacció de les revistes de més factor d'impacte sobre ultrasons i medicina perinatal, i és coeditor de cinc d'elles.

Voldria esmentar el seu paper durant la guerra dels Balcans. Recordo que l'any 1992, quan va venir a Barcelona per participar en un curs organitzat per l'Institut Universitari Dexeus, va rebre la medalla d'or d'aquesta institució, i en el discurs d'agraïment va fer al·lusió a la situació que vivia el seu país en aquells moments. Va ser molt emocionant veure com el professor Kurjak, amb llàgrimes als ulls, recordava moments dolorosos d'amics i membres de la seva família i explicava com ajudava a escapar de les persecucions moltes persones i malalts que no tenien res a veure amb la massacre a què estava sotmès el poble, fruit de les bogeries de certs governants. En aquella situació, deia: «Ens falta de tot, i aquí en aquest sopar ens sobra de tot. Això em fa sentir malament i no em mereixo més que compartir la meua pena amb el meu poble, i no els honors que vostès em donen avui». Així és el professor Kurjak, i aquest és el motiu pel qual tots els perinatòlegs el tenim com aquell científic que, tot i tenir moments de vent en contra, va superar amb escreix les adversitats i ens ha deixat l'exemple del científic honorat, perseverant, intel·lectualment impecable i, sobretot, generós amb la ciència i amb una gran estima pels malalts i pel món que els envolta.

L'actuació d'Asim Kurjak, durant el seu dilatat currículum acadèmic, restarà sempre clarament diferenciada i reconeguda en l'ingent esforç desenvolupat per investigadors i clínics que ha influït tan decisivament en el concepte de la medicina fetal durant els últims trenta anys.

I és per això, Excel·lentíssim i Magnífic Senyor Rector, que sol·licito que el professor Asim Kurjak sigui investit en el dia d'avui amb el grau de doctor *honoris causa* per la Universitat Autònoma de Barcelona, segons la proposta formulada al seu dia per la Facultat de Medicina i el Departament de Pediatria, d'Obstetrícia i Ginecologia i de Medicina Preventiva.

Moltes gràcies.

DISCURS
D'ASIM KURJAK

**ACCEPTANCE SPEECH BY PROFESSOR ASIM KURJAK
FOLLOWING THE AWARD OF THE DEGREE *HONORIS CAUSA***

Mr. Rector, Dean of Medical School,
colleagues of the University, ladies and gentlemen,

It is indeed unique and special honor to be in Barcelona today to be honored by this ancient University and this convocation. I am deeply aware of the tribute, granted by the award of the degree *honoris causa*, and mindful of the many previous and celebrated awards before me. I am sure that my sponsor, Professor Lluís Cabero, already gave a wonderfully clear description of my life and research, and I am deeply grateful to him for nominate me. I do not have the time to even allude to my professional work, which was deeply connected with perinatal medicine. A most challenging decision for me was to move to clinical work with malformed fetuses. When every new step would demand immense forethought and detailed counseling of patients and to achieve this aims, I had to work facing a battery of ethical issues and moral decisions, as our every step was watch by press, bishops, scientists, clinicians and ethicists. Fortunately we have been lucky that very early in this development I was trained in diagnostic ultrasound and made many collaborative studies with another good friend and remarkable scientists from Barcelona, professor Josep Maria Carrera. Looking back on tremendous development of ultrasonic technology, it is not overstating the fact to say that ultrasound has changed the thinking of our age. The magnitude of this step alone is incalculable. But, what we can say is that ultrasound, more than any other modern technique has made manifest that the fetus is an individual virtually from conception.

It is also evident that at an early stage of intrauterine existence we develop a remarkable individuality. Unfortunately this wonderful integration of events is subject to the malevolence of disease and chance just as much as in life after

birth. In fact, because of our vulnerability in utero after pregnancy and delivery we are not again subject to such risks of mortality until our old age. Hence, there is a logical demand for perinatal medicine and with it comes a need for fetal assessment from conception to birth. During the last twenty years I was and still am deeply involved in the study of beginning of individual human life and development of personality. It is of course, a subject of great controversies and proper answer on this question should definitely include not only science in medicine, but philosophy, ethics, morality and law. In my lecture, I am going to illustrate how scientific advances might help in better understanding of mystery of early human life.

LECTURE

Ladies and gentlemen,

All of this just mentioned our complex affairs what this award of the degree *honoris causa* really means. It salutes all the new things. It sends a message of respect and honor to my colleagues and me from Zagreb. For my part, I wish to thank all those who throughout my life thought me in setting standards and attaining objectives. I have been immensely fortunate to be supportive by my family, my close co-workers, parents who did all they could with they scant resources, sons whose support is never ending, and admirable teachers and students. Numerous professional colleagues who have joined in these studies with all their heart and energy, and my special thanks go out to Branko Rajhvajn, my first chief, and Sanja Kupesic, my best co-worker.

From today, I am privileged to hold an honorary doctorate of Autonomous University of Barcelona and I should do all possible to sustain this honor. May I again thank my sponsors thorough my heart my dear Spanish friends, Lluís Cabero and Josep Maria Carrera, and University Senate, Rector, Dean. I will long remember this day.

A. Kurjak

THE FACTS AND DOUBTS ABOUT THE BEGINNING OF THE HUMAN LIFE AND PERSONALITY

«What a piece of work is a man».
William Shakespeare, *Hamlet*

«To those of average curiosity about the wonders of nature, it is likely that two great mysteries have stirred the imagination; and each concerns a birth. Who has not gazed into the heavens on the starlit night and wondered about the birth of the universe? And who has not been stimulated by the sight of the newly born baby to the marvel at the unseen events within the mother's uterus that have led to the birth of such a perfect creation?»¹ These words written by the Professor Sir Graham (Mont) Liggins open Pandora's box of questions, dilemmas, doubts and controversies about human life and its beginning offering everybody lifelong challenge to solve mystery of life.

Entering this, filed scientists have been remiss in failing to translate science into the terms that allow mankind to share their excitement of discovering life before birth. Regardless to remarkable scientific development, curiosity, and speculations dating back to Hippocrates, life before birth still remains a big secret. Different kinds of intellectuals involved themselves trying to contribute to the solution of human life puzzle. They are led by the idea that each newborn child will only reach its full potential if its development in uterus is free from any adverse influence, providing the best possible environment for the embryo/fetus. Considering embryo/fetus, it should be always kept in mind amazing aspect of these parts of human life in which the mother and the embryo/fetus, although locked in the most intimate relationships, are at ALL TIMES two separate people. Accepting embryo/fetus as the person opened new set of questions about its personality and human rights. Today, synthesis between scientific data and hypotheses, philosophical thought, and issues in the humanities, has become

pressing necessity in order to deal with ethical, juridical and social problems arising from man's interference in many aspects and stages of life.²

Definition of the life

Proper answer to the question «How to define human life?» is complicated. Nowadays dilemmas consider the respect of human life from the birth to death involving not just biology but other sciences also. Philosophy, theology, psychology, sociology, law and politics evaluate this topic from different points of view. Integration of all would result proper definition.

When defining life it should be considered not just life as it is today but as it might have been in its primordial form and as it will be in the future. All present forms of life appear as something completely new. Life, then, is transferred and not conceived in each new generation. Furthermore, the phenomenon of life has existed on Earth for approximately 3.5 billion years. Consequently, although the genome of a new embryo is unique, the make-up of embryo is not new. If life is observed through the cell than every life (and human also) is considered as a continuum. Human cells and the mankind have been existing on the Earth continuously since the appearance of the first man. However, if definition refers to the single human being or present population, the statement «human life is a continuum» is not acceptable.³

Life, in a true sense of word, begins when the chemical matter gives rise, in a specific way to an autonomous, self-regulating, and self-reproducing system. Life is connected with a living being, and it created its own system as an indivisible whole, forms its individuality. One of the most important characteristics of living beings is reproduction. Reproduction is a mean of creating new life by transferring forms of old one into newly formed human being. Therefore, variability, individual development and harmony characterize human beings. Individuality is the most essential characteristic of human being consisting new life but also all human life forms through the evolution, characterized by phenotype, behavior and the capability to recognize and adapt. Human embryo and fetus gradually develop into these characteristics.

Although we should not forget that in the same way today's research is tomorrow's benefit (1), concerning human life conclusions should not be treated one-sidedly, from one perspective. This reality should be regarded in all its richness: embryo gives biologist, geneticist substance for consideration, but since we are talking about the beginning of an individual human life, it requires philosophical-anthropological consideration, theology and social sciences as well. In its protection, we have to include ethics and law. This approach leads to conclusion that it is necessary to reject reductionism as well as integrism and to find «golden middle» in between these two methodologies. (2)

Scientific approach

Biology characterizes human being by dynamics of the system and its self-control (homeostasis), excitability (response to stimuli of different nature and origins), self-reproducibility, the heredity of the characters, and the evolutive trend. (2)

For biologists it is important to specify which form of life phenomena, we are referring to: cell, organism population or species. The basic level of organization and the simplest form of life is the cell. Biologically speaking human cellular life never stops — or if it did, the extinction of the human species would result — and is passed on from one generation to another. Human individual organismic life is defined within its life cycle, which is temporary limited; i.e. it has a beginning and the end.⁴ It is obvious that life is a highly dynamic phenomenon, which could be described and explained through the careful study of life processes and interactions by interdisciplinary approach. In human spermatozoa and the oocyte are two essential cells involved in creating human life. It is clear that biologists are most qualified to render judgement on this matter. Understanding of beginning of human life and development of the embryo/fetus could provide definitive resolution. However, with a recent possibility of visualizing early human development virtually from conception, perinatologists should be those who by study, training, practice and research are singularly qualified.⁵

The science enables us data about physical development of the human being but does not provide information about its personality and personalhood.

Human embryogenesis

Only proper understanding of the process of human embryogenesis enables answering scientifically the question when the life cycle of human individual starts. Therefore, in the following text the main steps of the human developmental process are going to be briefly described, primarily during the first 15 days after fertilization.

A human being originates from two living cells: the oocyte and the spermatozoon transmitting the torch of life to the next generation. The oocyte is a cell approximately 120 μ in diameter with thick membrane, known as the zona pellucida. The spermatozoon moves, using the flagellum or tail, and the total length of the spermatozoon including the tail is 60 μ .⁶

After singamy, the zygote undergoes mitotic cell division as it moves down the fallopian tube toward the uterus. A series of mitotic divisions then leads to the development of the preembryo. The newly divided cells are called blastomeres. From 1 to 3 days after singamy, there is a division into two cells, then four cells. Blastomeres form cellular aggregates of distinct, totipotent, undifferentiated cells

that, during several early cell divisions, retain the capacity to develop independently into normal preembryos. As the blastocyst is in the process of attaching to the uterine wall, the cells increase in number and organize into two layers of cells. Implantation progresses as the outer cell layer of the blastocyst, the trophoblast, invades the uterine wall and erodes blood vessels and glands. Having begun 5 or more days after fertilization with the attachment of the blastocyst to the endometrial lining of the uterus, implantation is completed when the blastocyst is fully embedded in the endometrium several days later. Even during these 5-6 days, modern medicine introduces the possibility of making preimplantation genetic diagnosis.

However, at this time, these cells are not yet totally differentiated in terms of their determination to specific cells or organs of the embryo. The term preembryo, then, includes the developmental stages from the first cell division of the zygote through the morula and the blastocyst. By approximately the 14th day after the end of the process of fertilization, all cells, depending on their position, will have become parts of the placenta and membranes of the embryo. The «embryo» stage, therefore, begins approximately 16 days after the beginning of the fertilization process and continues until the end of 8 weeks after fertilization, when organogenesis is complete.⁷

Pre-embryo is the structure that exists from the end of the process of fertilization until the appearance of a single primitive streak. Until the completion of implantation pre-embryo is capable of dividing into multiple entities, but does not contain enough genetic information to develop into an embryo: it lacks of genetic material from maternal mitochondria and of maternal and parental genetic messages in the form of messenger RNA or proteins. So, during the preembryonic period has not yet been determined with certainty that a biological individual will result or would it be one or more (identical twins forming), so that the assignment of full rights of a human person is inconsistent with biological reality.

A conclusion is that the pre-embryo requires the establishment of special rules in the society: it cannot claim absolute protection based on claims of personhood; although meriting respect, it does not have the same moral value that a human person has.

Today, one largely accepted opinion is that, until the 14th day from fertilization or at least until implantation, the human embryo may not be considered, from the ontological point of view, as an individual.

Genetic uniqueness and singleness coincide only after implantation and restriction have completed, which is about 3 weeks after fertilization. Until that period, the zygote and its sequelae are in a fluid process, are not physical individual, and therefore cannot be a person.

It is well known that high percentages of oocytes, which have never been penetrated, proceed on to further development, and that many oocytes which do, are thwarted so early in their development that their presence is not even recognized. It is suggested that 30% of conceptions detected by positive

reactions to human chorionic gonadotropin (HCG) tests abort spontaneously before these pregnancies are clinically verified.

The newly conceived presents itself as a biologically defined reality. However, the status of the pre-embryo as an individual remains a great mystery. In the present scientific scene especially with the progress of ultrasound technologies, prenatal psychology and therapeutics opened a window into prenatal life of embryo and fetus confirming the evidence that the embryo/fetus is a true subject itself.⁸

Personality

Defining personality is very complex. There is still no clear definition of personality. One dictionary offers «what constitutes an individual as distinct person», but does not define what the «what» is. Another dictionary asserts «the state of existing as a thinking intelligent being». This definition might lead to the inference that personality increases pro rata with intelligence, or that some people may not have a personality at all if we followed Bertrand Russell's dictum that «most people would rather die than think and many, in fact, do!». Ken Stallworthy's *Manual of psychiatry* is more helpful with the definition that «personality is the individual as a whole with everything about him which makes him different from other people» because we can certainly distinguish fetuses from each other and from other people. With the next sentence —«personality is determined by what is born in the individual in the first place and by everything which subsequently happens to him in the second»— we are really in the field. (2)

Led by truism «No insignificant person was ever born»⁹ human being should be valued from the birth to natural death. But as always in nowadays world when truism is turned on its head when a person is selectively devalued, made insignificant on the basis, for example, of skin color, religious belief etc. Therefore, it is hard to establish proper values and exact definitions. This comes especially to sight when prenatal life is considered. Above stated truism opens important question: «Is the person —unborn a person in the first place and, if so, is the person— unborn a “significant” person?». (2)

Let us evaluate further present controversies. There is no doubt that the embryo and fetus in utero are human individuals prior to birth. The child that is born is the same developing human individual that was in the mother's womb. Birth alone cannot confer natural personhood or human individuality. This is confirmed by preterm deliveries of babies who are as truly human and almost as viable as those whose gestation goes to full term. All the known evidence support the human fetus being a true ontological human individual and consequently a human person in fact if not in law. A human being cannot begin before the appropriate brain structures are developed that are capable of

sustaining awareness. The same applies to a grossly malformed fetus. It would still be a human individual even if its human nature was not perfect nor its functions quite normal. Nobody questions the humanity of a Down's syndrome fetus or child. A fetus or child with severe open spina bifida is non the less a human being. The same should be said for the live anencephalic fetus or infant with only brain stem functions. It is a human individual even if it lacks a complete brain and usually survives birth by only a few hours or a day.

Human society created several standards in defining «person», «human being» based on what is familiar and easy recognizable. (2) For example: A human speaks, understands, and laughs. Absence of these characteristics (mutism, autism, and stoicism) does not disqualify. To the contrary, conclusion is that the characteristics we have come to associate with being a person may not be applicable to each individual person. Therefore, it is necessary to establish criteria for definition of «person» in society and in time. Italian Professors (8) committed themselves to care for embryo in such a way, the same dignity to every patient and the human conditions to grow and develop, to educate others inside and outside the speciality and carry out researches involving all the components of society.

Bioethical aspects

The idea of embryo/fetus as the miniaturized infant or adult is true in extent that the embryonic / fetal physiologist must be able to apply knowledge of every system obtained in born, yet quite untrue in failing to recognize the many ways in which life before birth differs fundamentally from life after birth. (1) The newly conceived form presents itself as the biologically defined reality: it is an individual that is completely human in development that autonomously, moment by moment without any discontinuity, actualizes its proper form in order to realize through intrinsic activity, a design present in its own genome. (8) Embryo as a patient is best understood as the subset of the concept of the fetus as the patient. These two concepts opened whole set of questions regarding ethical problems. The embryo as the patient is indivisible from its mother. However, balance is needed in protection interests of embryo/fetus and the mother. One prominent approach to understanding the concept of the embryo/fetus as a patient has involved attempts to show whether or not the embryo/fetus has independent moral status or personhood^{10,11}. Independent moral status for the fetus would mean that one or more of characteristics possessed either in, or of the embryo/fetus itself and, therefore, independently of the pregnant woman or any other factor, generate and therefore ground obligations to the embryo/fetus on the part of the pregnant woman and her physician.

A wide range of intrinsic characteristics has been considered for this role, e.g., moment of conception, implantation, central nervous system development,

quickening, and the moment of birth.¹² Given the variability of proposed characteristics, there are many views about when the embryo/fetus does or does not acquire independent moral status. Some take the view that the embryo/fetus possesses independent moral status from the moment of conception or implantation. Others believe that the embryo/fetus acquires independent moral status in degrees, thus resulting in «graded» moral status. Still others hold, at least implicitly, that the embryo/fetus never has independent moral status so long as it is in utero.¹³

Being a patient does not require that one possesses independent moral status.¹⁴ Being a patient means that one can benefit from the application of the clinical skills of the physician¹⁵. Put more precisely, a human being without independent moral status is properly regarded as a patient when the following conditions are met: that a human being is presented to the physician for the purpose of applying clinical interventions that are reliably expected to be efficacious, in that they are reliably expected to result in a greater balance of goods over harms in the future of the human being in question. (13) In other words, an individual is considered a patient when a physician has beneficence-based ethical obligations to that individual.

To clarify the concept the embryo/fetus as the patient, beneficence-based obligation is necessary to be provided. Beneficence-based obligations to the fetus and embryo exist when the fetus can later achieve independent moral status. (15) This leads to conclusion that ethical significance of unborn child is in direct link with the child to be born – the child it can become.

Legal status of the embryo

When discussing law, it should be always kept in mind that medicine is international, but law is not.

The status of the human embryo is not juridical defined and relies on the political, social, and religious influences in each country. It is hard to answer the question when human life should be legally protected. At the time of conception? At the time of implantation? At the time of birth? In all countries (except Ireland and Liechtenstein) juridical considerations are based on roman law. Roman civil law says that the fetus has right when it is born or if it is born-nasciturus.

Few countries agree with definition of beginning of human personality the time of conception. The majority does not grant legal status to the human embryo in vitro (i.e., during the 14 days after fertilization). Thus, even in the absence of legal rights, there is no denying that the embryo constitutes the beginning of human life, a member of the human family. Therefore, whatever the attitude, every country has to examine which practices are compatible with the respect of that dignity and the security of human genetic material.¹⁶

Arguments for beginning of human life and human person at fertilization

The fundamental approaches of biomedical and social practice must begin with the understanding that the subject before birth is a person and that «personhood» is conferred by successful fertilization of the egg. To hide from this in silence or ignorance should be unacceptable to all as stressed by Scarpelli (6).

View that human life begins when sperm and eggs fuse to give rise to a single cell human zygote whose genetic individuality and uniqueness remain unchanged during normal development is widely supported. Because the zygote has the capacity to become an adult human individual, it is thought it must be one already. The same zygote organizes itself into an embryo, a fetus, a child and an adult. By this account, the zygote is an actual human individual and not simple a potential one in much the same way as an infant is on actual human person with potential to develop to maturity and not just a potential person. As Scarpelli pointed out recently outside the realm of religious dogma, there has been no one, whose existence can be traced back to any entity other than the fertilized egg. The biological line of existence of each individual, without exception, begins precisely when fertilization of the egg is successful (6).

The process of fertilization actually begins with conditioning of the spermatozoon in the male and female reproductive tracts. Thereafter, fertilization involves not only the egg itself but also the various investments, which surround the egg at the time it is released from the ovary follicle. Fertilization, therefore, is not an event, but a complex biochemical process requiring a minimum of 24 hours to complete singamy, that is the formation of a diploid set of chromosomes. During this process, there is no commingling of maternal and paternal chromosomes within a single nuclear membrane (pre-zygote); after this process the parental chromosomes material is commingled (zygote).

Among the many other activities of this new cell, most important is the recognition of the new genome, which represents the principal information center for the development of the new human being and for all its further activities. For the better understanding of the very nature of the zygote, two main features are to be at least mentioned here. The first feature is that the zygote exists and operates from singly on as a being, ontologically one, and with a precise identity. The second feature is that the zygote is intrinsically oriented and determined to a definite development. Both identity and orientation are due essentially to the genetic information with which it is endowed. That is why many do believe that this cell represents the exact point in time and space where a new human individual organism initiates its own life cycle (2).

Arguments against beginning of human life at fertilization

Today, one largely accepted opinion is that, until the 14th day from fertilization or at least until implantation, the human embryo may not be considered, from the

ontological point of view, as an individual. There are at least five main reasons in favor of this opinion:

1. Before formation of embryonic disk embryo is «a mass of cells genetically human», «a cluster of distinct individual cells» which are each one «distinct ontological entities in simple contact with the others».¹⁷

2. Until approximately the 14th day after fertilization, all that happens is simply a preparation of the protective and nutritional systems required for the future needs of the embryo. Only when entity called embryonic disc is formed, it can develop into a fetus.¹⁸

3. Monozygotic twins phenomenon or chimeras can occur. In fact, this seems to be the strongest reason why the embryo is denied the quality of individuality and as a proof that the zygote cannot be an ontologically human being. In approximately one third of cases the embryo divides at about the two cells stage and in the other two thirds the inner cell mass divides within the blastocyst from day 38. Occasionally, the division takes place from day 8-12 but usually it is not complete thereby forming conjoined identical twins or two-headed individuals.

4. Co-existence of the embryo with its mother is a necessary condition for an embryo belonging to the human species and this condition can be obtained only at implantation (12). However, there is evidence that development of human embryo in vitro can continue well beyond the stage of implantation, and that mouse embryos implanted under the male renal capsule can reach the fetal stage. It is also argued, or at least implied, that so many human embryos die before or after implantation that it would be lacking in realism to accept that the human individual begins before implantation.

It is well known that high percentages of oocytes, which have never been penetrated, proceed on to further development, and that many oocytes which do, are thwarted so early in their development that their presence is not even recognized. Up to 50% of ovulated eggs and zygotes recovered after operations were found so grossly abnormal that it would be very unlikely that they would result in viable pregnancies. It is also suggested that 30% of conceptions detected by positive reactions to human chorionic gonadotropin (HCG) tests abort spontaneously before these pregnancies are clinically verified. The scientific literature is not unanimous on the incidence of natural wastage prior to, and during, implantation in humans, varying from 15% to as much as 50%. The vast majority of these losses are due to chromosomal defects caused during gametogenesis and fertilization.¹⁹

Genetic uniqueness and singleness coincide only after implantation and restriction have completed, which is about 3 weeks after fertilization. Until that period, the zygote and its sequelae are in a fluid process and are not physical individual and therefore cannot be a person.

5. The product of fertilization may be a tumor, an hydatidiform mole or chorioepithelioma. Though the mole is alive and of human origin, it is definitely

not a human individual or human being. It lacks a true human nature from the start and has no natural potential to begin human development.

A teratoma is another clear instance of cells developing abnormally that results from the product of fertilization, but which could not be considered to be a true human individual with a human nature. It has no potential to develop into an entire fetus or infant. Clearly, the fetus with the teratoma would be a human individual, but not the attached teratoma itself. Obviously, not all the living cells that develop from the conceptus, the early embryo or the fetus form an integral part of a developing human individual.

Different religious teachings and historical aspects

Catholic Church's teachings are clearly described in the Introduction *Donum Vitae*: «A human creature is to be respected and treated as a person from conception and therefore from that same time his (her) rights as a person must be recognized, among which in the first place is the invaluable right to life of each innocent human creature».

In 1997 the third Assembly of the pontifical Academy for life was held in Vatican City. It has been concluded that at the fusion of two gametes, a new real human individual initiates its own existence, or life cycle, during which—given all the necessary and sufficient conditions—it will autonomously realize all the potentialities with which it is intrinsically endowed. The embryo, therefore, from the time of gametes fuse, is a real human individual, not a potential human individual. It was even added that recent findings of human biological science recognize that in zygote resulting from fertilization the biological identity of a new human individual is already constituted.^{20, 21}

In Western Europe and in the North and South America these opinions are mostly based on Judeo-Christian theology, in Arabian Countries, in Africa and in Asia prevail the influences of the Islamic and Buddhist religions. Although their approach to the beginning of human life is impressively similar, each of these religions have different attitudes to the problem of embryo research, infertility and its therapy. In a fact, while the Jewish attitude towards infertility is expressed in the Talmud sayings and in the Bible (synthesized in the first commandment of God to Adam «Be fruitful and multiply»), the Christian point of view establishes no absolute right to parenthood. According to the Islamic views, attempts to cure infertility are not only permissible, but also a duty. Buddhism has imposed strict ethics on priests, but it has relatively lenient attitudes toward lay people, so if medical treatment for infertility is available, people should make use of it.

For about two thousand years the opinions of Aristotle, the great Greek philosopher and naturalist, on the beginning of the human being were commonly held. He argued that the male semen had a special power residing in it, *pneuma*,

to transform the menstrual blood, first into a living being with a vegetative soul after seven days and subsequently into one with a sensitive soul 40 days after contact with the male semen.²²

Aquinas adopted Aristotle's theory but specified that rational ensoulment took place through the creative act of God to transform the living creature into a human being once it had acquired a sensitive soul. The first conception took place over seven days while the second conception or complete formation of the living individual with a complete human nature lasted 40 days.²³

Hippocrates believed that entrance of the soul into the male embryo occurred on the thirtieth day of intrauterine life. It entered into the female embryo on the fortieth day. Actually, this idea was a considerable improvement on the scheme found in the Book of Leviticus, where it is suggested that the soul does not enter the female until forty days after the conception.²⁴

In short, the rational soul enables the matter to become a human being, an animated body, an embodied soul, a human person.

Harvey's experiments with deer in 1633 proved Aristotle's theory of human reproduction wrong, without himself finding a satisfactory explanation of human conception.

After modern scientists discovered the process of fertilization most people took for granted that human being, complete with a rational soul, began once fertilization had taken place.

It is clear that the answer to the question «When has the human being actually come to life?» could only be given by combining the cognition of different religions, philosophy and various biological scientific disciplines. There is a very fine line between the competence of science and the one of metaphysics, and it greatly depends on the individual's philosophical principles. Those two, more or less autonomous intellectual disciplines have very often tried dominating one another, or ignoring each other. It is only recently that the majority of scientists and some theologians have come to realize that the separate meanings of scientific and religious «truths» complement themselves thus representing methodologically independent entities. Current science is not interested in what Nature is, but in the facts that could be started regarding it, thus trying to explain the term, rather than inventing it. The main difference between science and religion can be seen in the fact that scientific «truths», unlike religious postulates, can and must be experimentally verified and the methods of scientific cognition can be easily explained and learnt. While religion favors irrationality, science prefers an entirely rational approach to matters of importance. Intellectual cognition when scientifically expressed usually is in a form of mathematical formulas and presented quantitatively. On the contrary, religion tends to keep its truths in a form of metaphoric expressions, preferring qualitative. Today, there is a tendency, on a higher level, to reopen the dialogue between the science and religion, which was present at the very beginning of our

culture. Religion had existed long before science came to life, but science is not to be thought of as a continuation of the religion. Each discipline should preserve its principles, its separate interpretations and its own conclusions. In the end, both of them represent different components of the one and indivisible culture of mankind.

Visualization of early human development

Significant advances have been made in recent years in visualizing and analyzing the earliest human development. Most of them have been done by introduction of three-dimensional color Doppler sonography.

Many new parameters about early human development are now studied by Doppler ultrasound. Considerable number of biochemical, morphological and vascular changes occur within the follicle during the process of ovulation and luteinization and most of them can be studied by transvaginal ultrasound with color Doppler and 3D facilities.²⁵ If the oocyte is fertilized the embryo is transported into the uterus where under a favorable hormonal and environmental conditions, it will implant and develop into a new and unique individual. The introduction of transvaginal color Doppler improved the recognition of blood vessels enabling detailed examination of small vessels such as arteries supplying preovulatory follicle, corpus luteum and endometrium. (18)

Perifollicular vascularization can help in identification of follicles containing high quality oocytes, with a high probability of recuperating, fertilizing, cleaving and implanting, while 3D ultrasound enables accurate morphological inspection and detection of cumulus oophorus. Follicles without visualization of the cumulus by multiplanar imaging are not likely to contain fertilizable oocytes. This information is especially useful in patients undergoing ovulation induction.

Following ovulation, the corpus luteum is formed as the result of many structural, functional and vascular changes in the former follicular wall. Color Doppler studies of the luteal blood flow velocities enable evaluation of the corpus luteum function in second phase of menstrual cycle and early pregnancy. When the placenta takes over the role of production of progesterone, the corpus luteum starts regressing.

After ovulation there is a short period during which the endometrial receptivity is maximal. During these few days a blastocyst can attach the endometrium and provoke increased vascular permeability and vasodilatation at the implantation site. Trophoblast produced proteolytic enzymes cause the penetration of the uterine mucosa and erode adjacent maternal capillaries. This results in formation of the intercommunicating lacunar network – the intervillous space of the placenta. A small intradecidual gestational sac can be visualized by transvaginal sonography between 32 and 34 days.²⁶

The secondary yolk sac is the earliest extraembryonic structure normally seen within the gestational sac in the beginning of the 5th gestational week. The yolk sac volume was found to increase from 5 to 10 weeks' gestation. When the yolk sac reaches its maximum volume at around 10 weeks it has already started to degenerate, which can be indirectly proved by a significant reduction in visualization rates of the yolk sac vascularity (17). Therefore, a combination of functional and volumetric studies by 3D power Doppler helps to identify some of the most important moments in early human development.

The embryonic heart begins beating on about day 22-23, accepting blood components from the yolk sac and pushing blood into the circulation. The embryonic blood begins circulating at the end of the 4th week of development.

The start of the embryo-chorionic circulation changes the source of nourishment to all intraembryonic tissues. The survival and further development of the embryo become dependent on the circulation of embryonic/fetal blood. If the embryo-chorionic circulation does not develop, or fails, the conceptus is aborted. The embryo cannot survive without the chorion (placenta) and the chorion will not survive without the embryo. Avascular degenerated chorionic villi constitute the hydatidiform mole.

Within the embryo, there are three distinct blood circulatory systems (6):

1. Vitelline circulation (from yolk sac to embryo)
2. Intraembryonic circulation
3. Two umbilical arteries (from embryo to placenta–fetoplacental circulation)

It is possible to visualize and assess them virtually from conception.^{27, 28, 29, 30, 31}

At five weeks from the maternal side of placenta, it is possible to obtain simultaneously three-dimensional imaging of the developing intervillous circulation during the first trimester of pregnancy. Three-dimensional power Doppler reveals intensive vascular activity surrounding the chorionic shell starting from the first sonographic evidence of the developing pregnancy during the 5th week of gestation.

At seven weeks three-dimensional power Doppler images depict aortic and umbilical blood flow. Initial branches of umbilical vessels are visible at the placental umbilical insertion.

During the 8th and 9th week, developing intestine is being herniated into the proximal umbilical cord.

At nine to ten weeks, herniation of the mid-gut is present. The arms with elbow and legs with knee are clearly visible, while feet can be seen approaching the midline.

At eleven weeks, three-dimensional power Doppler imaging allows visualization of the entire fetal and placental circulation.

During the 11th-12th week of pregnancy development of the head and neck continues. Facial details as nose, orbits, maxilla and mandibles are often visible. Herniated mid-gut returns into the abdominal cavity.

New possibilities for studying embryonic movements and behavior

The latest development of 3D and 4D sonography enables precise study of embryonic and fetal activity and behavior.³² With four-dimensional ultrasound movements of head, body and all four limbs and extremities can be seen simultaneously in three dimensions.³³ Therefore, the earliest phases of the human anatomical and motor development can be visualized and studied simultaneously. It is clear that neurologic development, early fetal motor activity and behavior, needs to be re-evaluated by this new technique.^{34, 35} Recently, our group studied the development of the complexity of spontaneous embryonic and fetal movements.³⁶ With advancing of the gestational age the movements become more and more complex. The increase in the number of axodendritic and axosomatic synapses between 8 and 10 and again between 12 and 15 weeks³⁷ correlates with the periods of fetal movement differentiation and of the onset of general movements and complex activity patterns such as swallowing, stretching and yawning, seen easily by 4D technique. Seven to eight weeks of pregnancy gross body movements appear. They consist of changing the position of head towards the body. Nine to ten weeks of pregnancy limb movements appear. They consist of changing of position of extremities towards the body without the extension or flexion in elbow and knee. Ten to twelve weeks of pregnancy complex limb movements appears. They consist of changes in position of limb segments towards each other, such as extension and flexion in elbow and knee.

Twelve to fifteen weeks of pregnancy swallowing, stretching and yawning activities appear. In addition to these activities, it is now feasible to study by 4D ultrasound a full range of facial expression including smiling, crying and eyelid movement.

It is hoped that new 4D technique will help us for better understanding of both somatic and motoric development of early embryo. It will also enable reliable study of fetal and even parental behavior (33).

Conclusion

The question when a human life begins and how to define it, could be answered only through the inner-connecting pathways of history, philosophy and medical science. It has not been easy to determine where to draw the fine line between the competence of science and metaphysics in this delicate philosophical field. To a large extent the drawing of this line depends on one's fundamental philosophical outlook.

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Kotor Varos

Married (two sons)

M.D., Zagreb, 1966

Postgraduate studies at the University of London, 1971-1972

Specialist in OB/GYN, 1974

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Professor and chairman of the Department of Obstetrics and Gynaecology at the University of Zagreb, Croatia

EXPERIENCE

1966 Director of Health Care Centre, Kotor Varos, Bosnia and Herzegovina

1979 Head of Ultrasonic Institute University of Zagreb

1985 Head of World Health Organization Collaborating Centre for Ultrasound in Developing Countries

1985-present

Head of the Department of Obstetrics and Gynaecology Medical School University of Zagreb «Sveti Duh» General Hospital, Zagreb

ACADEMIC AND RESEARCH INSTITUTIONS

1968 Appointed assistant professor in Department of Obstetrics and Gynaecology, University of Zagreb

1980 Appointed professor of obstetrics and gynaecology

1981 Lecturer at the post-graduate seminars on pediatrics, echocardiography, radiology, human genetic and perinatal medicine at the University of Zagreb

1986 Visiting professor at the University of Yonago, Japan

Visiting professor at the University of Jakarta, Indonesia

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Visiting professor at the Aim Shans University of Cairo, University of Ankara, Cornell Medical Centre, New York

ADMINISTRATIVE

1974-1985

President of the Organizing Committee of 7 international symposia organized in Dubrovnik

1980 Director of the postgraduate course in diagnostic ultrasound, University of Bari, Italy

1981 Chairman of the 4th European Congress on Ultrasound in Medicine, Dubrovnik, Croatia

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Director of «Ian Donald» Inter-University School of Medical Ultrasound, Dubrovnik, Croatia

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Director of the post-graduate studies Ultrasound in Clinical Medicine at the University of Zagreb

1984 Member of the Scientific Group of the World Health Organization

Chairman of the First International Symposium «The Fetus as a Patient», Dubrovnik – Sveti Stefan

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President of the International Society «The Fetus as a Patient»

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Director of Ian Donald Inter-University School for Ultrasound in Trieste, Granada and Istanbul

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Director of the postgraduate studies Ultrasound in Clinical medicine for foreign students organized at the University of Zagreb

1986 Chairman of the First World Congress Ultrasound in Developing Countries, Dubrovnik, Croatia

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Secretary General of International Society for Ultrasound in Obstetrics and Gynecology

since 1994

Member of Executive Board of European Movement - Croatia

since 1995

Secretary General of Croatian Association of the Club of Rome

since 2000

Vice-President of Croatian Association of the Club of Rome

Member of Committee for election of teachers in obstetrics and gynecology, Medical School University of Tuzla, Bosnia and Herzegovina

since 2001

President of Croatian Association of the Club of Rome

MEMBERSHIP IN THE EDITORIAL BOARD OF INTERNATIONAL JOURNALS

since 1979

Ultrasound in Medicine and Biology

since 1980

Journal of Perinatal Medicine

since 1981

Journal of Fetal Medicine

Core Journals in Obstetrics and Gynaecology

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since 1988

The International Journal of Prenatal and Perinatal Studies,
Stockholm, Sweden

Journal of Maternal-Fetal Investigation, USA

Journal of Fetal Diagnosis and Therapy, Paris, France

Member of the Scientific Committee of the journal *Archivio di Ostetricia e Ginecologia*

since 1995

Referee of manuscripts for more than 20 medical journals

since 1996

Advisor for the journal of Saudi Obstetrics and Gynaecological Society

since 1997

Archives of Perinatal Medicine

since 1999

Editorial Board Member of *Fetal Diagnosis and Therapy*

since 2000

Editorial Board Member of *Ippocrate*, Lugano, Switzerland

Member of the Board of the journal *Progresos en Obstetría y Ginecología*, Barcelona, Spain

Member of the 2000 *ad hoc* Editorial Board of *Fertility and Sterility*

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Member of the Editorial Board of the *Jordanian Journal of Obstetrics and Gynecology*

CO-EDITOR OF INTERNATIONAL JOURNALS

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Ultrasound in Obstetrics and Gynecology, London

Gynecologia et Perinatologia, Zagreb

since 1996

Prenatal and Neonatal Medicine, London

Area Editor of *Journal of Clinical Ultrasound*, New York

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Journal of Perinatal Medicine, Berlin

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The Ultrasound Review of Obstetrics and Gynecology

MEMBERSHIP IN PROFESSIONAL SOCIETIES

1975-1984

Vice-President of the European Federation for Ultrasound in Medicine and Biology

1978-1991

President of the Yugoslav Association of Societies for Ultrasound in Medicine and Biology

1991-1994

President of the Croatian Association of societies for Ultrasound in Medicine and Biology

1978-1979

President of the International Society for the Study of Physiology and Pathophysiology of Pregnancy (Organisation Gestosis), Basel

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Member of Italian Academy of Science and Art of Reggio Puglia, Italy

since 1983

Member of Croatian Academy of Medical Sciences

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Honorary Fellow of the American Institute of Ultrasound

1992

Chairman of the Basic Postgraduate Training Program Commission and chairman of European label of Excellency for the Extended European Board of Obstetrics and Gynecology (E-EBGO)

1993

Member of Executive Committee of the European Society for Gynecologic and Obstetric Investigation

since 1993

Member of Executive Board of Croatian Academy of Medical Sciences

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- 1993-1994
President of International Society for the Study of Pathophysiology of Pregnancy
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President-Elect of European Association of Perinatal Medicine
- 1996-1998
President of European Society of Perinatal Medicine
- since 1997
Member of European Academy of Science and Arts
- since 1998
Member of Academy of Medical Sciences of Catalonia
- 1999-2003
President of World Association of Perinatal Medicine
- 1999
Member of the International Advisory Committee for the Middle East 3D Ultrasound Society

Member of the International Society of Prenatal and Perinatal Psychology and Medicine
- 2000
President of Academy of Medical Sciences of Croatia
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Member of Fothergill Club
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Foundation member of the International School of Postgraduate Medical Education (ISPME)
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Member of Croatian Society for Calcified Tissues
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Member and professor of the Spanish School of Ultrasound and a representative member in the Rectoral Council of the Spanish Society of Ultrasound in Obstetrics and Gynecology

Member of Croatian Society for Medical Expertise of Croatian Medical Association

ACADEMIC AND PROFESSIONAL GRANTS AND AWARDS

1963-1965

Three first prizes of Rector of the University of Zagreb for distinguished students

1971 National Prize for Young Scientists

1975 Presidential Award–Medallion for the Order of Service to the Nation–Silver Star

1980 Italian national award for scientific work *Il Osimo d'Oro*

1985 Croatian national award «Ruder Boskovic» for scientific work

Honorary member of National Societies of Obstetrics and Gynaecology of Italy, Poland, Egypt, Hungary, Chile

Honorary member of Societies for Ultrasound of Australia, Indonesia, Egypt, Italy, Spain

1988 Honorary fellow of the American Institute of Ultrasound in Medicine.

1989 Honorary member of Society for Perinatal Medicine of Spain and Latin America

1990 Honorary member of Society for Radiology of Egypt

«Josip Juraj Strossmayer» Prize of Academy of Science of the Republic Croatia for the best scientific book (*The Fetus as a Patient*)

1992 Gold medal for Outstanding Scientific Merit

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1994 The First Prize of Academy of Science and Art of the Republic of Croatia for the achievements in medical science

1995 Doody's Best Health Sciences Book 1994-95

An Atlas of Transvaginal Color Doppler: *The Current State of Art*, 2nd edition

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- 1996 Prize «Europski krug» given by European Movement — Croatia for exceptional results in affirmation of European qualities in Croatia and Croatia worldwide
- Member of the Executive Committee of Croatian Academy of Medical Sciences
- Prize «Josip Juraj Strossmayer» of Croatian Academy of Science and Arts and Zagreb fair
- 1998 «William Liley» Prize for the best scientific paper from the field of fetal diagnostics and therapy
- Doctor *honoris causa*, Semmelweis University, Budapest, Hungary
- 2000 Honorary member of the Jordanian Society of Obstetricians and Gynaecologists
- Maternity Prize for contribution to perinatal medicine
- 2001 Award of Croatian Medical Association for the contribution to its work and affirmation
- Presidential decoration - The order of the Croatian starr with the effigy of Ruder Boskovic