One hundred years since Victor McKusick's birth: a tribute from Greece

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Victor A. McKusick has been recognized as the world leading authority in medical genetics. Among his numerous achievements, we should point out his inspiration and the training of a large number of leading geneticists, OMIM, the 'Bar Harbor' courses, and his contribution to the Human Genome Project. Nonetheless, little is known of McKusick's active participation in genetic education of a large number of physicians worldwide. Greece is an example of his frequent presence there, always eager to friendly advice, assist, teach, and offer his vast knowledge and his unique and excellent personality and friendship to everyone around. Victor McKusick's relationship and experience with the Greek genetics community is briefly accounted.

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Introduction

The identical twin brothers, Victor Almon and Vincent Lee McKusick (1921–1992), were born and raised in Maine on October 21, 1921. Victor's long academic career in Baltimore and the Johns Hopkins University School of Medicine, which he entered in 1943, is very well known to the genetics community. His amazing contributions to the development of medical genetics, began with his work running the Moore Clinic; initiating and editing the (online) Mendelian Inheritance in Man; the 'Bar Harbor Course' in collaboration with the Jackson Laboratory, Bar Harbor, Maine, USA; organizing the series of the 'Clinical Delineation of Birth Defects' conferences; and finally serving as the founding president of the Human Genome Organization (HUGO). Among the numerous recognitions of his achievements, he received the Lasker Award in 1997 and the National Medal of Science in 2002. Victor was very proud for this distinction awarded to him by President George W. Bush at the White House.

Nonetheless, Victor has been an inspiration as a mentor and friend to practically any medical geneticist in the past three decades of the 20th century. He was always available to advise and guide anyone asking for useful information and assistance for patients and families. I am sure that these feelings of mine are shared with all of us, who consider him as our spiritual 'father' and guide through our path in the development of medical genetics. Fig. 1, a photo taken at the Clinical Delineation of Birth Defects Conference held in Baltimore in 1974, demonstrates practically all his 'students'! It was a special honor and treat to be part in this magnificent genetic conference (Bartsocas and Crawford, 1974).

Victor McKusick in Greece

The author was fortunate to meet Victor during the course on Experimental Mammalian Genetics he was organizing with Earl Green and Elizabeth S. Russell (1913–2001) every year in the Jackson Laboratory in Bar Harbor, Maine. The ensuing friendship through successive genetics meetings followed for the next three decades. Of particular interest, however, were the International Clinical Genetics Seminars organized in Greece every 3 years since 1990, which he attended regularly with a very active contribution and a strong enthusiasm.

McKusick attended the sixth of these seminars, organized by the author, in Corfu in 1990. Main theme was 'The Genetics of Hematological Disorders.' A very detailed account of methods of gene mapping, the status of the human gene map, and the usefulness of genes, focusing on the Hematological Disorders, was given by Victor as an introduction to the Seminar. In a long list of entries and genetic map locations, the presentation covered all aspects of blood diseases, that is hemoglobinopathies, RBC enzymopathies, RBC membrane skeleton disorders, and heme synthesis disorders, with detailed clinical information.

In his long explanation of Human Gene Mapping, McKusick explained 'its usefulness to clinical medicine relating to the Mendelian disorders for

which no biochemical defect is known, so that specific diagnosis (prenatal, presymptomatic, and carrier) is not possible and rational therapy is difficult to plan. He concluded that, in the long run, the anatomic information that comes from gene mapping will be important to gene therapy also' (McKusick, 1992). Clearly, he stated that 'mapping has forced us to think in terms of more than the classic three categories of genetic disease: Mendelian, multifactorial, and chromosomal.' Of course, he did not neglect to include in his speech the '25th chromosome,' the mitochondrion that had been completely sequenced and mapped, with deletions and point mutations found at the basis of certain muscle and neurological disorders such as Leber's optic atrophy and the Kearns-Sayre syndrome.

Figure 1

Victor McKusick among some of his numerous international 'students,' Baltimore, USA, 1974.

Figure 2

Doctor's Degree Honoris Causa, University of Athens, Greece, 1999.

Victor McKusick was also present at the seventh International Clinical Genetics Seminar on 'Dysmorphology and Cardiovascular Disorder's conducted on the island of Samos (May 27–June 1, 1993). Forwarding the Seminar, he stated, 'The clinical genetics seminars that Professor Bartsocas and his colleagues have conducted are a successor to the week-long conferences entitled Clinical Delineation of Birth Defects.'

The Seminar was attended by several US geneticists, mostly McKusick's 'students,' and many Europeans, including Judy G. Hall, Jean-Pierre Fryns, Robert J. Gorlin, Peter Beighton, Anne Child, David L. Rimoin, Jules G. Leroy, Elizabeth Barrett-Connor, and others, providing an excellent environment for extended discussions and debates.

Three questions were opened to discussion during the 8th International Clinical Genetics Seminar, which was held aboard the MTS 'ARCADIA,' cruising the Aegean Sea in June 1996:

(1) What is the present status of Genetic Counseling?
(2) Who is to provide Genetic Counseling in the 21st century?
(3) How Genetic Counseling should be provided?

Victor McKusick (1998) made a few important prophetic remarks to answer these questions in his forward, which was published in the 'Genetic Counseling in the Dawn

Figure 3

Press conference on the HGP, Athens, 1999.

of the 21st Century,' C.S. Bartsocas and P. Beighton (ed.), ZHTA Medical Publications, Athens 1998.

'Everyone – all healthcare providers – should do genetic counseling. Genetic counseling should be part of the warp-and-woof of clinical medicine. Primary care providers, as well as specialists and subspecialists in all branches of medicine, must be prepared to counsel concerning the genetic problems of families and individuals that come under their care. There cannot possible be enough master's degree genetic counselors or board certified medical geneticists to do more than a small portion – the more complex portion – of genetic counseling.

What is required for genetic counseling (the second question) is the fullest possible understanding of the human genome […] and understanding of how variations in the genome lead to disease and other deviant phenotypes […] Focus on gene structure will shift to a focus on gene function; focus on basic etiology of genetic disease (the nature of the specific causative mutations) will shift to focus on mechanisms and pathogenesis. […]

The HGP will provide the technology and background information for determining susceptibilities to disorders that may develop later in life, to diagnose disorders in the unborn at stages as early as preimplantation, and to identify the carrier status for disorders that can become manifest in our children. […] The psychologic and psychosocial aspects of genetic counseling are important also and require improvement.'

Listening to the authority of McKusick's speeches was a captivating experience for the audience, aboard MTS 'ARCADIA,' cruising the Aegean Sea. Faculty included again several US and European geneticists, which included Judy G. Hall, David L. Rimoin (1936-2012), Tom Gelehrter, Elizabeth Barrett-Connor (1935–2019), Robert J. Gorlin (1923–2006), Rodney Harris (1932–2017), Giovanni Romeo, Jules G. Leroy, Albert Schinzel, and others. As previously, hot discussions followed practically on all topics covered during the 4-day cruise.

McKusick's important prophesying remarks were, 'As a result of the HGP, medicine can be expected to become powerfully more predictive than it now is. On the therapeutic side… perhaps with some exaggeration, by the year 2000 half of pharmaceutical research will be genome based. Clearly, genetic counseling enters all aspects of the application of New Genetics to medicine of the future' (McKusick, 1998).

The Human Genome Project was almost completed by October 1999, when Victor was honored by the University of Athens.

In a grandiose ceremony in the Aula, held in October 1999, the Rector and the Senate of the National and Kapodistrian University of Athens welcomed and honored Victor McKusick. In the crowded Aula (the Main Hall of the University from 1837), Victor received the Doctorate Degree Honoris Causa and delivered a fascinating lecture on the progress of the almost fully accomplished Human Genome Project (Fig. 2).

Figure 4

Ταυτότητα υγείας μέσω γενετικής

Εγκαιρη διάγνωση ασθενειών, γενονός στο εγγύς μέλλον

Της ΓΑΛΗΝΗΣ ΦΟΥΡΑ

McKusick's interview on the Future of Genetics, in the main daily Athens newspaper KATHIMERINI, October 16, 1999.

Figure 5

Preparing for a donkey ride in Santorini.

Figure 6

The McKusick couple in Mykonos.

Figure 7

Dining at the Yachting Club of Greece with the Jules Leroy and Rodney Harris couples, and other friends.

Figure 8

Nicosia, Cyprus. The local organizer Violetta Anastasiadou (front) with Betty Bazopoulou, Victor, Salvatore di Mauro (Columbia U.), Bartsocas and Vazken der Kaloustian (McGill U).

He stated that 'the achievements of genetics are overwhelming, and as a result it is impossible for someone to predict their future applications.'

The Athens Press (Foura, 1999) was full of praising comments of Victor's achievements and his contributions as the 'Father of Medical Genetics' (Figs. 3 and 4).

Predictions reach the area of fantasy. It is like the novels of Jules Verne, which however became a reality. The Mapping of the Human Genome, which began in 1985 and was expected to continue through 2005, will be completed within the year 2000. Since 1968, the year that the first human gene was recognized, until 1985, 750 genes were identified with great usefulness in genetics. We have data for the genes of more than 1000 diseases, stored in the electronic archives of the National Library in Washington.'

As the patriarch of genetics, Victor dealt with ethical issues. He stated that 'genetic standards could be used for other non-medical science purposes, with the possibility of ostracizing a few individuals. We should be able to determine the duration of human life. Unfortunately, we still don't know the gene for longevity.' With reference to cloning humans, McKusick was categorical. 'There is no perfect similarity in the human species. Even monozygotic twins differ in their fingertips. A scenario of the type making humans to obtain their organs is disgusting.'

Victor referred to a scientific meeting organized by Hilary Clinton in the White House on 'Information Technology meets the Genome' and applications for treatment of ailments, as blindness or deafness with insertion of microchips.

Victor's presence was always attracting attention by his wise speeches in a soft reassuring tone. He was there to discuss, advise, debate, and provide every recent scientific detail. He was amazing in remembering

Figure 9

Victor, wine tasting in Cyprus.

names, references, facts, and opinions. Indeed, he was a living genetic encyclopedia.

Nonetheless, he was ready to embark in new experiences. Although he lacked classic education, he was eager to learn, when visiting museums and important sites, that is Delphi and Knossos. He was interested to travel around and to obtain new experiences (Fig. 5–7). He visited several places in Greece and Cyprus, where he attended the ninth Seminar, whose topic was 'Non-Traditional Inheritance and Prenatal Diagnosis.' He was eager to learn from us, while we desired his continuous never-ending teaching (Figs. 8 and 9).

We were flattered when he stated 'As a participant in the seminar I could not help but reflect on the progress that has taken place in dysmorphology in the 25 years since the 1968 Clinical Delineation of Birth Defects Conference' (McKusick, 1998).

Anne, Victor's charismatic wife, was always accompanying him in his long trips to Greece. She was a charming elegant lady, who occasionally made exceptional comments when she had to add information to her husband's answers. She corresponded with us, especially when dealing in nongenetic items. Unfortunately, she revealed the news of Victor's cancer in a rather optimistic fashion. Later (December 29, 2007), on a Christmas card from the McKusicks, Anne sadly but optimistic wrote 'Victor had a cancer discovered last July but is doing well on chemotherapy.' Victor died on July 22, 2008. The world lost the father of medical genetics, while we lost and miss very much a fabulous mentor and a very good friend.

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