

Interview with Eugenio Mira.

Aldo Messina

To be a teacher, it is not enough to be a university lecturer, but one must be good to intuit the abilities of each student, to inspire him to give the best of himself and to discover a knowledge that he already possesses.

In my opinion, Professor Eugenio Mira has all these qualities.

Currently, he is the former Director of the Department of Otolaryngology, University of Pavia, Policlinico S. Matteo. In this interview I would like to share with you his professional history, that made him one of the most internationally renowned Italian otoneurologists.

A.M. Professor, when were you born?

E.M. I was born in Lecco on March 21, 1936, so I'm 85 years old now.

A.M. I presume you graduated in Medicine and Surgery in Pavia?

E.M. Yes, I attended the Alessandro Manzoni high school in Lecco and then I started to study medicine in Pavia with a scholarship at Ghislieri college, one of the great historic colleges of the University of Pavia.

During my last years at university I did an internship at the Institute of Comparative Anatomy. I honed my knowledge of Histochemistry, which was an emerging discipline in the 1960s. I became a student of its director, Professor Maffo Vialli, a great teacher and talented researcher. In that period and immediately after I published several scientific works about the histochemistry of DNA, mucopolysaccharides and proteins. Because of the few practical perspectives offered by the histochemistry I decided after my graduation in November 1960 to introduce myself to Professor Mario Cherubino, Director of the Department of Otolaryngology, pointing out to him that I was interested in doing his speciality without any commitment for the future.

A.M. Why Otorhinolaryngology?

E.M. I would say it was quite random: the advice of friends, the idea of something new, the idea of doing something clinical anyway. When I met Professor Cherubino, I became his first student in Pavia and in this way I was introduced to the otorhinolaryngology, bringing with me my background as a researcher in histochemistry.

So, in the years after graduation I published some further articles on histochemistry applied to otolaryngology such as on salivary glands and epithelia of nasal and tracheal mucosa. I like to remember a work from 1966, the first one related to the inner ear, which showed the high concentration of oxidoreductive and hydrolytic enzymes in the stria vascularis, testifying the high metabolism of its epithelium. In 1964, I obtained my first professorship as free lecturer in Histochemistry.

At the same time I deepened the clinical aspects of otorhinolaryngology and I started to be fascinated by vertigo, dizziness and balance disorders, symptoms whose requires for diagnosis not only to "work with hands and eyes", like a craftsman surgeon, but to "use the head". I gradually left histochemistry for vestibology, maintaining the imprinting of a researcher. In 1965 I obtained my second free professorship in Otolaryngology.

In those years the study of vestibular function was dominated by electronystagmography (ENG) and all the specialists were intent on defining the criteria for the analysis of ENG recordings, trying to identify procedures and algorithms that would allow an automatic analysis of the tracings. In this context that I began my collaboration with a group of young bioengineers from the Institute of Informatics and Systems Engineering at the

University of Pavia (Mario Stefanelli, Roberto Schmid, Giovanni Magenes, Angelo Buizza), to define the most significant parameters of the nystagmographic tracings.

In the 1970s, in the field of basic research it seemed natural to me to collaborate with other young researchers from the Institute of General Physiology at the University of Pavia (Paolo Valli, Emanuele Musso, Gianni Zucca, Laura Botta and Paola Perin) who had developed an innovative preparation: the isolated posterior semicircular canal of the frog. Thanks to this collaboration, we created an experimental model that was then (and still is) suitable for in-depth research into hair cell activity and mechano-neural transduction of the vestibular receptors.

I was quite satisfied with the results but I missed the human aspects of otolaryngology: the clinic and the relationship with the patient. I pursued my academic career to the Department of Otorhinolaryngology of the University of Pavia directed by Professor Cherubino, first as a volunteer, then as part-time assistant, then as a full assistant, focusing on the surgical aspects of the discipline and in particular the diagnosis and treatment of head and neck tumors. To deepen my clinical knowledge of the vestibular system I decided, as a Muslim goes to Mecca or a Catholic to Rome, to complete my clinical experience at the Besta Neurological Institute in Milan, where there was an otolaryngology consulting room run by Professor Aldo Dufour and his collaborators, otolaryngologists from the Fatebenefratelli Hospital in Milan. For years I travelled between Pavia and Besta, Besta and Pavia, and I became Aldo's pupil, then a scientific collaborator, and finally a friend; we carried out together a series of basic, clinical and educational research initiatives, all centered on the vestibular system. These studies laid the birth of a sub-specialty or super-specialty that was beginning to differentiate itself from otolaryngology and audiology and that we started to call vestibology.

A.M. Milano became at that time the national reference center for vestibology thanks to Aldo Dufour but also for audiology thanks to the school of Ettore Bocca, in particular Antonio Antonelli, and Massimo Del Bo. The two disciplines are obviously complementary, therefore did you consider yourself an expert

in audiology or just a vestibologist? How did you manage it?

E.M. It wasn't easy because they are twin disciplines. For me, to give a definition, *vestibology* is the discipline that deals exclusively with the vestibular system, peripheral and central, in all its aspects: anatomy, physiology, pathophysiology, clinic and therapy.

Vestibology is a recent term coined mainly in Italy. If we consult PubMed, under the heading vestibology, we find a few dozen articles, 90% of which are written by Italians. Vestibology is therefore a term, mainly of Italian origin, which had not yet fully entered the international language. In my memory, I first found it in the volume "Vestibologia - Manuale pratico" by Dufour, Mira and Pignataro edited by CRS Amplifon in 1980. In the scientific world, in English, the terms *otoneurology* and *neurotology* are more common. Of the two, I personally believe the latter is more correct, since historically, from the middle of the 19th century, the study of the vestibular system has been detached from neurology, in parallel with studies of the auditory system (audiology) or the visual system (ophthalmology).

The research on the vestibular system originated in France with Marie Jean Pierre Flourens, who addressed the role of the vestibular system in positioning the eyes in relation to head movements and in maintaining balance. At the same time, alongside the great French, Austrian and German neurologists, emerged in Vienna the Politzer school, whose many students included Robert Barany. Barany researches on nystagmus and thermal stimulation of the labyrinth won him the Nobel Prize. The attention of clinicians shifted from the study of vestibulo-spinal reflexes, with Romberg test, past-pointing test and stepping test, to that of eye movements, mainly the vestibulo-oculomotor reflex, and therefore the study of ocular nystagmus. Because nystagmus is a transitory phenomenon for more in-depth research into its characteristics it needs to be recorded. For this reason we used at first mechanical or cinematographic methods and then, from the 1930s and 1940s, we started to use electronystagmography.

After forty years of glory, in the 1980s, the nystagmography showed its limits and with the morphological analysis of the ENG re-

cordings, without a precise knowledge of the physiological and physiopathological mechanisms that underlie nystagmus, it entered in a phase of decadence until end itself. Shortly afterwards, a real cultural revolution took place: there was a return to the clinic, to the vestibular examination at the patient's bedside, the *bed-side vestibular examination* was born.

A.M. And in Italy?

E.M. In Italy, we can first of all remember the name of Tullio, a professor of Physiology in the early twentieth century, who had the intuition to describe a vestibular manifestation, the nystagmus, resulting from a sound stimulation, known today as Tullio's phenomenon. But Tullio was essentially a researcher, a physiologist, and remained an isolated case. In the 50s and 60s in Italy studies on the vestibular system have been carried out mainly from the school of Padua, directed by Michele Arslan. He was a man of exceptional intelligence and culture, of great charisma: a great figure in international panorama, a great director of a university department, a great politician of science, today I would say a great "*barone*". Thanks to him the first meeting of the Barany Society was held in Padua in 1960 and one of the first world congresses of otorhinolaryngology was held in Venice. In Padua, research and clinical works on the vestibular system were done from Arslan's students, including Oscar Sala and David Meghian, author in 1959 of a treatise on electronystagmography.

In those years a reference text for us, Italian researchers, was the 1956 report by Michele Arslan at the national congress of the Italian Society of Otolaryngology "*Fisiopatologia e clinica delle vie vestibolari centrali*" and the 1957 french treatise "*Maladies de l' Oreille interne et Otoneurologie*", by Aubry and Pialoux.

A.M. Going back to your experience, you met Aldo Dufour at the Besta Institute in Milan, a neurological department where, at that time, even rare pathologies from all over Italy converged and which provided you with the clinical background you were looking for. And then?

E.M. Once the Dufour-Mira duo was established, the vestibology trio of that period was completed by Professor Oreste Pignataro,

from the Milan school of Pietrantonio, Bocca and Calero. Pignataro, a friend, had acquired otoneurological skills because, as a young specialist, he had attended the Otorhinolaryngology Department in Geneva directed by Professor Montandon.

Under the guidance of Aldo Dufour, we passed from students to collaborators and together with younger colleagues of Fatebenefratelli (Matteo Richichi, Franco Cocchini) we started in Milan the first vestibular courses organized by "Centro Ricerche e Studi (CRS) Amplifon", modeled on the existing audiology courses of the same CRS. On the same theme, and still under the guide of Aldo Dufour, Italian vestibology grew with the congresses "Giornate Italiane di Nistagmografia Clinica", then "Giornate Italiane di Otoneurologia", organised by the Formenti Company.

I like to remember the first one: the one in Torre Pedrera (Rimini) in 1981. The Amplifon courses and the Formenti days brought a considerable number of specialists up to date and on the other launched a number of professionals in the sector, including Claudio Vicini and Giorgio Guidetti, along with a number of Tuscan colleagues. Dufour's baton was picked up by Paolo Pagnini with the CRS Amplifon courses in Florence and the San Miniato days, together with Daniele Nuti, Mario Gufoni, Augusto Casani and Paolo Vannucchi, the fathers the Tuscan school of Italic vestibology.

Aldo Dufour's golden years were from the 1970s to the 1990s. In that period Dufour was the author of two reports at the national congresses of the Italian Society of Otorhinolaryngology: one in Capri (1975) on central vestibular syndromes and the other in Milan (1980) on clinical nystagmography. These reports represented the highest point of electronystagmography in Italy, but after this a change of direction has taken place. As in the rest of the world, vestibology has evolved over time: from the exasperated analysis of ENG recordings to a clinical vestibology, to bed-side vestibular examination.

The first signs of this can be found in our already mentioned volume "*Vestibologia - Manuale pratico*", by Dufour, Mira and Pignataro in 1980, published only one year after the US second edition of the vestibular "bible" "*Clinical neurophysiology of the vestibular*

system” by Robert Baloh and Vicente Honrubia. Our volume was then republished in 1999, this time, don't ask me why, with the title “Otoneurologia clinica”.

A.M. Can we identify here a new moment in which vestibological thought spread in Italy?

E.M. We mentioned the year 1980, in which our volume was published. But the person who ensured that vestibology became a widely diffused discipline, let me say, was my colleague and friend Giorgio Guidetti, who managed this subject with great constancy and competence and founded, with Augusto Casani, Marco Manfrin, Alessandro Martini and Aldo Messina, the Italian Society of Vestibology (VIS).

The real impetus for the diffusion of vestibology in Italy is the work of Giorgio Guidetti who, unfortunately, was recently a victim of COVID-19, leaving an unbridgeable void. And allow me to recall other vestibologist friends who are no longer with us: Franco Cocchini, Luciano Cipparrone, Gianni Modugno, Dario Alpini.

A.M. I willingly join in the remembrance.

Continuing, how was since then the relation between our scholars and those of other countries and with the Barany Society?

E.M. I believe I can take some credit for the fact that the nascent Italian vestibology took a leap beyond the Alps in the 70s and 80s. With one of the bioengineers, Emanuele Anzaldi, with whom I collaborated on the analysis of nystagmographic tracings, we attended the Course of Vestibolométrie Clinique in Strasbourg, held by Professor Greiner and his pupils Maurice Collard and Claude Conraux. There, the French colleagues recognised the validity of our approach about the automatic analysis of ENG tracings and invited us to their meetings and to join their society called “Les Pélérins”: the pilgrims of vestibology. This name seems to have been given by Michele Arslan. Many of these French “pilgrims” had an international connection and in particular with the Barany Society, the world empyrean of vestibology, the summa of basic researchers and clinicians. It was not easy to join it, at the time, only a few members were Italian, such as Michele Arslan and the physiologist Ottavio Pompeiano. I attended the Barany meetings at first as a simple auditor, then as a full member and speaker, then as coordina-

tor and member of the Membership Committee. I started to travel into the world: after France, to London, Queen's Square Hospital, with Hallpike, Cairns, Dix, Hood, then, across the Atlantic, to California, Los Angeles, UCLA, with Honrubia and Baloh, or on the East Coast, Baltimore, Johns Hopkins, with David Zee and David Robinson. With me the young Italian vestibologists started to travel into the world and to be recognized in the international context as excellent otoneurologists. The French colleagues came to the Dufour conferences and all the great world leaders participated in the legendary International Symposium of Otoneurology organized in Florence in 1999 with Paolo Pagnini

A.M. What is the scientific contribution of Italian vestibology at international level?

E.M. Certainly the studies on paroxysmal positional vertigo and vestibular migraine left their mark. Canalo-cupolithiasis was recognised as vertigo by the Italians. Let us not forget canalolithiasis of the lateral canal, described in 1985 by Pagnini, with Nuti, Vannucchi and Cipparrone, at the same time as McClure, or the repositioning manoeuvres, such as that of Semont, studied by Guidetti in Paris in collaboration with Michel Toupet, and those devised by Gufoni, Vannucchi and Asprella.

A.M. On your own personal level, what have been the most appreciated elements of study at international level?

E.M. I would say two or three.

The first series relates to the aforementioned research on the isolated semicircular canal, with colleagues from General Physiology. This work is still cited today because if paroxysmal vertigo is also called “benign” it is because we have demonstrated that the otoconia dispersed in the endolymph dissolve after a certain time, due to chemical-physical processes, and the series of vertiginous attacks resolves, unless they recur again when there is a further detachment of otoconia.

The second series is computer-based, with colleagues from Bioengineering and led to the creation of a mathematical model of the vestibulo-oculomotor reflex and then, in the 1980s, to the formulation of an expert system and algorithm for the automatic diagnosis of vertigo, mainly on the basis of anamnestic data.

Finally, in the 1980s, with Giacomina Piacentino and colleagues from Child Neuropsychiatry we arrived at the recognition of benign paroxysmal vertigo in children as a migraine equivalent or a migraine precursor. Today an almost obvious link, but then innovative.

A.M. How did Guidetti change the Italian vestibology?

E.M. Above all, I recognise Giorgio's great determination and ability as a weaver. He was the Cavour of otoneurology in our country, capable of bringing together great expertise and great intuition. He was one of the first to talk about the relationship between vertigo and migraine and also to jump to the higher levels of the vestibular system, i.e. to move from the simple analysis of vestibulo-ocular and vestibulo-spinal reflexes to the influences that the vestibular system can have on cognitive functions, such as spatial memory. And the Vestibology Italian Society (VIS) is his baby.

A.M. And the third generation in Pavia, the one formed by you, who are you represented by?

E.M. Both my first students, Paolo Castelnovo and Marco Benazzo were involved in vestibology, but then they took other paths: Paolo Castelnovo in nasosinusoidal endoscopic surgery in Varese, where he went on to become Director of the Department, Marco Benazzo, now Director of the Department in Pavia, in head and neck oncological surgery. The Pavia otoneurological expertise sees a prominent element in Marco Manfrin and more recently in Silvia Quagliari. From Pavia also comes Maurizio Versino, the only Italian neurologist who, after his training at Johns Hopkins with David Zee, has in-depth knowledge of the vestibular system.

A.M. What about the rest of Italy?

E.M. The centers of otoneurological excellence are now spread throughout the country. From a predominantly northern-central competence, the model is now spread throughout the peninsula and the larger islands.

A.M. We can say that knowledge of the vestibular system and its pathologies is at a good level throughout Italy. What about electronystagmography today?

E.M. Nystagmography died at the end of the 1980s. Vestibology, like all scientific disciplines, moves forward on three pillars: basic

research, clinical research and technology. In the 1980s, on the input of basic research by international physiologists, the strictly technological approach, represented by electronystagmography, was abandoned and a diagnostic model based on the simple (so to speak) clinical examination was proposed: the bedside examination. The bedside examination of the vertiginous patient is performed at the patient's bedside with the aid not of expensive and complex instrumentation such as the electronystagmograph, but with the aid of the hands, the eyes, and above all the brain, within which the knowledge of the physiopathology of the vestibular system must be clear. This was truly the revolution that we owe to the likes of Honrubia, Baloh, Zee, Brandt, authors of the fundamental texts, the gospels of today. However, later on, towards the end of the 90s, the technology which had been put aside with the decline of electronystagmography came back into vogue: videonystagmography, video-HIT, VEMPs. I accept and practice these innovative methods but let us remember that behind them there is always the patient, with his clinical history, his anamnesis, his symptoms, his personality: let us not slip into another technological dead end.

A.M. So what is the future of vestibology today?

E.M. Otoneurology has taken on a dignity of its own and deserves to be recognised at a European level as a speciality school. I believe that by taking on board Giorgio Guidetti's message, the current leaders of the Italian Society of Vestibology will fight for this.

A.M. The therapeutic approach cannot be omitted. Otolaryngologists and audiologists who deal with vestibology are able to make correct topographic diagnoses. But this does not seem to have changed their therapeutic skills and they often delegate the therapeutic conclusion to other specialists. Shouldn't they be given the basics of neuropharmacology in their specialisation courses?

E.M. It would be implicit in the teaching activities of Schools of Specialisation in Vestibology, if they were established. And alongside the fundamentals of therapy, some fundamentals of rehabilitation. Vestibular rehabilitation, which originated in the United States with Susan Herdman, which we brought to

Italy with Claudio Vicini's courses at Bertinoro in the 1990s, and which grew in Italy with Giorgio Guidetti, is one of the bases, if not the main base, of the treatment of vestibular pathologies.

A.M. It was a good chat, thanks.



Daniele Nuti, Eugenio Mira and Paolo Pagnini, National Congress of the Italian Society of Otolaryngology (SIO), 1988