YEAR VI (XLIII) - n. 1 - MARCH 2020

Quarterly medical and scientific magazine

Advanced neurosurgery and personal grit



A cement for the vertebrae



Childhood Absence Epilepsy



A sky-high research



How a drug is born

BIOLOGIA MOLECOLARE



un contributo importante per la diagnosi e terapia dei tumori cerebrali

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Come la biologia molecolare può essere utile agli oncologi?

Con la sua capacità di analizzare le caratteristiche genetiche delle cellule tumorali, la biologia molecolare è di grande aiuto per gli oncologi. Conoscere a fondo un tumore cerebrale infatti significa fornire delle importantissime indicazioni per le scelte terapeutiche da seguire. Un esempio molto valido può essere quello dell'analisi del gene MGMT in caso di glioblastoma, la forma più aggressiva di tumore cerebrale. I risultati di questo esame ci consentiranno di comprendere il grado di farmaco-resistenza del tumore e quindi aluteranno gli oncologi a non perdere tempo prezioso scegliendo le terapie più adatte. Convenzionato con II SSN.

Per approfondimenti http://www.neuromed.it/sezione/laboratorio-di-neuropatologia/





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In the story of a sportsman, the fusion between advanced neurosurgery and personal determination



ita Charon, author of the book "Narrative medicine: honoring the stories of ilness", speaks of the need for a medicine capable of "recognizing, absorbing, interpreting and being moved by stories".

The stories, the lived experience characterizes all human culture, starting from the most ancient myths. And even medicine, many decades ago, was marked by stories, a habit lost in the face of the great successes of procedures and technologies. But the story remains important, to understand, share, identify. So it is precisely a story of disease (and of strength) that we want to tell in this issue of Neuromed News. Angelo Magliulo describes his journey into a serious pathology such as brain tumor, without ever separating his personal experience from the relationship established with Professor Vincenzo Esposito and the whole team following him.

But, above all, Angelo tells us a story of life, strength, persistence. Of a disease faced with concreteness and awareness, indispensable elements to deal with wake up surgery. And then he is back from the operating room, to sports trophies, never losing sight of values and life goals, without compromise, to use his words.

Sport is crucial also in another story that found place in newsmedia: Antonio De Benedetto, a footballer who, after a challenge very similar to Magliulo's one, likewise "launched" in the Neuromed, returned to score on the playing fields.

After all, these episodes show us one of the fundamental concepts of Neuromed Institute: the alliance between patient and clinicians, the making of a team in which the person on the operating table is protagonist together with those around him. Only a perfect fusion between advanced medicine and humanity can give us stories like these.



ard to find a more unusual combination: the cup of a Bodybuilding tournament together with a pack of 730 tax return models. But for Angelo Magliulo they are important symbols of that attitude ("grit" in his own words) that led him to face such a serious pathology like a brain tumor.

Probably that day in August 2016, when there was a visit to plan the surgery, must have seemed strange to doctors. "The fact -Magliulo continues - is that I had a contest on December 11th, for which I had been training for long time. I didn't want to miss it. So we scheduled the surgery for February 2017, and of course I continued to train and

44 years old, from Torre del Greco in the province of Naples, accountant and bodybuilder, Angelo never lost sight of the objectives he considered most important: work and sport. "If you bask in illness - he says - you never get out. Of course, when you live an experience like this things you see differently, but then there is the return to everyday, normal life. And that's where you measure yourself, when you find the right determination to do the things you like".

This story begins in

2015 with the first symptoms. "They were light - he says – something like losing the sense of orientation. Then came the real crises, and at that point the situation was clearly outlined. Medical evaluation quickly clarified that the position of the tumor, wedged between brain structures very important for movement and speech, required very advanced surgery, to be performed awake, and this led me to Neuromed Neurosurgery".



work as usual". Not only did he make the race, but he made the podium, third place.

Eight hours of surgery awaited him, experienced firsthand. Because the awake technique provides, in fact, that the patient is awake during the whole operation, in order to constantly check which brain areas the surgeon can intervene without causing damage (see Box). "The first ten days after surgery - he says - I had problems in my right arm, loss of strength until complete paralysis and slight dysarthria of the Angelo Magliulo (center) with the neurosurgical team that assists him in Neuromed. To the left of Angelo: Professor Vincenzo Esposito







During our interview with Angelo Magliulo

language, but then the situation quickly normalized, as expected by the team and by Prof. Esposito, also thanks to the intense rehabilitation". So Angelo achieves the goal of getting back to work quickly, fifteen days later, while it took thirty days for the gym. Hard training, as always, led him to participate in two contests, in November and December of the same year, earning fourth place in the qualification for the Europeans and fifth in the qualification for the Mediterranean and World Games. And other competitions are already scheduled for the month of May.

One wonders if this experience could be useful to anyone who is facing a serious disease like his. "I never thought of stopping, of being 'serene' - he comments with the same expression he probably has before starting a workout - I always wanted to go back to my real life dimension, made up of work and sport, I always thought that what really matters is adding life to years rather than years to life, without compromise, because "disease" is just a simple word, not a sentence. For me, this represents a very important part of the treatment ".

When the patient is part of the surgical team

In awake neurosurgery the patient is an active protagonist

"In the field of brain surgery this is one of those cases where we have to put in place all the most advanced technology available. In addition to that, there must be a careful and precise preparation work, to be done together, side by side with the patient". Professor Vincenzo Esposito, Head of the Neuromed Neurosurgery Unit 2, summarizes in these few lines the main features allowing his team to deal with situations like the one involving Angelo. "I could say - Esposito continues - that there is not a single moment in which the clinical team works regardless of the person who will have surgery. It takes a deep planning, requiring time and great constancy".

These are the tumors localized in a critical area, very near, if not inside, to brain structures essential for the patient's life. Surgery becomes a human and technological challenge: removing the diseased cells leaving the surrounding brain areas intact. It means restoring hope to the patient, without however diminishing the quality of his life. The answer is in "awake" surgery: the patient is operated while he is conscious, without general anesthesia. This allows the team to talk to him, subject him to continuous tests and then constantly monitor brain functions. Surgery, thanks also to the use of a high-magnification microscope, thus becomes a highly precise operation, during which the neurosurgeon can "navigate" in the brain knowing exactly what to expect from each single move.

"In Angelo's case - explains Esposito - the brain areas concerned fundamental functions, such as language, motor and sensitive activities. The precision had to be maximum, therefore the investigations carried out before surgery are of the utmost importance. Here the neuropsychologist comes into play: the professional who accompanies the person towards the intervention by studying his brain and its functions, but also explaining what we are going to do and what we expect. All this is crucial because it increases the information in our possession and helps the patient to face a very complex path".

"The first step - says Dr. Marco Ciavarro, neuropsychologist - is the preoperative study, through the administration of tests that allow us to have a complete picture of how that particular brain works and the execution of a Functional Magnetic Resonance Imaging (allowing doctors to see the brain "at work", editor's note). Thanks to these exams, we can precisely



identify the critical areas presiding over fundamental functions, drawing a map that will help the neurosurgeon in taking the right decisions. Subsequently, all the details of surgery are exposed to the patient, including risks and possibilities. There is also a psychological work, because we face a person who, in awake surgery, will face considerable stress".

Then we arrive in the operating room. Here the information collected must be further refined. "We perform - says Esposito - a continuous monitoring of brain functions. Through the electrical stimulation of the brain structures involved, evaluating the patient's responses, who constantly collaborate with us, we gradually confirm the functional magnetic resonance imaging data and proceed gradually with the removal of the tumor".



A cement for the vertebrae

In the treatment of vertebral fractures, Neuromed puts in place a high-tech combination: percutaneous vertebroplasty and EOS



Dr Marcello Bartolo

ertebral fractures represent a larger problem than one can think, given that nearly one and a half million cases are counted in Europe every year. Excluding those due to traumas, which are quickly identified in the emergency room, the vast majority of nontraumatic fractures is due to complications of osteoporosis: it is estimated that one in four women after the age of 60 is soon or later affected by vertebral fracture due to this condition. But the problem does not leave men unscathed, especially in old age, and it can affect also people with spine tumors, or with metastatic tumor lesions. Neuromed's approach to this problem combines two high-tech procedures:



radiological examination obtained with the EOS device and the minimally invasive percutaneous vertebroplasty.

"Typically - says Dr. Marcello Bartolo, Head of Diagnostic and Therapeutic Neuroradiology Unit – patients with nontraumatic vertebral fractures report abrupt onset of back pain, which can also be very intense. As an example, the affected person may even find painful to turn over in bed. This is the classic alarm bell that brings the patient to the attention of the emergency room or GP. At that point, a diagnostic





process consisting of careful clinical and instrumental tests must start".

This is where EOS comes into play at Neuromed. The device only apparently performs a "classic" X-ray exam. "EOS explains Bartolo - is a very sophisticated tool that allows us to examine the spine with a very low radiation dose, corresponding to about 10% of that absorbed during a CT scan. In addition, the examination is performed in less than 60 seconds and, very importantly, in orthostatism (in a vertical position, editor's note), with the possibility of performing 3D reconstructions and measurements of angles. But let's not forget another fundamental element in the correct diagnosis of vertebral fractures: magnetic resonance imaging, which allows us to establish if we are facing an old or recent fracture, and this will be a crucial element in guiding subsequent therapeutic choices".

Once the vertebral fracture has been diagnosed and classified, it is time to decide for intervention. "In Neuromed - continues the Director of the Unit - we have a great tradition in the use of percutaneous vertebroplasty, and the last ten years have seen an average of two hundred treatments per year. It is an intervention aimed specifically at recent fractures, which have occurred in the last 2/3 months. It is very rapid (about 20

Nuclear physics and medicine: a long love story

Geneva CERN, the largest scientific experiment in the world, is famous for nuclear physics studies, which may seem very far from medicine. But it is from such laboratories that technologies now widely used for the diagnosis and treatment of patients have come. For example, the well-known nuclear magnetic resonance, born thanks to the development of superconducting magnets. And then there is EOS, a radiological device originating from the ideas of the physicist Georges Charpak, who designed the "Multi-wire proportional chamber", originally aimed at the detection of subatomic particles. An invention that earned him the Nobel Prize in Physics in 1992.





minutes), minimally invasive and, in 99% of cases, it is performed under local anesthesia. Basically, a metallic needle is introduced through the skin of the back, in correspondence of the vertebra affected by fracture. Then an acrylic cement, (PMMA), polymethylmethacrylate is injected. It solidifies in a few minutes and consolidates the fractured vertebra, restoring its consistency and stability. The very low radiation dose of EOS, then, allows us to perform a new X-ray examination of the column after the operation, in order to evaluate changes and improvements occurred in patient's posture ".

The benefits are almost immediate, as Bartolo points out: "The recovery of a vertebral fracture with traditional techniques (the brace, in practice) can take 5-6 months. With vertebroplasty we have a patient who in two days sees the pain disappearing, and can return to his work and social life in a few days ".





Childhood Absence Epilepsy

Willie

Children getting "stuck" during normal activities. A kind of epilepsy in which early diagnosis and targeted therapies can guarantee normal development and life

ike a stop motion movie, or like when you press the pause in a video: a child or a teenager is engaged in the usual things, maybe at school or watching television or even talking to someone, and suddenly he/she stops and does not respond to stimulus anymore.



He/she stays like this for a few seconds, sometimes gazing, then picks up exactly from the point in which the "freeze" started. And, from their point of view nothing strange happened.

Such events, called "epileptic absences", are

short-lived and often people around, parents or teachers, may think that the child is simply "distracted or thoughtless".

"Absences - says Dr. Giancarlo Di Gennaro, Head of the Neuromed Center for the Study and Treatment of Epilepsy – are full-fledged



generalized epileptic seizures. Childhood absences are among the most frequent forms in school-age children, and once they were known as 'petite mal' to distinguish them from seizures, or "grand mal". They are generally due to a genetic predisposition and have an excellent prognosis, since they respond very well to drugs and tend to disappear in adolescence."

"These children - adds Dr. Alfredo D'Aniello, child neuropsychiatrist at the Neuromed Epilepsy Center - do not have any neurological or cognitive disorders. But absences can be very frequent, up to dozens of times in a day. In this case, if not properly managed, they could adversely affect school performance. That's why it is important to recognize and treat them as

Research

New therapeutic targets investigated by the Neuropharmacology unit

The search for new drugs in the field of epileptic absences is a challenge fought on two fronts: molecular and technological. "The commitment of our group in this field - says Professor Ferdinando Nicoletti, Head of the Neuromed Department of Neuropharmacology

 aims at identifying new therapeutic targets that can complement existing drugs.
We want to offer to clinicians new weapons to expand therapeutic possibilities for those patients in whom traditional drugs are not sufficiently effective or have important adverse effects ".

"We focus - explains Dr. Roberta Celli, pharmacologist who is guiding this line of study - on the mechanisms of action linked to specific nerve cell receptors, mGlu5, and on possible innovative pharmacological actions that could exploit them".

One of the tools used for this research is a real technological innovation: wireless







The team involved in the development of sensors for wireless electroencephalography. From the left: Dr Anna Prioriello, Dr Roberta Celli and engineer Luigi Pavone

soon as possible. Of course, the first to notice that something is wrong are parents and sometimes teachers. Accurate collection of clinical history with detailed descriptions of episodes by observers is very important for diagnosis. The electroencephalogram (EEG) is the pivotal test in confirming the diagnostic hypotesis because it has typical characteristics, and





sometimes, given their high frequency, it is also possible to record a crisis during examination".

"We have many drugs available - explains Di Gennaro – to cure absences until they disappear by themselves. These are welltolerated drugs, allowing young patients to live their life without particular limitations. In most cases, childhood absences will tend to disappear in the adolescence, so anti-epileptic therapy can be gradually stopped.

Promoting a healthy information

World Epilepsy Day is always an important time to address not only medical problems, but also issues, sometimes running deeper, regarding prejudice, if not hostility.

"I have to admit - says Dr. Liliana Grammaldo, Neuropsychologist at the Center for Surgical Treatment of Epilepsy - that unfortunately there is no substantial difference between today and the past with respect to the prejudice and stereotype that this disease brings. This makes us think that it is still important to promote healthy information, starting at a young age. That's why we are constantly engaged in meetings with children in schools, and we are always very surprised by how young people react. They are motivated kids, wanting to know and fully capable of asking good questions".

"Epilepsy - adds Dr. Alfredo D'Aniello, Child Neuropsychiatrist of the Center - is one of the most frequent neurological diseases. It affects one percent of the population, an estimated 500-600,000 people in Italy. It is a pathology that has two peaks of incidence, and one of them is in childhood. Too often epilepsy is still surrounded by stigma and prejudice, partly due to the lack of correct information. This is why we promote meetings in schools, aimed at providing information on epilepsy and its manifestations. Finally, we know that children and adolescents spend many hours of their day at school, making classrooms important environments for providing information on what to do to help someone with a seizure".



A sky-high research

In collaboration with the Italian Space Agency, Neuromed experiences the effects of flight on the body

nyone involved in aeronautics or space flights has two historical phrases in mind. The first is by Leonardo Da Vinci: "The big bird will take the first flight, above the bump of his great Cecero, filling the universe with amazement, the writings with fame and eternal glory the nest where he was born". The second of the Russian Konstantin Tsiolkovsky (1857-1935): "The earth is the cradle of humanity, but you cannot live forever in a cradle".

Both of these men dreamed of a future that has now become reality, in which humans

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The team involved in the Neuromed - Italian Space Agency project. From the left: Milena Cannella, Roxana Ginerete, Domenico Bucci, Nico Antenucci, Tiziana Imbriglio and Giada Mascio are getting used to living far from the ground. At any moment of a day, between eight thousand and twenty thousand planes are in flight. It means that, as you read this article, more than half a million people are suspended in the air. And in the past years the International Space Station has been hosting six astronauts who, during sixmonth shifts, literally "inhabit" space. Finally, by 2021 the first tourists will travel aboard a spaceships.

It is time to study with increasing attention

could find just over two thousand meters. It is a higher altitude than what we are used to in our towns, but we can still breathe regularly without problems. However, while we passengers fly rather rarely, the crew, pilots and assistants, experience these conditions several times a day, with atmospheric pressure going from ground to flight conditions and vice versa ".

Such changes could have effects on the body. This is why the Neuromed – ASI project aims to verify their effects. "We are



A project aiming to study the effects of oxygen deficiency on flight crews"

what consequences can have for the human organism exposition to flight conditions. Neuromed is doing its part with a project conducted by the Department of Neuropharmacology, in collaboration with the Italian Space Agency (ASI), investigating the effects of the so-called "hypoxia" (oxygen deficiency) on airlines flight crew.

"A jet airliner - explains Dr. Giada Mascio flights at an altitude between 8,500 and 12,000 meters. Of course passengers and crew could not survive, due to the low concentration of oxygen in the atmosphere. This is why planes have systems maintaining the air at a pressure we not only evaluating the lower atmospheric pressure - says Professor Ferdinando Nicoletti, Head of the Department - but also the stressful conditions to which the crew members may be subjected during the various phases of the flight, some very demanding. The experiments are carried out on animal models, exposed both to in flight atmospheric pressure and to repeated stress ".

The results will come in the coming months, and will constitute more knowledge to add to the road started by Leonardo, leading more and more humans to "leave the cradle".



HEDITERHANED

TECNOLOGIA D'AVANGUARDIA PER DIAGNOSI TEMPESTIVE ED ACCURATE in campo oncologico e neurologico

"F-COLINA PET/TC indicata nella valutazione dei pazienti con carcinoma prestatico

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"F-DOPA PET/TC indicata nella valutazione dei tumori cerebrali, neuroendocrini e sospetto per malattio di Parkinson



F-FLORBETABEN E "F-FLORBETAPIR per pazienti con decadimento cognitivo e malattia di Alzheimer



"F-FDG PET/TC indicata nelle patologie neoplastiche per la ricerca del tumore primitivo e di eventuali metastasi, nella valutazione post terapeutica dei tumori e in campo neurologico

1



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An innovative line of research born from the collaboration between four prestigious Italian scientific institutions

Understanding the genetic mechanisms of brain tumors in infants and children, this is the aim of a work, published in the journal Nature Communications, born from a collaboration involving the Molecular Neuropathology

Laboratory of the Neuropathology Unit in the I.R.C.C.S. Neuromed. Under the coordination of the Armenise-Harvard Laboratory of Brain Cancer at the Cibio Department of the University of Trento, the research groups of Neuromed, Sapienza University of Rome and





Professor Felice Giangaspero



Bambino Gesù Hospital of Rome paved the way to the possibility of creating "test tube tumors" on which new drugs can be tested.

Thanks to the support of the Armenise-Harvard Foundation, the Airc Foundation for Cancer Research and the Caritro Foundation of Trento, researchers created "organoids", small test-tube brains in the form of irregular spheres. Developed from stem cells from healthy donors, they will allow laboratories to understand the genetic mechanisms underlying the onset and development of brain tumors. Organoids are grown from stem cells, which can be modeled in various ways to recreate the actual functioning of an organ or to study only one aspect. It means conducting a complex series of experiments with greater ease than using animal models, and at much lower costs. They represent a very reliable tool for developing innovative and personalized therapies.

The attention of the researchers in this specific scientific work, which saw the contribution of Professor Felice Giangaspero (Department of Radiological, Oncological and Anatomo Pathological Sciences, Sapienza University of Rome; Neuropathology IRCCS Neuromed) and Dr. Francesca Gianno (PhD student of the Department of Radiological, Oncological and Anatomo-Pathological Sciences, Sapienza Universitv of Rome: Neuropathology IRCCS Neuromed), was focused on medulloblastoma, the primary malignant neoplasm of the central nervous system most frequent in children. Current conventional therapies allow 5-year survival in 70% of patients, but this result is burdened by side effects that significantly limit the quality of life of the children. New therapies capable of acting on specific molecular targets are strongly needed, and they can be tested on tumor models as close as possible to the human cancer. Organoids today represent the ideal tool for such research.

Developed from stem cells from healthy donors, organoids will allow laboratories to understand the genetic mechanisms underlying the onset and development of brain tumors



Cardiac arbythe Mediterranean Clinic

The commitment of the Mediterranean Clinic to the fight against health tourism

he Center of Arrhythmology and Heart Failure of the Mediterranean Clinic of Naples is increasingly engaged in the fight against health migration. In 2019, some 1000 patients were surgically treated for arrhythmias, sparing them the necessity to seek care outside the region. Among them, 130 patients already treated outside Campania needed a second surgery to solve their problem.

"Health tourism - explains Dr. Giuseppe De Martino, Head of the Department of Arrhythmology and Heart Failure – happens when a patient must go out of his region to seek treatment. We are talking about a situation generating a double damage: a higher cost for the families of patients, facing travel and accommodation expenses, and a higher load on the Campania region, which has to pay the health services to the other regions. At Mediterranea we created a unique Center, the only one performing specific types of intervention, such as hybrid ablation with a transcatheter endo-epicardial approach. Thanks to this technique, we are able to cure arrhythmias that otherwise cannot be fully treated with traditional ablation".

Only a few days ago the latest case. "A young girl, Valeria - says the head of the department - suffering for years from an atrial arrhythmia provoking strong tachycardia. She already underwent a first ablation in a south Italy clinic, and then a

To find out more: Clinica Mediterranea

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A unique Center, performing cutting-edge intervention





Dr Giampiero Esposito

second in a facility in Milan, without having her problem cured. In Mediterranea we performed the hybrid technique, solving the situation. The case of Valeria, however, is emblematic because the origin of the arrhythmia was on the outside of the heart, and only hybrid approach was capable to eliminate it".

The technique used by Dr. De Martino is very innovative and allows his team to achieve results otherwise impossible with traditional techniques. The concept of "hybrid" arises from the fact that, in addition to the classic groin puncture, by which internal surface of the heart is reached, a very small cut is also made on the chest, allowing to reach cardiac external surface.

In the Clinica Mediterranea, Dr Giampiero Esposito, since January is head of the Cardiac Surgery Unit. Esposito, specialized in Cardio-Angio Surgery and Thoracic Surgery, has various clinical experiences abroad at the Harefield Hospital in London, the KliniKunt Charlottemburg University in Berlin and the Withenshave Hospital in Manchester. He performed about 9,000 major cardiovascular surgeries. Over 20 years he has been dedicated to minimally invasive aortic, mitral and coronary heart surgery, hybrid surgery of the aortic arch and surgery of obstructive hypertrophic myocardiopathy. He is member of the STS (Society of Thoracic Surgery), EACTS (European Association of Cardio-Thoracic Surgery), SICCH (Italian Society of Cardiac Surgery) of the International Society for Minimally Invasive Cardiothoracic Surgery (ISMICS). Professor in the Postgraduate School of Cardiac Surgery at the University of Varese from 2014 to 2016, he published 53 scientific papers in prestigious international journals and he is the author of "Innovative Grafts for Aortic Arch Replacement", a book published by Minerva Medica. In 2010 he filed American, Japanese and Chinese patents for the "Lupiae" vascular prosthesis produced by Terumo Vascutek. Esposito has been awarded Cavaliere of the Italian Republic.



New weapons against heart failure

The scientific contribution of the Trusso Cardiology Clinic

cientific contributions can come to light not only from labs, but also from clinics, where doctors are in contact with patients every day. An example comes from the Trusso nursing home in Ottaviano with a study conducted by Dr. Antonio Cerciello on new treatment options for



Dr Antonio Cerciello during the last PLACE 2019 Congress chronic heart failure with reduced ejection fraction.

The research was presented by Dr. Cerciello, Head of the Cardiology Unit (Outpatient Clinic for Heart Failure) of the Trusso Clinic in Ottaviano, together with Professor Norman Lamaida, during the last PLACE 2019 Congress, in Rome.

The study aimed to improve the treatment of a disease that is the primary cause of

hospitalization among patients over 65 years of age, weighting heavily on the costs of national health system, as well as deeply affecting people's quality of life. Heart failure in fact becomes progressively disabling and, in the long run, despite the progress made, it remains an important cause of death.

The research conducted in Ottaviano, focused on a new drug consisting of two active ingredients, has a very important feature for this type of studies: the high number of patients treated. "Over three years - explains Dr. Cerciello - we involved 156 patients suffering from heart failure. Results showed the advantages of using the new drug in patients with chronic heart failure not responding to the optimal therapy recommended by the ESC 2016 guidelines. The drug is well tolerated, has improved the patient's functional capacity and ventricular remodeling with total absence, or very few, side effects".

"A very important finding emerging from the research - said Cerciello during the conference - lies in the fact that the earlier the drug is administered the most quality of life of the patient improves, with a significant reduction in the evolution of the disease. So much so that the use of Sacubitril / Valsartan is also being considered in heart failure patients with normal ejection fraction. An aspect that we plan to explore in a future investigation".







Scopri il nuovo Centro Odontoiatrico del Neuromed

I sorriso è il nostro biglietto da visita: ce no prendiamo cura attraverso una sana alimentazione, a buone abitudini quotidiane e corretti stili di vita. Il nuovo Centro Odontoiatrico di Neuromedinasce per aiutare il pazienti in questo compito, offrendo un servizio di qualità e competenza in ogni singola branca dell'odontoiatria.

Con l'ausilio di team medici altamente esperti e qualificati, il Centro Odontoiatrico raggiunge ogri giorno questo obiettivo proponendo piani di cura e trattamenti personalizzati grazie a diagnosi cliniche approfondite.

Offre a tutti i pazienti, adulti e bambini, servizi odontoiatrici qualit check-up completi, igiene orale, ortodonzia, odontoiatria conservativa, protesi fisse e mobili, implantologia, odontoiatria infantile, estetica dentale e parodontologia. Ivi è possibile eseguire anche radiografie odontoiatriche e tac dentali come OPT e TC 3D, al fine di individuare il trattamento più specifico per la salute dentale del paziente.

Il Centro Odonioiatrico di Neuromed è ubicato al Primo Piano della Piattaforma Ambulatoriale ed è possibile prenotare una visita dal Lunedi al Venerdi dalle 9:00 alle 19:00 e il Sabato dalle 9:00 alle 13:00 contattando il Tel. 0865 929 730.

Equipe multidisciplinari e tecnologia d'avanguardia per la salute del vostro sorriso.



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L'edontoiatria infantile, detta anche pedodonzia, si occupa della salute orale di bambini ed adolescenti. Si prevengono malocclusioni dentali infantili con la prevenzione e monitoraggio dello sviluppo dentale procedendo, dove si necessita, di tempestivi interventi correttivi. Lo scopo è assicurare, sin dalla giovane età, la salute orale dell'adulto del domani attraverso piani personalizzati e tecnologia d'avanguardia,

GIENE DENTALE ED ESTETICA

Per la salute della nostra bocca un'accurata igiene orale quotidiana è importante ma non è sufficiente. Per rimuovere in profondità placca, tartaro e batteri (soprattutto negli spazi meno raggiungibili da strumenti domiciliari ed evitare l'insorgenza di carie e malattie come la gengivite o la piorrea) occorre dirigersi dagli specialisti almeno ogni 6 mesi.

intervenire tempestivamente può evitare cure più invasive nel futuro.

inoltre presso il nostro centro è possibile svolgere anche trattamenti specializzati per recuperare l'originaria estetica dentale predisponendo soluzioni professionali ed efficaci con risultati del tutto naturali.

PARODONTOLOGIA

Per salvaguardare i nostri denti occorre prendersi cura anche delle gengive, dell'osso alveolare e del legamento parodontile. Sono i sostegni dei nostri denti, per non perderil occorre ricorrere alla parodontologia per prevenire e curare gengiviti e parodontiti.

Circa il 75% degli adulti di età compresa tra i 45 e i 65 anni ha perso almeno un dente. Cosa possiamo fare?

PROTESI

Per una masticazione adeguata e una fonetica corretta occorre colmare le mancanze dentali con una protesi al fine di riabilitare la funzionalità della bocca. La protesi fissa garantisce ottima stabilità mentre la protesi mobile agevola la pulizia.

IMPLANTOLOGIA

In caso di mancanza totale o parziale di elementi dentali è possibile riabilitare la funzionalità e l'estetica del sorriso ricorrendo a moderne tecniche chirurgiche implantologiche.

Gli impianti sostituiscono la radice persa permettendo l'applicazione di una corona.

La mancanza di un dente non è solo un problema estetico, è correlato a disturbi di masticazione, di digestione, forti emicranie e dolori cervicali.

Inoltre se le condizioni cliniche lo consentono, si può ricorrere alla tecnica del carico immediato per ripristinare in un solo giorno il nostro sorriso.

Stanza con poltrona completamente attrezzata per la gestione del paziente con disabilità fisiche.

Druken Den Gierrine PETRECCA

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Food and health

the label is not enough, you need a food pyramid



ot everyone likes the Nutri-Score, and in Italy it is becoming a real National issue. The French labeling system, supposed to help people in making healthier food choices, is not well accepted in the "belpaese". Among the reasons for this attitude, an unfair penalty of some Italian products, starting with olive oil which, according to the Nutri-Score

criteria, would be treated like other vegetable oils, without emphasizing substantial differences between the various types of oil.

Located on the front of a product packaging, the Nutri-Score system indicates the individual nutritional values by a scale of five colors, ranging from red to





Prevention of the IRCCS Neuromed, authors of numerous studies on the Mediterranean diet, comment - A potential problem whit this labelling system is that it isolates the single product from a global diet. The Mediterranean diet is a lifestyle that must be considered as a whole, in the wise choice of foods and in the knowledge on how to combine them. It is not a

green and corresponding to the first five letters of the alphabet, A-B-C-D-E.

Considered as a simple, intuitive and understandable tool by some Italian researchers, Nutri-Score is viewed with reserve by others.

"The proposal to help people make healthier food choices is definitely worth sharing. However, the proposed system risks being too simplistic and only partially conveying the message - researchers of the Department of Epidemiology and ranking or a shopping list, but it reflects a century-old history that could disappear if we begin to consider foods as atoms not communicating each other".

"The long life secret of the Mediterranean diet certainly lies in the way in which the food is combined and then served on the table - explains Licia lacoviello, head of the Department and professor of Hygiene at the Insubria University of Varese - it is unthinkable to evaluate olive oil outside the context in which it is commonly used by



Mediterranean populations, as a seasoning for fresh and cooked vegetables. Something similar is happening for moderate alcohol consumption: it must be viewed in the broader picture of a tradition in which a glass of wine is consumed during main meals".

"Adopting a food assessment score such as the one proposed by the Nutri-Score, without referring to food frequency or pairing, risks making the true essence of the Mediterranean diet disappear - comments Marialaura Bonaccio, epidemiologist in the Department. - We must also remember that Mediterranean food model is based on fresh or minimally processed products. So an effective preventive action should also pay attention to industrial processing, which in itself represents a potential threat to our health, beyond nutritional content".

"Our proposal - explains Giovanni de Gaetano, president of the IRCCS Neuromed - is to combine the Nutri-Score label with the traditional Mediterranean pyramid, allowing people to have an broad view on healthy eating habits. The pyramid clearly indicates what and how much to consume daily, placing the various foods in a wider food context. Moreover, the Mediterranean pyramid reminds us of a fundamental teaching: there are no foods to demonize, but only quantities and frequencies to respect. The dessert at the end of the meal is fine, but only on Sunday, for example. So also red meat, which can be consumed in moderation and without too much guilt, provided that it is done according to the Mediterranean rule, that is once a week, accompanied by vegetables seasoned with olive oil and a glass of good wine. By isolating foods from the diet, there is a risk of significantly unbalancing nutrition. What we propose is 'lifestyle at the table', inspired by moderation and common sense".

Neuromed researchers, therefore, suggest to include on the packaging of the various food products, together with Nutri-Score labeling, a color reproduction of the Mediterranean diet pyramid, with all its foods and with the specific food well highlighted in that context. The Department of Epidemiology and Prevention of Neuromed

> Researchers propose to combine the Nutri-Score label with the traditional Mediterranean pyramid





A new diagnostic frontier aiming to make a contribution to early diagnosis and management of cancer patients

enetic information is increasingly important in the context of oncology. In fact, specific genetic mutations in tumor cells can provide crucial indications for the classification of the cancer, prediction of its aggressiveness and, above all, response to drug therapies. Genetic profiling, especially in solid tumors, is normally carried out on tissues taken from the tumor itself, through biopsy or surgery. In this context, the "liquid biopsy" constitutes a new diagnostic frontier. "The release of tumor DNA into the

blood - explains Stefano Gambardella, head of Molecular Genetics at Neuromed - can allow us, through the use of highly sensitive methods, to identify mutations relevant for therapeutic choices without having to resort to traditional biopsy. Although today the main clinical application of liquid biopsy is on nonsmall cell lung cancer, this technique is constantly acquiring greater sensitivity and specificity also in other fields of oncology". Possibilities offered by liquid biopsy are very promising, as Gambardella says: "Further



potential applications are early screening of malignant neoplasms, diagnosis of minimum residual disease and development of personalized tumor management strategies for the individual patient".

We are talking about innovative technological methods because "They will allow us to search – adds the responsible of Molecular Genetics - for something that is present in the blood in an infinitesimal percentage. There are three important phases: the pre-analytical one, linked to the conservation of these molecules, which degrade quickly, then the phases in which we collect and analyze them". On the perspectives of this method Gambardella concludes: "the data we have are encouraging because we know that they can be improved a lot. For example, today we only have a sensitivity of 30% on some types of cancer, but we are confident that the evolution of scientific research will lead to a significant increase in this number".

A long term project aimed to improve available data NEWS

Studying at Neuromed

The Institute awarded scholarships to the most deserving students to promote a better technical and professional approach

As announced by President Giovanni de Gaetano, the I.R.C.C.S. Neuromed awarded scholarships to the best graduates at the Institute's educational centre. Scholarships provide for courses of study aimed at acquiring further skills and at extending experience within the framework of research projects.

Five new doctors already started their service in the Institute: two nurses (Paride Buonomo and Biancamaria Masi) and two medical radiology technicians (Salvatore Santangelo and Angela Clarissa De Prata), for "Sapienza" University of Rome; a neurophysiopathology technician (Giorgia Malinconico), for the Tor Vergata University, also in Rome. "The basic goal of this initiative - explains Professor Pasquale Passarelli - is to better train professionals to future challenges. But, even more, there is the establishment of a true community aimed at technical and professional advancement for those who choose to study at Neuromed ".

Teaching is one of the pillars of the institute, fully integrating with research and care activities. Born in 1997, the Neuromed teaching activity every year offers a wide and high-quality training. Courses affiliated with Sapienza University are: Nursing, Biomedical laboratory technicians, Physiotherapy, Medical radiology technicians. The courses of Neurophysiopathology and Speech Therapy are affiliated with Tor Vergata University.

To find out more: Polo Didattico IRCCS Neuromed

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Sieep appeas An underestimated problem

In the Neuromed Sleep Center, therapy is accompanied by reliable information

NEUROMED NEWS

ccording to estimates, 10% of adults suffer from sleep apneas (OSAS), a condition in which there is an excessive and repeated interruption, or slowing down, of breathing during sleep. The condition is often caused by complete or partial obstruction or compression of the upper airways. This usually causes a sudden awakening, with sleep interruption until normal breathing is restored. Multiple episodes during the night lead to poor sleep quality, affecting everyday life.

Often underestimated, this condition may pave the way to very serious problems, first of all daytime sleepiness, due to poor quality of night rest. Beyond poor concentration throughout the day, it can becomes a real danger, for example while driving or at work. Moreover, OSAS is often associated with an increase in cardiovascular risk.

Typical risk factor is an anatomicalfunctional alteration, directly causing or contributing to a narrowing of the upper airways. In order to diagnose OSAS in adults, instrumental tests, such as night cardiorespiratory monitoring or polysomnography, are essential.

Once the diagnosis is made, the treatment aims at eliminating or reducing the causes of the obstruction. International guidelines indicate different approaches, ranging from behavioral ones, such as reduction of overweight, to the use at night of orthodontic appliances able to reduce the obstruction or devices that can help the patient to breathe. The most recent guidelines recommend the use of positive pressure mechanical ventilation (PAP) as a first choice treatment.





A larger problem than you think

Sleep apneas are a frequent problem in the world population, with significant health, social and economic consequences. The most recent epidemiological data, obtained with polysomnography in people between 40 and 85 years of age and published by Italian Ministry of Health, indicate a prevalence of 49.7% in men and 23.4% in women. In the course of the last twenty years, it has been observed an increase mainly associated with obesity, but we see significant percentages also in people with normal body weight. Regarding women, the prevalence increases after menopause, while in pregnancy it can reach values between 14% and 45%. Despite the spread of the problem among the population, a large majority of people suffering from sleep apnea are not identified, leading to a delay in diagnosis and appropriate therapies.



Much can be done for prevention, especially by adopting a healthy and balanced lifestyle, with proper nutrition and constant physical activity: simple precautions that can prevent overweight and obesity, important factors in increasing the risk of disease. But there is a time when early diagnosis and correct treatment make the difference. This is where specialized structures, such as the Neuromed Center for Study and Treatment of Sleep Disorders, come into play.

"Sleep disturbances can negatively affect age-related issues, such as cognitive disorders. - says Dr. Andrea Romigi from the Neuromed sleep center - This has been seen, as an example, in neurodegenerative diseases like Alzheimer's. Frequent sleep disturbances seem to be associated to a dysfunction of orexin, the protein regulating

Sleeping apneas complications

According to current medical knowledge, complications of sleep apnea syndrome can involve:

• Respiratory system (respiratory failure)

• Cardio-circulatory system (hypertension, which initially appears at night, then during the day and is resistant to therapy; cardiac arrhythmias; coronary heart disease; cerebrovascular diseases

• Neurological system (cognitive and mood disorders, anxiety, emotional instability, depression. These issues can affect relational life)

Furthermore, this syndrome can be an important risk factor for the development of numerous chronic non-communicable diseases (renal failure, obesity, diabetes and, according to recent studies, also an increased risk for some cancers)

sleep-wake cycle, and we know that some sleep disorders could also predispose to Alzheimer's disease. We observed that, if sleep apnea is well treated, there is a lesser extent of neurodegenerative processes underlying the pathology. This translates into a real prevention action".

Beyond simple rest, sleep is also a way to keep our nervous system young. "The importance of sleep must always be taken into account. - concludes Romigi - Sleep deprivation implies many consequences, starting from daytime sleepiness to increased blood pressure, vascular risk factors and cognitive problems. Taking care of your sleep must therefore become an integral part of your commitment to prevention".



Therapies

• behavioral therapy: if overweight or obesity is present, it is important to aim for a reduction in body weight through healthy nutrition and adequate physical activity

• positional therapy: in case of OSAS occurring only in supine position, the adoption of a socalled "position dissuader" can be indicated

• prosthetic-orthodontic therapy: night use of mandibular advancement orthodontic devices, able to increase the retro-pharyngeal space and, therefore, reduce obstruction

• surgical therapy: surgery of the upper airways

• prosthetic-ventilatory therapy: night use of a mask generating positive pressure that will help breathing. Positive pressure can be applied continuously (Continuous Positive Airway Pressure - CPAP) or intermittently (BILEVEL Positive Airway Pressure).

To find out more:

Centro per lo studio e la cura dei disturbi del sonno

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The commitment of the I.R.C.C.S. Neuromed and its Foundation to draw attention to the pathology, as well as on the misunderstandings and fears that still surround it

Epilepsy Day

The purple color to fight prejudice

e are winning the battle against prejudices on epilepsy, but we still need energy. International Epilepsy Day was celebrated on 10 February. On this occasion, Neuromed Foundation promoted a series of meetings and initiatives aimed at knowing the disease and reflect on the latest scientific approaches. Meetings with schools are the most effective because children are often the first to deal with this disease. The onset, in fact, usually is at school age, and the simple fact of not recognizing a seizure epileptic crisis often leads young people to exclude those affected. Removing the sense of fear, through knowledge, turns out to be the most effective tool to make sure that, from an early age, it is possible to fight

not only the pathology, but also the prejudice that always surrounded it.

"What we are working on - says Mario Pietracupa, President of the Neuromed Foundation - is not just a clinical action, addressed to patients and family members. With our initiatives we aim to involve the whole population, because epilepsy has a long history of prejudice and discrimination behind it. Today, thanks to science innovations and social awareness, we can say that, luckily, those times are almost over, but our commitment must be steady. So we light up in purple (the color of the International Epilepsy Day) the most representative buildings and monuments. And we bring the voice of our experts to young people ".

Rare diseases

A better knowledge helps us in fighting fear and raising hope in scientific research

are diseases' disabling aspects are heterogeneous, and the lack of specific policies for these conditions, together with insufficient knowledge, often lead to delays in diagnosis, difficulties in accessing proper treatments and loss of trust in the health system.

The key condition for improving global strategies regarding rare diseases is to recognize their existence. In order to improve diagnosis and treatment, moreover, proper identification must be accompanied by the dissemination of information fulfilling the needs of health workers and patients. Doing so, we can support not only scientific research, but also the many families daily dealing with these problems.

"Our goal is to make these people not feeling alone, because they are not - says the President of the Neuromed Foundation Mario Pietracupa - We always promote a series of public initiatives among schools, institutions and citizens aimed at increasing knowledge of rare diseases. We bring patients to Neuromed, so they can know our researchers. We want to give hope to these people, and we want them to understand that many experts are looking for treatments, studying daily to add an extra piece to scientific knowledge".

During 2020 World Rare Disease Day, Neuromed Foundation promoted various initiatives. But the commitment is not limited to just a single day: it continues throughout the year. An example is the meeting "A look at Rare Diseases", promoted together with patient associations, clinicians, researchers and health managers. From diagnosis to therapies to assistance, every aspect regarding rare disease patient care was examined.

To find out more: Centro Malattie Rare

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How a drug is born

The most delicate phases: clinical studies

n a previous issue of this magazine we talked about the early stages of drug development, from the design of new molecules to tests on animal models. These are procedures designed to optimize the molecule under study, evaluate its effective pharmacological properties, both in the laboratory and on complex organisms, and establish safety level.

Only after a molecule has been completely optimized for all preclinical attributes (in technical terms: pharmacology, pharmacokinetics, efficacy and safety) can it be tested on humans and patients. This is the phase of the so-called "Clinical trials". They represent a narrow and impervious road on which all new medical therapies must pass. It is also a very long way: years pass before a new therapy can see the light.

Clinical trials are traditionally divided into four phases: In phase I only the safety of the drug and possible side effects are evaluated. About 70% of experimental drugs pass this test phase. For those molecules that make it, phase II studies will come to test their



effectiveness. Generally the objective of phase 2 is achieved using a "surrogate marker" of the disease (for example, an MRI or a laboratory examination).

Here comes a concept that is often heard of and which is the basis of all modern medicine: randomized controlled trials: one group of patients receives the experimental drug, while a second "control" group receives standard treatment or a placebo, a substance devoid of any pharmacological action. Most of the time these studies are also "blind", that is, neither patients nor researchers know who received the experimental drug and who received the placebo. This avoids a well-known drawback: a person who receives a new drug will feel better simply because he/she is strongly convinced of its effectiveness, a the market. But research continues even when a new drug is regularly used. This is phase IV, in which all the effects continues to be monitored.

Neuromed is heavily involved in clinical trials, starting from phase II and for all subsequent phases. There are 36 active trials, and for eight of them the Institute is a coordinating center. "Participating in clinical



Professor Giuseppe Lembo (right) with the team dedicated to clinical trials

belief that can also affect doctors themselves when they evaluate the patient. If nobody directly involved in the prescription knows who is having the drug and who is not, the observation of the effects will be as impartial as possible.

Phase III studies are carried on in similar ways, but they aim to demonstrate the efficacy of the drug on actual clinical elements, such as the evolution of the disease itself, and no longer only on "markers" (as occurs in phase II). They can involve several hundred or thousand patients and last for years. Only if a molecule passes one, or more often two, phase III studies can it be evaluated to enter

trials - says Professor Diego Centonze, Head of the Neurology Unit - has important effects not only for the progress of therapies, but also for the level of assistance that a center can offer to its patients. Clinical trials put us in international networks, with a clear advantage in terms of knowledge and updating. Furthermore, knowing which molecules are appearing on the horizon allows us to adapt our independent research, perhaps discovering new and interesting elements starting from them".

It is the concept at the basis of every clinical institute following a high scientific



Professor Diego Centonze (third from left) with the team dedicated to clinical trials

approach: patients are better treated where research is done. "The clinical trials - says Professor Giuseppe Lembo, Head of the Department of Angio-Cardio-Neurology - are part of a broader concept, that of Evidence based medicine". The definition of evidence-based medicine refers to the use of the best scientific evidence in making decisions in medical practice. So patient care is always based on solid foundations. "All medicine continues Lembo - today needs this approach. It can be a new drug, of course, but it can also be a particular clinical practice, or the use of old strategies that need to be reconsidered. A clinic that follows this approach guarantees its patients the best possible care". At the heart of the study there can be a new drug or a particular clinical procedure

A nutraceutical formulation to fight hypertension

Adding a combination of three natural extracts to standard pharmacological treatments could help to fight hypertension, improving cardiovascular function especially in those patients whose blood pressure remains not well controlled. These are the conclusions of a study conducted by the Vascular Pathophysiology Laboratory of I.R.C.C.S. Neuromed in Pozzilli, in collaboration with the Medical University of Salerno, Federico II University in Naples, I.R.C.C.S. Multimedica in Milan, and Sapienza University of Rome. The findings were published in the Journal of the American Heart Association.

Extracts used in this nutraceutical formulation come from Bacopa Monnieri, Ginko biloba and green tea leaves, complexed with phosphatidylcholine, a natural phospholipid. Researchers evaluated its effects on a group of hypertensive patients, all of them receiving standard therapies. The main characteristic of the selected patients was that, despite pharmacological treatments, their blood pressure remained not well controlled.

Albino Carrizzo, PhD; Ornella Moltedo, MSc; Antonio Damato, BSc; Katiuscia Martinello, PhD; Paola Di Pietro, MSc; Marco Oliveti, BSc; Fausto Acernese, PhD; Giuseppe Giugliano, MD; Raffaele Izzo, MD; Eduardo Sommella, PhD; Serena Migliarino, MD; Ornella Piazza, MD; Carmine Izzo, MSc; Nicola Virtuoso, MD; Andrea Strianese, MD; Valentina Trimarco, PhD; Pietro Campiglia, PhD; Sergio Fucile, PhD: Annibale Puca, MD: Bruno Trimarco, MD; Carmine Vecchione, MD, New Nutraceutical Combination Reduces Blood Pressure and Improves Exercise Capacity in Hypertensive Patients Via a Nitric Oxide-Dependent Mechanism. J Am Heart Assoc. DOI: 10. 1161/JAHA.119.014923

New interaction between nerve cell receptors discovered: possibilities open up for therapies against Parkinson's disease

> One of the main weapons in the treatment of Parkinson's disease is levodopa (L-Dopa), capable of counteracting the tremors and other manifestations of the pathology derived from the lack of dopamine in a particular area of the brain. But over time this drug causes growing side



effects, mainly involuntary movements (dyskinesias) which significantly worsen the patient's quality of life. Now a research born from the collaboration between the Neuromed Neuropharmacology Laboratory, the Swedish University of Lund, the INSERM of Montpellier in France, the Sapienza University of Rome and the UCB Pharma in Belgium, opens an innovative path towards the possibility of fighting these side effects.

The study, carried out on animal models and published in the prestigious scientific journal

lavori

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prodotti



"The Journal of Clinical Investigation", was focused on the interaction between two types of receptors (molecules present on the surface of nerve cells, capable of receiving the chemical signals of neurotransmitters): dopamine (D1) and mGlu5, the latter for glutamic acid. The research shows that D1 and mGlu5 receptors interact with each other forming a molecular complex. This complex would give rise to changes in the transmission systems between neurons which, during a prolonged treatment with L-Dopa, would lead to the appearance of dyskinesias. Irene Sebastianutto, Elise Goyet, Laura Andreoli, Joan Font-Ingles, David Moreno-Delgado, Nathalie Bouquier, Celine Jahannault-Talignani, Enora Moutin, Luisa Di Menna, Natallia Maslava, Jean-Philippe Pin, Laurent Fagni, Ferdinando Nicoletti, Fabrice Ango, M. Angela Cenci, and Julie Perroy. D1-mGlu5 heteromers mediate non-canonical dopamine signaling in Parkinson's disease. J Clin Invest. 2020 Feb 10 doi: 10.1172/JCl126361. [Epub ahead of print]

L'INTERVISTA

Tim Nawrot Lifelong consequences of air pollution

Tim Nawrot, Professor in the Universities of Hasselt and Leuven, Belgium, was at Neuromed at the invitation of the Department of Epidemiology and Prevention for a Neuroseminar entitled "Air pollution and consequences for health throughout life"

Professor Nawrot, air pollution is becoming an increasingly serious problem, and institutions are struggling to deal with it. What do your research tell us about the effects on human health?

The consequences of air pollution extend throughout a person's life, starting from the first days. Infants may already have a lower birth

weight, and we know how important this is for their future health. Moreover, in adults we see effects on the cardiovascular system. In the past, there was a lot of focus on respiratory problems, but today we know that heart and blood vessels are also seriously affected by pollution.

What pollutants are we talking about?

Naturally there are gases, such as ozone. But we have to consider that one of the most toxic components of air pollution is the so-called particulate matter: extremely small particles which, once into the lungs, can reach all organs of the body.

Particulate matter is the main reason behind traffic blocks imposed on various European cities. But, in the current



situation, should the effects you are studying be considered as a major public health problem in the European Union?

We must bear in mind that even for values below European limits we start to observe negative health effects that can extend throughout life. We see that DNA damage can occur, by shortening of telomeres, an important factor in the biological processes of aging. And it is estimated that 5 percent of heart attacks are due to air pollution. To make a comparison, health risks are much lower than those related to cigarettes smoking, but there are a huge number of people exposed to air pollution. This is why we are talking about a public health problem. Drastic interventions on air pollution would therefore have a great impact on the well-being of an important part of the population.