Cerebrovascular diseases at the C. Mondino National Institute of Neurology: from Ottorino Rossi to the present day

Giuseppe Micieli, MD\textsuperscript{a} Emilia Martignoni, MD\textsuperscript{b,}\textsuperscript{†} Giorgio Sandrini, MD\textsuperscript{a,c} Giorgio Bono, MD\textsuperscript{b} Giuseppe Nappi, MD\textsuperscript{a}  
\textsuperscript{a} IRCCS C. Mondino National Institute of Neurology Foundation, Pavia, Italy \textsuperscript{b} Faculty of Medicine and Surgery, Department of Clinical Medicine, University of Varese, Italy \textsuperscript{c} Faculty of Medicine and Surgery, Department of Public Health and Neurosciences – Section of Neurological Sciences, University of Pavia, Italy  
Corresponding author: Giuseppe Micieli  
IRCCS C. Mondino National Institute of Neurology  
Via Mondino 2, 27100 Pavia, Italy  
E-mail: giuseppe.micieli@mondino.it

Summary

This paper traces the development of research and healthcare models in the field of cerebrovascular disorders at the C. Mondino National Institute of Neurology in Pavia, Italy. It starts with a description of the original experiences of Ottorino Rossi and his thesis on atherosclerosis which date back to the beginning of the last century; it then illustrates the connections between his seminal essay and the future directions followed by research in this institute, through to the development of one of the first stroke units in Italy.

In this context, we examine a large range of scientific approaches, many related to cerebrovascular diseases (such as headaches) and autonomic disorders, and some of their biological and physiological markers. The originality of an approach also based on tools of advanced technology, including information technology, is emphasised, as is the importance of passion and perseverance in the pursuit of extraordinary results in what is an extremely complex and difficult field.

KEY WORDS: atherothrombosis, autonomic nervous system dysfunction, cerebrovascular disease, emergency neurology, neuropsychology, stroke unit, stroke registry

Many years ago: Ottorino Rossi’s essay on atherosclerosis

Founded in 1907, the University of Pavia’s Clinica Neuropatologica (Clinic for Nervous and Mental Diseases) was created as an institution for the diagnosis and treatment of neuropsychiatric disorders and, in line with what was happening (or would later happen) to similar institutions, it was built outside the complex of the city’s main hospital (the San Matteo Hospital). In the years immediately following its foundation, the institute’s location was actually to prove its fortune, endowing it with those peculiar characteristics and qualities that still today identify it in the minds of the people of the city and province of Pavia; however, as was to prove the case for all clinics similarly located, this circumstance was to end up leaving the institute in “splendid” isolation, excluded from the organisational, and even cultural, developments of more recent years. The move to the new site in via Mondino, a modern and much more comfortable building, was not to succeed in resolving this problem completely, given the institute’s new orientation as, primarily, a hospital health care facility; indeed, as such, it feels acutely, and at times painfully, its isolation from hospitals in which it could fulfil the role that, correctly, is now starting to be envisaged for neurology, today and in the future.

Over time there has emerged a growing contraposition between two different models, or versions, of neurology. On the one hand, we have “academic” (or classical) neurology, which, while boasting a refined diagnostic approach, remains one of the few disciplines using a semiological framework that has moved on very little, if at all, from the body of knowledge of the past century; furthermore, it also has the severe drawback of offering few or no treatment options. On the other hand, we have “emergency” neurology, which, being primarily geared at the management of critical conditions on admission to hospital or during hospitalisation, is deeply integrated with the other (more or less general) medical specialties, and has an operational approach that is at odds with the erudite, sometimes almost philosophical, case discussion that has become a feature of the first “version” of this discipline. The intensive care hospital is the right setting for the practice of emergency neurology, which involves semi-intensive type care and close contact with other intensive and semi-intensive care units and departments, such as the coronary unit and emergency room or accident and emergency department. Operating
in this way, the emergency neurology unit is able to “intercept” the neurological needs of patients on their admission to hospital, or at the onset of specific complications in other units of the same hospital. As such, it can be seen as the natural evolution of the model of organisation represented by the stroke unit, which is given over to the diagnosis and treatment of acute cerebrovascular diseases and is a technologically and culturally advanced area for the management of critical neurological conditions that would otherwise have to be treated in non-specialist settings, with all the attendant drawbacks and problems (low diagnostic specificity, more diagnostic tests, longer hospitalisations, uncertain impact of non-specialistic therapies). In view of these considerations, it can reasonably be asserted that stroke care has been the driving force behind the definitive development of (emergency) neurology, given that it is, precisely, changing ideas on diagnosis and treatment that have allowed the transition from a “nihilistic” to an “interventional” approach, characterised by interventions within the very first hours of the acute event, links with emergency services (but also with rehabilitation services) and, finally, the development of management outlooks that are completely new and, above all, geared at reducing mortality and disability, not only from stroke but also from other acute neurological diseases. At the present time, the “classical model” (high specialty) of neurology is still in operation in the Mondino Institute; but alongside it there is also an emergency neurology unit and a neurorehabilitation unit which has close links with a widespread territorial network. In this way the institute is able to offer a complete range of neurological services in line with the direction this discipline is taking. At first glance, this whole process may seem to have very little to do with the historical figure of Ottorino Rossi and his activities within the University of Pavia. However, in actual fact, in Rossi’s 1906 essay “L’artherosclerosi dei centri cerebrali e spinali”, which he wrote while still an assistant at the Clinic of Nervous and Mental Diseases of the University of Pavia (directed by Professor Casimiro Mondino), we encounter a rather unusual, or at least unexpected (i.e. not particularly “contemplative”) approach to the problem of cerebrovascular disease, which he interpreted in an essentially anatomo-pathological way (the only one possible at the time), also identifying some therapeutic possibilities, which were interesting not least because of their scope for further development. What Rossi wrote in 1906 is clearly in line with what, in much more recent times, has been written about the approach to cardiovascular and cerebrovascular risk in the atherothrombotic patient. In short, he showed the benefit of a holistic view of the problem and accepted, in part, the more classically cardiological view of the local acute coronary event as a complication of atherosclerotic plaque rupture.

Atherothrombosis is characterised by an unpredictable and sudden disintegration (rupture or fissure) of an atherosclerotic plaque; this causes platelet activation leading to thrombus formation and occlusion of the vessel where the plaque is located. It is the basic condition that determines the events leading to myocardial infarction, ischaemic stroke, peripheral artery disease and vascular death, and it is the final consequence of atherosclerosis, which, instead, develops over a period of several decades. Indeed, although the atherosclerotic process begins in an individual’s late teens or twenties, with the formation of fatty streaks and fibrous plaques, the clinical manifestations of the disease are rarely evident before the age of 40 years. Atherothrombosis is a progressive process over time that affects the entire vascular system; it is potentially fatal and it is unpredictable (as regards both the timing of the clinical event and the long-term outcomes). Rossi’s essay did not fail to point out the pathological complications (or rather consequences) of atherosclerotic lesions of both extracranial and intracranial vessels, and here again it is possible to discern a modern approach to the problem of cerebrovascular disease, i.e. the one that focuses on altered cerebral circulation, whose role is, even today, still not fully and definitively clarified, especially with regard to the possible therapeutic approaches that it might imply. Leaving aside the obvious differences from extracranial large vessel disease, it is clearly apparent that intracranial vessels are still little studied (especially in acute settings) and rarely considered candidate sites for recanalisation procedures in ischaemic disease (mechanical or pharmacological thrombectomy); above all, no appropriate long-term therapeutic approaches (as valid as those used to treat the same condition in the major vessels) are known. Finally, appealing as the hypothesis is, the role of genetic factors in the phenotypic expression of intracranial disease has not yet been fully identified (and, with it, possible therapeutic approaches).

Leaving aside observations that are still in part sub judice, like those on vertiginous syndromes linked to atherosclerosis, Rossi’s essay also introduces the important topic of vascular cognitive decline, in other words the condition that, many years later, was to be sweepingly labelled (albeit, unfortunately, in the absence of diagnostic-therapeutic certainties) “vascular dementia”. As chapter 16 of the Italian SPREAD stroke guidelines (Psycho-Cognitive Complications) clearly shows, vascular dementia can be seen as a condition in which the cognitive decline may result from a range of very diverse pathological conditions. Indeed, there exist vari-

Figure 2 - Ottorino Rossi’s essay on atherosclerosis.
ous forms of vascular dementia: the multi-infarct form (i.e., related to multiple infarcts, even in different arterial territories, as in the case of cardioembolic stroke); the form associated with a single strategic lesion – this often involves a single acute ischaemic event –, which is characterised by the occurrence of a (sometimes peculiar) cognitive disorder resulting from an injury that interrupts (sometimes permanently) the cortico-subcortical circuits that underlie the major cognitive functions; the form associated with cerebral small-vessel disease; the acute and/or chronic hypoperfusion form, seen prevalently in conditions of chronic hypotension (iatrogenic hypotension, chronic autonomic failure, chronic heart failure) or acute prolonged hypotension (heart or carotid surgery); finally, the haemorrhagic form.

Of all these, the one that has attracted the most interest on the part of researchers in recent years is undoubtedly the “small-vessel disease” form, previously also described asBinswanger’s disease.

In reality, the definition “small-vessel disease” includes cerebral white matter disorder characterised by diffuse changes of vascular origin (leukoencephalopathy), or by the presence of diffuse lacunar or microlacunar lesions (most often asymptomatic), or by an association of the two. From the anatomo-pathological point of view, these structural white matter alterations are underlain by changes in the walls of small cerebral vessels, which lead to the appearance of lipohyalinosis, microaneurysms, microatheromas and even fibrinoid necrosis. These are conditions that can, of course, translate into a clear susceptibility to hypoperfusion phenomena (occurring, for example, as a response to arterial hypertension that would otherwise be harmful to the microcirculation and the cerebral haemodynamic, possibly leading to leukoaraiosis), haemorrhagic lesions (usually detectable on gradient echo MRI or CT as microbleeds, or larger haemorrhagic lesions, as in the case of typical spontaneous intraparenchymal bleeding), or small focal lesions definable as ischaemic lacunar infarcts, whose physiopathogenetic significance and, particularly, therapeutic implications are still debated today. Additionally, of course, cerebral atrophy alone may be present as a possible anatomo-pathological picture underlying the clinical manifestations of vascular dementia.

All this adds up to a complex morphological picture, in which the clinical features can have very different, or excessively similar, connotations. The differential diagnosis of vascular dementia may have to be made versus other forms of dementia, such as Alzheimer’s dementia, even though numerous clinical and neuropsychological findings seem to clearly differentiate the latter. However, it should not be forgotten that the phenotypic expression of vascular cognitive impairment, too, appears to result from a genetic background that only in some cases corresponds to a monogenic disease (CADASIL, CARASIL, CAA); in other cases it is likely that it is the combination of gene polymorphisms (in themselves insufficient to cause the disease) with vascular risk factors (hypertension, diabetes, smoking, hypercholesterolaemia), and in general with certain environmental conditions, which gives rise to a wide spectrum of clinical conditions. Ottorino Rossi’s descriptions of cases observed at the Clinic for Nervous and Mental Diseases constitute accounts of phenomena that would, many years later, be observed using more appropriate research tools. At the same time, Rossi provided descriptions, even classical ones, of alterations of sensorimotor function possibly dependent on acute-subacute vascular lesions, located both supra- and subaortic or, in the spinal cord.

Perhaps because it was following in the wake of a method oscillating between clinical observation (necessary and “compulsory”) and instrumental diagnostic investigation, the Clinica Neuropatologica where Rossi conducted his studies did not fail to equip itself, over the years, with a set (initially simple, even minimal) of instrumental tools. This was enriched in more recent times (early 1970s) with the acquisition of a brain CT scanner (the institute was one of the first in Italy to purchase one); this addition was an important step towards better understanding (and, in part, confirmation) of what had previously been described purely on the basis of anatomo-pathological observations.

**Attempts to establish a functional approach to vascular pathology**

Thus, the whole neurology scenario was set to change and, as proved to be the case for all the branches of modern medicine, to do so in an increasingly rapid and specific manner. Moreover, the Pavia Clinica Neuropatologica had, during the 70s, brought together, under Prof. Kauchtschischvili, a group of young researchers through whom it was ready to take up, once again, the line of investigation concerning, precisely, cerebrovascular disorders and the haemodynamic, degenerative and functional conditions that can cause them. These young researchers included, among others, Giuseppe Nappi, Marco Poloni, Giorgio Bono, Paola Bo, and Gianpaolo Papandrea. Adopting an approach characterised by openness to collaborations outside the institute, a spirit that would continue in the years that followed, they studied, among other things, cerebral transit time with radioactive tracers (in collaboration with A. Favino of the Institute of Occupational Medicine, University of Pavia).

**Figure 3 - From the left: G. Papandrea (now general practitioner in Villanterio, Pavia), G. Bono (Chair of Neurology at the Insubria University, Varese), P. Bo (deceased, 2008), G.M. Kauchtschischvili (deceased, 1976), M. Poloni (Head of Neurology Unit, Ospedali Riuniti, Bergamo), G. Nappi (Scientific Director of IRCCS C. Mondino Foundation).**
In the early 1970s, this group published papers (3-8) on the influence of smoking and other “harmful” exogenous factors, such as chronic alcohol abuse, aging and induced hypoglycaemia, on the functional status of cerebral circulation. The latter was evaluated mainly using a rheograph, a rather rudimentary instrument from whose results it was easy to intuit the involvement of purely mechanical factors capable of influencing the characteristics of the sphygmic wave which this technique claimed to depict. This instrument was used to photograph a “functional abnormality” – no longer an anatomopathological one (as in Rossi’s times) – in the context of diseases whose evolutionary pattern was already quite easy to understand. This was also the period of pharmacological studies using vasoactive substances such as ergot derivatives (vincamine) in the “treatment” of chronic disorders of cerebral circulation. These studies, in addition to rheography, also used another method that might today be considered “curious”, namely ophthalmodynamometry, i.e. the determination of blood pressure in the retinal artery through the application, to the orbit, of an inflatable balloon in order to determine the disappearance of the pressure wave, and thus the evaluation of “intracerebral” circulation (as well as of the efficacy of possible mechanisms of compensation in the presence of intracranial and/or extracranial vessel disease).

Thanks to the work of the same group, it was not long before these studies of cerebral haemodynamics were embracing other methods, namely the Doppler method and angiography, allowing the description of cases with dolichobasilar and megadolichobasilar artery abnormalities (and also consideration of their possible role in hemifacial spasm, in an early interpretation of what would later more correctly be identified and described as a neurovascular conflict involving the VII cranial nerve) (9,10). At the same time, a National Research Council study – this study was coded ATS-OD2 and its aim was to conduct an instrumental assessment and follow up of patients with cerebrovascular diseases (TIA or minor strokes) observed in the acute or subacute phase – was using methods now fortunately obsolete and long since abandoned, such as EEG recording during carotid compression. This particular application of electroencephalography was, indeed, not free from risks, associated with the possible presence of unstable plaques in the compressed carotid artery. Furthermore, it was not unusual for the sinus stimulation that could derive from this procedure to cause the appearance of a worrying asystole (fortunately short-lasting). Mainly, however, it rarely expressed, in reality, the state of cerebral circulation, and its compensations, following an acute event (11,12).

Finally, following the acquisition of the cerebral CT scanner, this remarkable tool of investigation also began to be applied to clinical research, particularly research into cerebrovascular diseases, both acute and chronic, through investigations geared mainly at defining clinical pictures related to chronic vascular white matter disease and at describing findings that might be considered topical today, given the fresh interest that has been shown in this disease in recent years, in part thanks to the efforts of a large number researchers, both Italian and foreign (13).

For both the institute and the working group created over many years and coordinated by Prof. Giuseppe Nappi (who co-authors this article), which was mainly oriented towards the study of functional disorders of the nervous system, particularly headaches, this period also constituted a valuable opportunity to investigate the possible links between headache and acute cerebrovascular episodes, especially minor strokes and those episodes that, at the start of the 1980s, were still known as RIAs (reversible ischaemic attacks). These investigations of the presence of headache before and/or during and/or after the onset of the ischaemic cerebrovascular symptoms constituted, for the school of the Mondino Institute of Neurology, the moment that marked a real revival of interest in vascular disease in the strict sense, even though some years were still to go by before its organisational, management and research endeavours led to setting up of lines of research and healthcare activity specifically devoted to this problem (14,15).

At present, however, what is really worth emphasising is the importance of the categorisation of headaches as the point of transition between affective and cerebrovascular disorders, which, unlike the former, are hallmarked by the final (ischaemic) damage. Indeed, it is always a predisposition to develop headache that, depending on risk factors that are linked to aspects of the internal and...
external environment, underlies the appearance of the “complication”, and can be inserted among the comorbidities of the two classes of disorders that lie at the two ends of the spectrum.

There was, in this period, no lack of experimental models simulating the relationship between migraine and vascular disease, a relationship demonstrated, for example, in the response of the cerebral endothelium to nitrates, which are known for their headache-inducing effect and also provide a reliable measure of cerebral vascular reactivity both in physiological and in pathological conditions (diabetes, carotid stenosis, etc.). A similar experimental model allowed the Mondino group to discover the clinical relevance of the use of NO donors, both in acute and in chronic cerebrovascular disease, especially in patients with traditional risk factors, such as diabetes and hypertension (16,17).

In short, the study of cerebrovascular diseases by the Pavia neurological school was well under way again, as is shown by the fact that, from its use of models, both clinical and speculative, borrowed from other interesting diseases such as those affecting the autonomic nervous system (investigated at length in this period, also within the context of various forms of primary headache), it succeeded in making connections that are still very much appreciated today; these include the interesting and useful relationship, supported by a more recent review published in Clinical Autonomic Research, between the autonomic nervous system and ischaemic stroke. Discussion of the activity of the autonomic nervous system was still serving to complement and enrich epidemiological, clinical and/or therapeutic data, providing some very interesting interpretations of pathological events that, in some cases, prompted the opening of new lines of research in the field (17,18).

The relationship between the autonomic nervous system and stroke is perhaps best enshrined in a very common and increasingly frequent condition (not only among the elderly), namely, atrial fibrillation which, of course, particularly with advancing age, can cause stroke (cardioembolic). However, there exist many other relationships between ischaemic (or haemorrhagic) cerebrovascular disease and changes in vegetative functions. It was for these reasons that the Pavia neurological group, in conjunction with a group of Pavia cardiologists, founded the Italian Society of Cardioneurology, through which, in 1989, an international meeting was organised in Palmi Calabro (Reggio Calabria) which brought together specialists in both disciplines from every part of the world, and came shortly after another interesting meeting held in Pavia (19). The proceedings of this international meeting were published in the book “Neurocardiology Update” (20).

A stroke unit is established at the C. Mondino Foundation

It was in the early nineties, when the institute was still located at the old site in via Palestro, that we began to develop the necessary know-how, cultural, scientific and organisational, to care for cerebrovascular patients, sometimes in the acute phase. The work, in those early years, was done without a dedicated area. In other words, it was carried out, within the various departments, by an “itinerant” medical team (stroke team). In this period, initial ideas began to take shape on the organisation of what, in 1996, was to become one of Italy’s first stroke units. An area for this unit was selected: one of the large rooms (traditionally occupied by as many as 13 beds) located within the department, at the time directed by Prof. Nappi, was transformed into an open space designed to accommodate six closely monitored beds, a nursing area and a specially equipped bathroom.

Outside the department, in what had previously (in the old Clinica Neuropatologica) been the “verandah”, i.e. the space given over communal activities, including meals, a small area was created to house the computer equipment. Its purpose was to collect data from the stroke unit monitors, as well as from the computerised patient monitor.
records that were gradually being introduced in this period, and from nursing folders. This use of advanced IT solutions and software revolutionised many aspects of the care of cerebrovascular patients in our stroke unit (workflow management, compliance with Italian SPREAD guidelines, assessment of clinical risk, and so on).

The stroke unit was enthusiastically welcomed by the nursing staff, some of whom still work there today (the unit was transferred to the institute’s new site in 2003), as well as by the physicians and all those who, over the years, have made a crucial contribution to the work done there (rehabilitation therapists, physiotherapists, psychologists, social workers and bioengineers). Its inauguration provided the opportunity for a congress, held at the “old” Mondino site, which was attended by the specialists (vascular surgeons, neurosurgeons and others) who, with sacrifice and enthusiasm over many years of joint collaboration, had taken part in all the work on cerebrovascular diseases (21).

The stroke unit, thanks to its well-known organisational and management features, was a setting ideally equipped for ensuring accurate identification of a patient’s risk profile, continuous monitoring of vital signs, prompt therapeutic interventions in response to neurological and/or medical complications, standardisation of specific treatment procedures for stroke, and effective and rapid multidisciplinary consultations.

At the same time, it opened the way for the development of management models for improvement of nursing and for initiatives geared at involving, and raising awareness among, the general public; examples in this regard include information campaigns carried out first in the province of Pavia and then at regional level (PRESTO and ASL MI2 projects), and projects developed for the Ministry of Health (on more advanced and effective computer-based models of care).

The intensive work carried out in recent years in the sphere of information, aimed both at the public and, in particular, at patients and their families, is illustrated by the publication (in early 2003) of the booklet entitled “The stroke patient: what do I do when he comes home?” This booklet, born of the collaboration between all the professionals who took part in the information campaigns held at provincial level (especially those organised in rehabilitation centres), was published in no less than 100,000 copies and quickly became a “must” from which many other healthcare professionals have drawn inspiration for similar initiatives.

Similarly, the intensive and enthusiastic collaboration with the Department of Computer Science and Systems Engineering of the University of Pavia (in particular with the late Mario Stefanelli, and with Silvana Quaglini and Silvia Panzarasa, among others) allowed us to develop and test some extremely interesting management models (22). The Pavia group came to international renown through its study and demonstration of the important benefits to be obtained from adherence to guidelines (first those of the AHA and then the Italian SPREAD guidelines), namely reduction of mortality and disability as well as of hospitalisation costs. The collaboration with this group led to the development of computerised medical record systems equipped with software, such as that for assisted clinical decision-making (workflow management), whose applications continue to be used in both the nursing and the medical areas.

At the same time, the capacity, thanks to the computer systems used, to store numerous data has allowed us to publish some extremely interesting studies, including...
one on the importance of monitoring in the care of the acute cerebrovascular patient (23). The up-to-date models developed and the results obtained have allowed the centre based at the C. Mondino Institute to be among the first and the most advanced stroke units in Italy, and also to participate (as the only Italian centre) in the Stroke Unit Trialist Collaboration, coordinated by Peter Langhorne.

The experience gained through these projects, as well as through the everyday care of the patients regularly referred to the stroke unit (both at the “new” and the “old” site) — in spite of the absence, already noted, of an accident and emergency department —, contributed, in the early 2000s, to the development of regional health care models. These models were finalised after the important PROSIT project (the first author of this piece was also a member of the scientific committee of that project, coordinated by Livia Candelise, Milan, which demonstrated the superiority of the stroke unit compared with traditional departments: a net reduction [9]% of mortality and disability), and included the stroke unit in the Lombardy Regional Health Plan 2002-2004, in the subsequent regional “Cardiocerebrovascular Plan”, and in the documents of the regional Cardiocerebrovascular Commission. All this led to decisions, at regional level, of great importance from the perspective of the organisation of stroke units and their integration with emergency and rehabilitation services (24-26).

A stroke registry and emergency neurology

Alongside these developments, there also began to develop, within a joint SIN-SNO (Italian Society of Neurology and Society of Hospital Neurosciences), group founded in Milan in 2008 during the annual meeting of the SNO, the concept of emergency neurology herein discussed; its postulates were collected in a position paper of these two Italian neurological societies which is now being circulated in Italian (27) and in English, in the journal Neurological Sciences.

In 2001, the Pavia group, acting on a mandate from the coordinating SIN-SNO group, began to develop the network that would subsequently be named SUN (Stroke Unit Network) Lombardia; this network was created as means of sharing information tools so as to unify and standardise health care practices at regional level. This project subsequently led to the birth, at the end of 2006, of the Lombardia Stroke Unit Registry, the first (and still the only) registry of this kind in Italy, which has a data base now shared by as many as 37 neurology departments equipped with stroke units spread across the region (28). The registry, currently being released as a Lombardy Region Electronic Health Record, contains data on an average of 12,000 stroke patients hospitalised in the region’s stroke units; it employs advanced computer applications (such as those for verifying application of the Italian SPREAD stroke guidelines, or process mining techniques used to define the optimal care pathway, in terms of the timing and sequence of interventions, within hospitals that receive patients with stroke and have, naturally, a stroke unit). Because of its particular features and innovative character, it was recently compared with other registries in Europe and elsewhere in the world at a workshop hosted, on February 4, 2011, by the Regione Lombardia (regional government) in its prestigious headquarters on the 31st floor of the Pirelli building in Milan.
While the feverish activity on the database for this registry continues, with widespread interest also forthcoming from other Italian regions, another regionally funded project has come to light which, through the collaboration of all the centres in the region that treat stroke, should make it possible to study the genotype of that common but poorly understood cerebral small-vessel disease, of which monogenic variants are known, but that mostly seems to be attributable, as said earlier, to the classic and dynamic interaction between genes (polymorphisms) and the environment. The SVE- LA (Small VEssel and LAcunar) project, like other projects of the Stroke Centre and Emergency Neurology Trust (SCENT) at the C. Mondino Institute, bear witness to the existence of a true vocation which has ancient roots in the research and treatment of cerebrovascular diseases. That said, nothing can be achieved without the contribution of people who, passionate about their work, are, prepared, over the passing days, months and years, to work long hours and, indefatigably, to devote their resources (intelligence, passion, efficiency) to the achievement of excellent results.

Acknowledgements

In addition to the people mentioned in the text, it is appropriate and proper to point out that much of the work described herein could not have been achieved without the contribution of Dr Anna Cavallini, now head of the Mondino Cerebrovascular Diseases and Stroke Unit. Sincere thanks are also due to our collaborators from at the present Department of Emergency Neurology and Emergency Room: Alessandra Persico, Elisa Candido, Maurizia Maurelli, Franca Moschiano, Simona Fanucchi, Alfredo Costa and Isabella Ghione. Dr Anna Bersano has recently begun a close collaboration with the institute in the field of genetics, and it is she who is to be thanked for designing the institute’s projects on the genetics of cerebrovascular diseases. To her go our best wishes for a bright and well deserved future as a researcher in this field. We hope that her collaboration will contribute to the institute’s ongoing success and affirmation in this difficult, but stimulating, field. Finally, particularly warm thanks go to all those individuals — nurses (particularly those who, like Federica Negri, Serafino D’Amico, Veronica Tosca, Adriana Negro, Flavia Bocchino, and Monica Bianchi, among others, have generously and enthusiastically worked in the Stroke Unit since 1996), nurse coordinators (Emanuela Sacchi, Fiorenza Montini), physiotherapists, and nurse’s manager Claudia Fiore, — who, over the years, have worked in the care of our stroke unit patients, helping, with patience and courage, to change the approach to and organisation of cerebrovascular patient care.

Essential bibliography

1. O. Rossi. L’arteriosclerosi dei centri cerebrali e spinali. Pavia; Tipografia e Leg. Cooperativa 1906