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Decizie de indexare a faptei de plagiat la poziţia 00341 / 07.11.2016 şi pentru admitere la publicare în volum tipărit

care se bazează pe:

A. **Nota de constatare şi confirmare a indiciilor de plagiat** prin fişa suspiciunii inclusă în decizie.

Fişa suspiciunii de plagiat / Sheet of plagiarism's suspicion	
Opera suspicionată (OS)	**Opera autentică (OA)**
Suspicious work	**Authentic work**
OS	DĂNĂILĂ Leon.The cordocyte. *Proc.Rom.Acad. Series B*. **16**(2). 2014. p.83-102.
OA	PAIS Viorel, DĂNĂILĂ, Leon and PAIS Emil.Cordocytes-stem cells cooperation in the human brain with emphasis on pivotal role of cordocytes in perivascular areas of broken and thrombosed vessels.*Ultrastructural Pathology*. **37**(6). 2013. p.425-432.
Incidenţa minimă a suspiciunii / Minimum incidence of suspicion	
p.83:04 abstract - p.83:07 abstract	p.425:01 abstract - p.425: 04 abstract
p.83:11 abstract - p.83:14 abstract	p.425:09 abstract - p.425:13 abstract
p.85:07s – p.85:09s; p.83:04 - p.83:05 abstract	p.425:01 abstract
p.93:14s - p.93:54s	p.426:35s - p.426:48s; p.426:53s - p.426:07d; p.426:10d - p.426:11d; p.426:12d - p.426:21d
p.93:01d - p.93:54d	p.426:21d - p.427:01d
p.94:00s - p.94:46s	p.427:03d - p.428:06s; p.429:02s - p.429: 08s
p.94:53s - p.94:16s	p.428:06s-p.428:10s; p.428:14s -p.428:29s
p.94:17d - p.94:43d	p.428:05d-p.429:02s; p.428:30s - p.428:33s p.431:44s - p.431:00d; p.431:26d -p.431:28d; p.431:36d - p.431:39d
p.95:04d - p.95:15d	p.425:10s-02d
p.96:Fig.10b	p.427:Fig.2
p.97:Fig.12	p.427:Fig.3
p.97:Fig.13	p.428:Fig.4
p.98:Fig.15	p.428:Fig.6
Fişa întocmită pentru includerea suspiciunii în Indexul Operelor Plagiate în România de la Sheet drawn up for including the suspicion in the Index of Plagiarized Works in Romania at www.plagiate.ro	

Notă: Prin „p.72:00" se înţelege paragraful care se termină la finele pag.72. Notaţia „p.00:00" semnifică până la ultima pagină a capitolului curent, în întregime de la punctul iniţial al preluării.

Note: By „p.72:00" one understands the text ending with the end of the page 72. By „p.00:00" one understands the taking over from the initial point till the last page of the current chapter, entirely.

B. **Fişa de argumentare a calificării** de plagiat alăturată, fişă care la rândul său este parte a deciziei.

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Fişa de argumentare a calificării

Nr. crt.	Descrierea situaţiei care este încadrată drept plagiat	Se confirmă
1.	Preluarea identică a unor pasaje (piese de creaţie de tip text) dintr-o operă autentică publicată, fără precizarea întinderii şi menţionarea provenienţei şi însuşirea acestora într-o lucrare ulterioară celei autentice.	✓
2.	Preluarea a unor pasaje (piese de creaţie de tip text) dintr-o operă autentică publicată, care sunt rezumate ale unor opere anterioare operei autentice, fără precizarea întinderii şi menţionarea provenienţei şi însuşirea acestora într-o lucrare ulterioară celei autentice.	
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5.	Republicarea unei opere anterioare publicate, prin includerea unui nou autor sau de noi autori fără contribuţie explicită în lista de autori	
6.	Republicarea unei opere anterioare publicate, prin excluderea unui autor sau a unor autori din lista iniţială de autori.	
7.	Preluarea identică de pasaje (piese de creaţie) dintr-o operă autentică publicată, fără precizarea întinderii şi menţionarea provenienţei, fără nici o intervenţie personală care să justifice exemplificarea sau critica prin aportul creator al autorului care preia şi însuşirea acestora într-o lucrare ulterioară celei autentice.	✓
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10.	Preluarea identică a unor fragmente de demonstraţie sau de deducere a unor relaţii matematice care nu se justifică în regăsirea unei relaţii matematice finale necesare aplicării efective dintr-o operă autentică publicată, fără menţionarea provenienţei, fără nici o intervenţie care să justifice exemplificarea sau critica prin aportul creator al autorului care preia şi însuşirea acestora într-o lucrare ulterioară celei autentice.	
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12.	Preluarea identică de pasaje (piese de creaţie de tip text) ale unui cuvânt înainte sau ale unei prefeţe care se referă la două opere, diferite, publicate în două momente diferite de timp.	

Notă:

a) Prin „provenienţă" se înţelege informaţia din care se pot identifica cel puţin numele autorului / autorilor, titlul operei, anul apariţiei.

b) Plagiatul este definit prin textul legii[1].

> *„ …plagiatul – expunerea într-o operă scrisă sau o comunicare orală, inclusiv în format electronic, a unor texte, idei, demonstraţii, date, ipoteze, teorii, rezultate ori metode ştiinţifice extrase din opere scrise, inclusiv în format electronic, ale altor autori, fără a menţiona acest lucru şi fără a face trimitere la operele originale…".*

Tehnic, plagiatul are la bază conceptul de **piesă de creaţie** care[2]:

> *„…este un element de comunicare prezentat în formă scrisă, ca text, imagine sau combinat, care posedă un subiect, o organizare sau o construcţie logică şi de argumentare care presupune nişte premise, un raţionament şi o concluzie. Piesa de creaţie presupune în mod necesar o formă de exprimare specifică unei persoane. Piesa de creaţie se poate asocia cu întreaga operă autentică sau cu o parte a acesteia…"*

cu care se poate face identificarea operei plagiate sau suspicionate de plagiat[3]:

> *„…O operă de creaţie se găseşte în poziţia de operă plagiată sau operă suspicionată de plagiat în raport cu o altă operă considerată autentică dacă:*
> *i) Cele două opere tratează acelaşi subiect sau subiecte înrudite.*
> *ii) Opera autentică a fost făcută publică anterior operei suspicionate.*
> *iii) Cele două opere conţin piese de creaţie identificabile comune care posedă, fiecare în parte, un subiect şi o formă de prezentare bine definită.*
> *iv) Pentru piesele de creaţie comune, adică prezente în opera autentică şi în opera suspicionată, nu există o menţionare explicită a provenienţei. Menţionarea provenienţei se face printr-o citare care permite identificarea piesei de creaţie preluate din opera autentică.*
> *v) Simpla menţionare a titlului unei opere autentice într-un capitol de bibliografie sau similar acestuia fără delimitarea întinderii preluării nu este de natură să evite punerea în discuţie a suspiciunii de plagiat.*
> *vi) Piesele de creaţie preluate din opera autentică se utilizează la construcţii realizate prin juxtapunere fără ca acestea să fie tratate de autorul operei suspicionate prin poziţia sa explicită.*
> *vii) In opera suspicionată se identifică un fir sau mai multe fire logice de argumentare şi tratare care leagă aceleaşi premise cu aceleaşi concluzii ca în opera autentică…"*

[1] Legea nr. 206/2004 privind buna conduită în cercetarea ştiinţifică, dezvoltarea tehnologică şi inovare, publicată în Monitorul Oficial al României, Partea I, nr. 505 din 4 iunie 2004
[2] ISOC, D. *Ghid de acţiune împotriva plagiatului: bună-conduită, prevenire, combatere*. Cluj-Napoca: Ecou Transilvan, 2012.
[3] ISOC, D. *Prevenitor de plagiat*. Cluj-Napoca: Ecou Transilvan, 2014.

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MEDICINE
Research article

THE CORDOCYTE

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My research work, which led us to discover this cerebral cell (Cordocyte) has started in the 2000 years, when I have highlighted it for the first time, during a study upon clarification of some undiscovered aspects of cerebral atherosclerosis. In 2005, I have initiated the publishing our results in two atlases and at Cape Town congress in 2006. This work is based on data analysis by light and transmission electron microscopy of the surgical cases operated by me in the last 13 years. We examined cortical arteries and veins, perivascular areas with old hematic masses, vasculogenetic foci, broken large vessels, moyamoya disease, thromboses, tumors and cerebrovascular malformations, to identify and characterize different phenotypes belonging to a new interstitial cell recently described ultrastructurally in the brain and here, named cordocyte. Also, we attempted to identify and characterize precursor/stem cells for cordocytic lineage in the perivascular areas, within perivascular nerves, choroid plexus and pia mater (now considered a cordocytic-vascular tissue). This cytohistopathological study illustrates and explains some facets of cordocytes-stem cells cooperation around on the fundamental role of cordocytes in response to vascular injuries.

Key words: human brain, vessels, cordocytes, stem cells ultrastructure.

INTRODUCTION

History

My research is based on the well-known fact according to which, the brain is devoid of lymphatic tissue and lymphatic circulation.

Considering this phenomenon, I asked myself if it is possible that its functions are taken over by other elements of the central nervous system (CNS) which had not been known until today.

As a neurosurgeon, I had studied day by day, with great patience and attention, with the help of the optical microscope and of the electron microscopy, all the expansive processes and the cerebral biopsies harvested from the patients I had operated on.

In this way, beginning with 2000, I had observed the existence within the brain of a thin and elongated interstitial cell with a protective and defensive role against the various internal and external aggressions, of the most noble and most complex structure in the universe – the brain (Danaila *et al.*, 2000; Danaila *et al.*, 2002 a, b; Danaila *et al.*, 2003 a, b; Danaila *et al.*, 2004 a, b; Danaila and Pais, 2004; Danaila *et al.*, 2005).

The referred to observation, which I had initially considered to be insufficient, did not allow me to make public this new morpho-functional cerebral cytological entity.

It wasn't until the year 2005 when, following the positive rendering evident of the most important morphological (Figure 1) and physiological features, about which I did not have any doubts anymore, I had made public and I had described in two atlases the new cerebral cell I had discovered (Danaila *et al.*, 2005; Danaila and Pais, 2005).

I had postponed the official announcement of my discovery because the analized cell was very thin and thus below the resolution of the optical microscope.

The enormous amount of the material which required analyzing had made me to take on as collaborator the biologist Viorel Pais who, although

We consider it to be a genuine maestro in health and diseases because of its biological potential within the cerebral parenchyma, in the areas surrounding the blood vessels, in the choroid plexuses, in the pia mater, etc.

MATERIAL AND METHODS

This work is based on the data analysis by light scanning and transmission electron microscopy of the surgical cases operated by Danaila during the last 13 years.

The ages of the patients from whom there had been harvesteed the cerebral bioptic material had been between 4 and 90 years old.

The analyzed pathological processes had included thromboses of the carotid system, cerebro-vascular malformations, aneurysms, primary hematomas, Moyamoya disease, perivascular hemorrhages, infarctions, traumatic brain injuries, metastatic brain tumors, tuberculomas, cysts, tumors (tumors of the normal choroid plexus, pineocytomas, germinomas, medulloblastomas, glioblastomas, astrocytomas, schwannomas, meningiomas, hemangiopericytomas, lymphoma craniopharyngioma, hypophyseal tumors, chordomas), abscesses, cysticercosis, hydatidosis, etc.

The normal cerebral cortex and the white matter had been harvested from the patients which had been operated for unbroken cerebral aneurysms (Danaila and Pascu, 2001; Danaila *et al.*, 2002; Danaila *et al.*, 2006; Danaila and Ştefănescu, 2007; Danaila *et al.*, 2008; 2009; 2010 a, b, c; Danaila, 2012; Danaila *et al.*, 2012 a, b, c; Danaila, 2013 a, b, c; Danaila *et al.*, 2013; Danaila and Rădoi, 2013; Danaila and Pascu, 2013).

The samples which had been studied under an optical microscope had been fixed with 2.5% buffered glutaraldehyde and post-fixed with 1% buffered osmium tetroxide, dehydrated in alcohols and embedded in resin epoxy (Epon 812). There had been cut sections with a thickness of 4-6µ using an ultramicrotome which had been then mounted on glass slides, stained with 1% toluidine blue, and examined using optical microscopy. There had also been cut with the ultramicrotome multiple ultrathin sections, with a thickness of 70 nm, which had been then treated with 2% uranyl acetate, as well as with Reynolds lead citrate solution. The specimens were then examined using the JEM 1200 EX (JEOL) transmission electron microscope.

The electron micrographs had been processed on a computer and then converted into images.

Ultrastructurally, there had been identified, characterized and compared both undifferentiated cells and well-differentiated cordocytes found in different locations, from the outer cerebral cortex to the choroid plexus, and in areas with old hematic masses, vasculogenetic foci, heterotopic neural tissue, encapsulation, broken arteries and abnormal proliferations, such as microtumors.

We had demonstrated the existence of phenotypical changes of the cells, and our findings had especially shed light on the roles of these cells which might facilitate the beneficial actions and delay the pathological processes, they being involved in the fundamental processes of the development of the central nervous system.

RESULTS

Several new histopathological features

The protective role of the pia mater cordocytes

The cordocytes, which form the pia mater together with the with blood vessels, are involved postnatally in the normal corticogenesis (which had been demonstrated in the cerebral ectocortex), in the maintenance of the appropriate pericortical microenvironment, in the vasculogenesis, vasomotion and vascular repair / remodeling, in the inhibition of the hematic invasion into the brain parenchyma as physical barriers, especially in the hypertensive human individuals, in the inhibition of the microtumoral growth and of any aberrant cellular migration towards the cerebral cortex, etc. (Figure 2).

Thus, the pia mater is composed of cordocytes. This assembly of cordocytes as the ultimate and active defender of the cerebral cortex and of the cortical vessels is a very dynamic structure, it undergoing numerous phenotypical modulation changes and accompanying various events, both in healthy individuals and during pathological processes, as a barrier within the immune surveillance.

The cordocytes and the blood-brain-barrier (BBB)

The blood-brain-barrier concept is based on the fact according to which the vital dyestuffs introduced into the blood flow do not color the brain.

Therefore, the blood-brain-barrier is the morphofunctional system which selectively regulates the access and the exit of the biological substances and of the cells, in order to control and to preserve the normal microenvironment, the morphology and the physiology of the brain.

To that effect, we had ascertained that not only the close interendothelial junctions have such a role, but the entire wall of the capillaries, of the arteries and of the veins are overprotected on the outside by well defined layers of cordocytes. (Figures 3 and 4).

The cordocytes prevent the access into the brain especially of the red blood cells, whose degradation products have a nocuous effect not only on the cerebral parenchyma, but also on the blood vessels, in which they have a spasmodic effect.

Its consequences, which can sometimes be even fatal, can be found in the patients with subarachnoid hemorrhage.

The cordocytes block the uncontrolled spreading within the brain of the red blood cells

which cross the intercellular junctional complexes which tightly connect the endothelial cells among themselves.

Our microscopic observations had been focused on the periarterial areas.

In this way, we had observed that the extravasated red blood cells are detained by the cordocytes either through adhesion or through catching. Finally, the red blood cells which had been loaded on the cordocytes are hemolyzed.

Whenever the protective cordocytic network is overwhelmed by the large quantity of red blood cells, or when these die, there are generated self-signals which concentrates numerous perivascular stem cells in the injured area (Figure 5).

In such situations, in the respective area there can be found unidentified cells, transitional forms and well defined cells.

Generally, most of our body is constantly renewed. The adult neurogenesis is the production of new functional neurons in the adult brain (Figure 6, adapted from Altman and Dass, 1965).

The cordocyte and its antitumoral role

The defensive means of the human body against cancers are equally numerous as their causes.

Therefore, during his or her lifetime, an individual can suffer and can be cured of cancer several times.

Actually, the human body can sometimes survive even the most terrible diseases.

Among the multiple defensive possibilities of the brain against the abnormally proliferating cells we can also find the cordocyte.

In such circumstances, every single cell which usually surrounds an artery can be activated, and they will position themselves in front of the abnormal cellular mass, with the nuclear long axis perpendicular to the advancing cell mass (Figure 7).

This peculiar inhibitory role of the abnormal cell proliferations is demonstrated by this cell type in the genuine tumoral cases, when large perivascular formations are closely surrounded by cordocytes, which inhibit and delay both the cell growth and their movement (Figure 8). This property to impede / delay both the cell growth and any motion is easily observable in the cases with arteriovenous malformations, where the cordocytes seem to have an efficient role in controlling the development of the neural tissue, closely surrounding all the neuroepithelial cells, and extending their filopodia towards the target cells. Moreover, overlapping cordocytes form a thick barrier between the neuroepithelial and the lymphocytic population, with the lymphocytes being separated from the neural cells (Figure 9).

In the analysis performed by Pais, Danaila and Pais (2013) there had been observed certain important aspects which we shall present as follows.

Thus, we had ascertained the interesting fact that the tumor formation is often surrounded by a thin basement membrane consisting of fibrils. The referred to thin fibrils surround each one of the tumoral cells, but not the immune cells infiltrated within the tumor mass.

The presence of the long and thin protrusions of the cordocytes around the microtumor suggests their role of antitumoral barrier.

Nevertheless, this barrier is missing here and there, while in other areas, where it is degenerated, there are found numerous peripheral thin connective fibrils.

In the zone surrounding the microtumoral mass, with areas of autophagy, the white matter is degenerated, the axons are caricatured, the oligodendrocytes are in an apoptotic phase, while the microglial cells are loaded with autophagosomes, secondary lysosomes and vascular cytoplasmic areas.

At the analysis of the transmission electron microscopy images of another tumoral node located within the white matter, in a female patient with a traumatic brain injury, we had observed an increased density of cells which appeared to be derived from the perivascular cells and the modified endothelial cells of the staghorn-shaped vessels.

These proliferated polygonal cells which surround the endothelial cells in the so-called staghorn pattern are characteristic for a hemangiopericytoma, which can metamorphose later into a true intraparenchymal tumor.

The traumatic injury could have been an etiological factor for the tumor.

In conclusion, in some tumors, the cause can be represented by the traumatic brain injury.

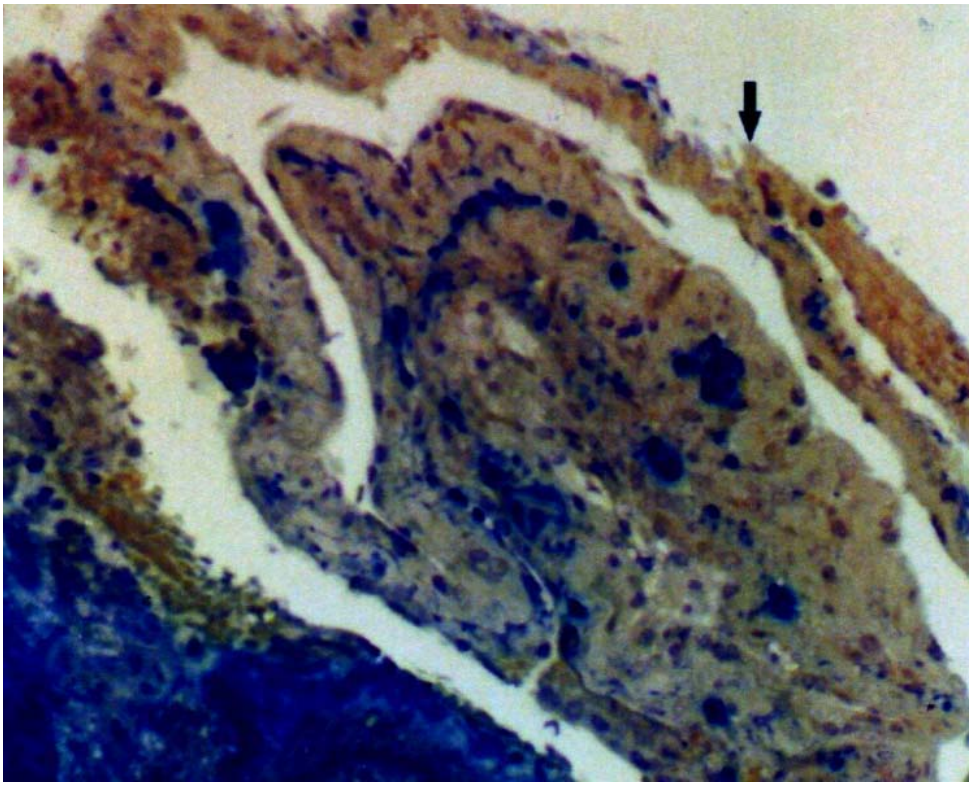

Figure 8. A solid and contorted cellular cord surrounded by cordocytes which impede the cell migration and proliferation in a case with a cerebral metastasis of a carcinoma. The arrow indicates a cordocyte firmly attached to the abnormal cells. (*OM ×200*).

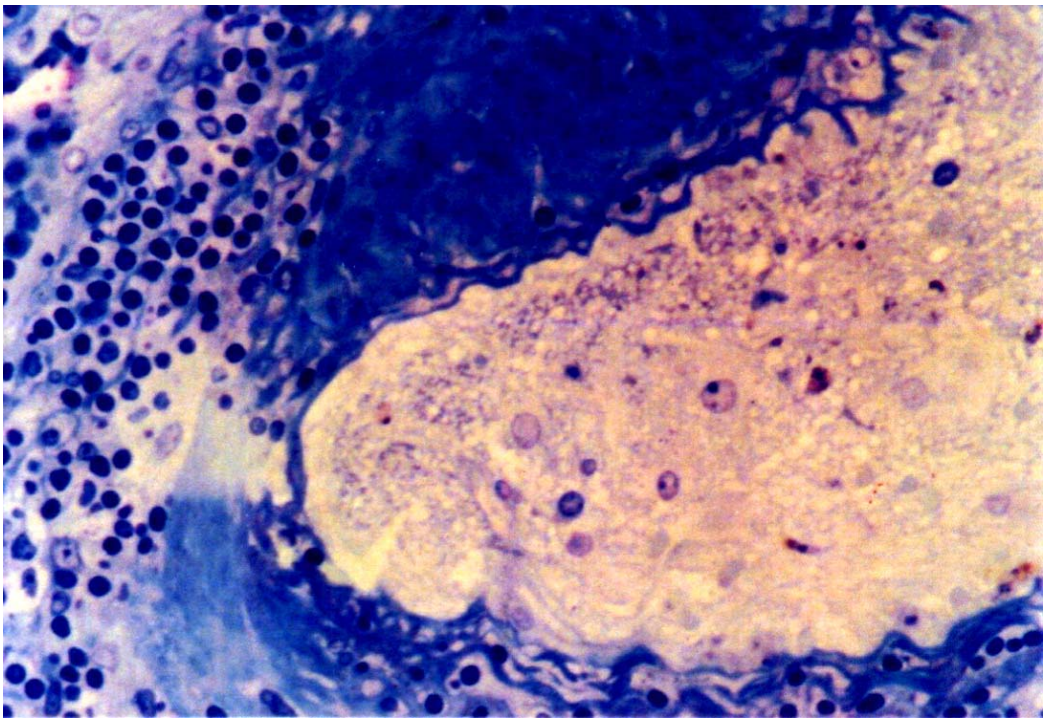

Figure 9. Neural tissue surrounded by a dense lymphocytic infiltrate, in a case with an arteriovenous malformation. All the lymphocytes seem to be separated from the neural tissue through this thick barrier formed by cordocytes. (*OM ×400*).

The repair and the regeneration of the cerebral blood vessels with the help of the stem cells, of the undifferentiated cells and of the mature or well-differentiated cordocytes

Following the study of the biopsies we had harvested from the patients with high blood pressure, from those with arteriovenous malformations (AVM) or venous malformations, as well as from those with arterial thromboses, we had ascertained the presence of the ruptures (Figure 10) and of the defects of the vascular wall (Figure 11) and the existence of the cytogenetic (vasculogenetic) foci.

In the cases of perivascular hemorrhages, the mature cordocytes surrounding the arteries and the veins have most of the times spatial and temporal relations with the undifferentiated cells and with the mesenchymal stem cells.

The cordocytes not only make a supportive interstitial network for the stem cells, but they act as regulators and modulators for the different cellular types in all the stages of the processes, they being particularly sensitive to any local damage.

In this kind of situations, some of the cordocytes remain in the proximity of the adventitial layer, while others move to the perivascular space, where they have close relationships with the isolated undifferentiated cells and with the mesenchymal stem cells from which emerge new cordocytes (cytogenetic foci) in order to clean the perivascular spaces.

Al the small cytogenetic foci contain both progenitors of the vascular cell lineage and precursor cells for the cordocytic lineage. On the other hand, all the cytogenetic foci with only several precursor / stem cells are already surrounded by one or two well-differentiated cordocyte layers, fact which suggests their important morphological roles in the early events of the vascular morphogenesis.

In this way, the well-differentiated cordocytes gradually eliminate the red blood cells from the future vasculogenetic foci.

However, in some arteriovenous malformations, multilayered cordocytes surround the proliferating precursor / stem cells, whereas the hematic mass is surrounded by a single layer of well-differentiated cells, due to the different cytokinetic mechanisms which are present in the different cell types.

Normally, the long and thin cordocyte prolongations which surround the nascent vessels suggest a controlling role of the proliferation, migration and differentiation processes.

The cordocytes gradually orchestrate all the cellular events in the vasculogenetic sequence, because they are in direct contact with the stem cells and with the different progenitors, and surround each cytogenetic focus, indifferent of its age, until the formation of the mature vessel.

All cellular divisions, migrations, and differentiations are in direct relation with the well-differentiated cordocytes which send thin prolongations toward the target cells, or surround the massive formations which contain many differentiating cells originating from the hematopoietic stem cells or from the perivascular mesenchymal stem cells.

When the well-differentiated cordocytes are absent, the precursor / stem cells are spreading in the space and not in the vascular lineages.

In the vascular segments with narrowed lumen or with occlusions, there can be observed at the vascular surface an accumulation of precursor / stem cells in association with cordocytes, or cytogenetic foci where only the cordocytes are present. Thus, these cytogenetic foci are positioned in the immediate vicinity of the disrupted vascular walls.

These are prompt reactions of the protective cells which are located around the vessels (Figure 12).

In the transmural erythrodiapedesis, sometimes the tunica adventitia is thickened and contains numerous precursor / stem cells, but not differentiated cells, cordocytic phenotypes, or vascular lineage.

The remodeling begins with the mobilization of the stem cells, followed by the proliferation and the migration toward the place of rupture of the differentiating cells of cordocytic lineage, and finally ends with the new cordocytic coverage of the vascular surface.

These spatial and temporal modification mechanisms are regulated by the cellular dynamics and morphology.

Responsible for such mechanisms are the well-differentiated cordocytes, because they come in direct contact with the stem cells through their long and thin prolongations.

Moreover, other well-differentiated cordocytes come to the damaged place, fact which suggests precise and specific signaling pathways.

Finally, when the arterial rupture is resolved through the cell cooperation, which also includes the smooth muscle cell activity within the tunica media, a new layer of cordocytes and other elements and cells covers the vascular surface (Figure 12).

However, cordocytes playing a key role are observed in some cases with arteriovenous malformations in which the tunica media is lacking in some of the vascular segments.

In this areas, well-differentiated cordocytes gather stem cells which become adherent to the cell membranes in the damaged area (Figure 12).

In the veins, there are found stem cells which are clustered together through long prolongations and short filopodia of the local cordocytes at the level of the damaged vascular wall (Figure 13).

Additionally, other mature cordocytes, reinforced by collagen fibers they produce themselves, are directed toward a crossing cell column which prevents the venous wall to collapse due to the focal degeneration.

In the patients with thromboses, there is also present a perivascular reaction of the cordocytic lineage, with polymorph nuclei, in conjunction with mature cordocytes.

Now there can be identified stem cells in symmetrical divisions in small cytogenetic foci, as well as undifferentiated or morphologically transitional cells and mature or well-differentiated cordocytes, with their characteristic ovoid nucleus and prominent and marginal nucleolus.

However, these protective cells occupy a peripheral position, at the vascular surface, surrounding the different cellular foci, in direct contact with the fibroblasts and the macrophages in the perivascular areas with new arterioles and numerous foam cells.

A thrombosed branch originating in the middle cerebral artery had showed the involvement of the cordocytes, both during the early vasculogenetic events and in the maturing vessels.

Matured and interconnected cordocytes surrounded the totally thrombosed main artery, and there could be seen both the incipient cytogenetic focus (Figure 14) and the collateral vessels in formation.

The cordocytes are always distributed to the peripheral zones of the cytogenetic / vasculogenetic foci to support the cellular actions and to protect the delicate cellular building, they producing themselves an amount of collagenic extracellular matrix as supporting connective material.

The referred to vasculogenetic process attracts from the beginning other cordocytes which position themselves at the periphery, so that in the end, at the exterior of the mature vessels there is sometimes an excess of cordocytes showing apoptosis processes (Danaila *et al.*, 2002).

At another level, a thick cell column emerges from the other adventitial layer including cordocytes and a few stem cells.

In the core of nascent vessels it is visible a segregation of the differentiating cells, some of them becoming endothelial cells, while others evolve into smooth muscle cells. The surplus cells, either endothelial or smooth muscle cells, may undergo apoptosis or autoschisis processes which are identified using the electron microscopy.

However, the continuous involvement of the cordocytes is evident in all the stages of vascular morphogenesis. Whenever a vasculogenetic focus increases in size, it is surrounded by interconnected mature cordocytes which keep inside all the cells (both undifferentiated and differentiated, i.e., stem cells, progenitors of endothelial cells, smooth muscle cells and fibroblasts) which participate in histoarchitecture of the vascular wall.

Our electron microscopy observations demonstrate a very close rapport between the perivascular cordocytes and the stem cells in the early phase of collateral vasculogenesis, when the cordocytes surround from the beginning until the end all the proliferating and differentiating cells during their maturation process towards endothelial cells, smooth muscle cells, fibroblasts and well-differentiated cordocytes.

Therefore, it is clear that the cordocyte act as a guide and as a protective cell for a cytogenetic / vasculogenetic focus, despite the reduced number of stem cells within the vascular niche (Figure 15).

The principles which control the embryonic stem cells, the proliferation versus differentiation, the paracrine mechanisms, as well as the identification of the different messenger molecules they secret themselves, remain to be comprehensively established.

According to Belting and Wittrup (2008), the novel pathways for the cell to cell communication involve nanotubes, exosomes, apoptotic bodies, and nucleic acid-binding peptides.

In conclusion, the perivascular cordocytes cooperate closely with the stem cells in the vascular repair and in de novo vessel formation through cell proliferation and cellular differentiation.

The cordocytes as anti-hematic barrier

In the cases with recent hemorrhagic foci, we had ascertained in their periphery the presence of a long and thin cordocyte with the role of anti-hematic barrier (Figure 16 a, b).

The lysed cells from the hematic mass probably generate chemoattracting agents for the referred to delimitating and neuroprotective cordocytes.

The neuroprotective action is demonstrated by the fact that there cannot be found any red blood cells beyond the cordocytes.

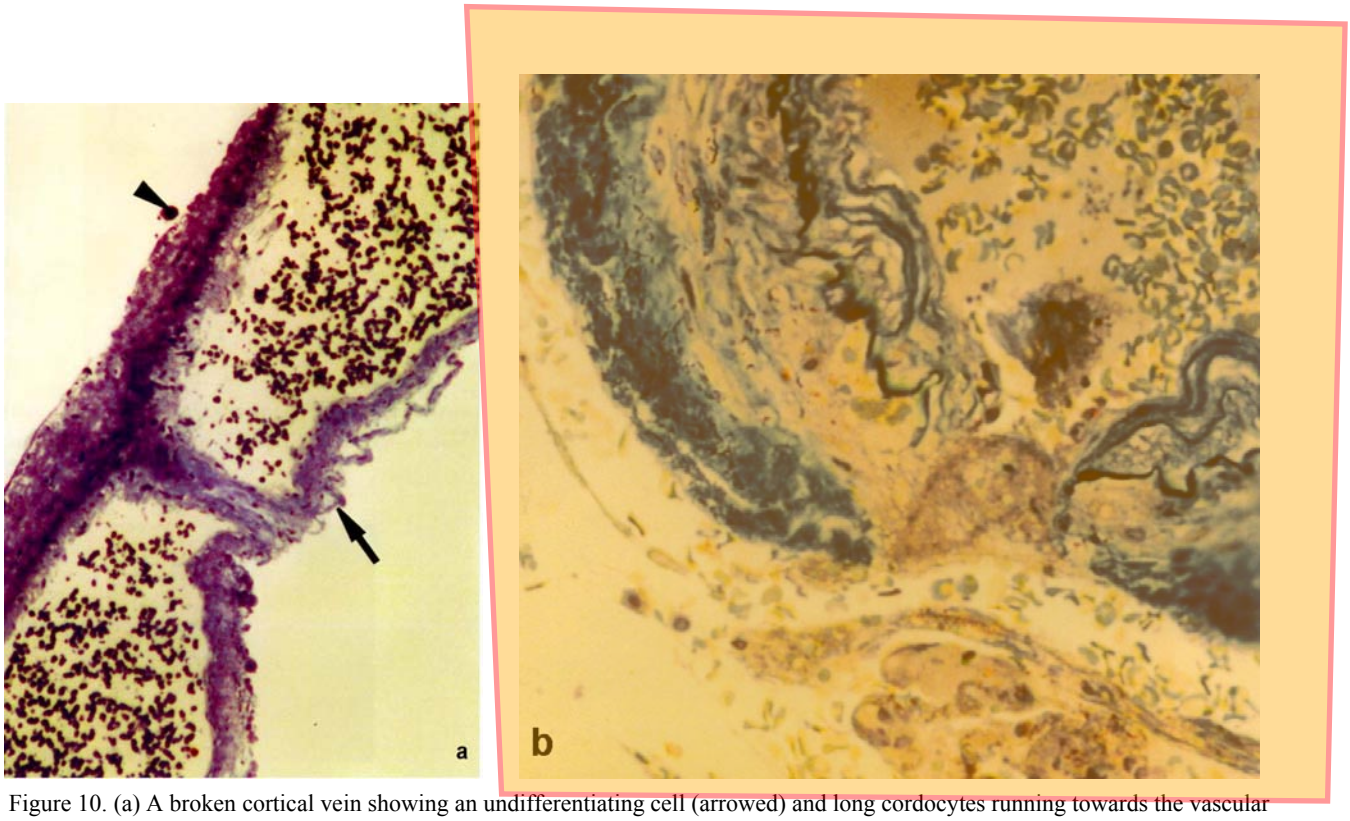

Figure 10. (a) A broken cortical vein showing an undifferentiating cell (arrowed) and long cordocytes running towards the vascular wall. (b) A broken cortical artery showing the mobilization of the precursor / stem cells and of the well-differentiated cordocytes in front of a vascular rupture, while other mature cordocytes retain the isolated red blood cells (*OM ×400*).

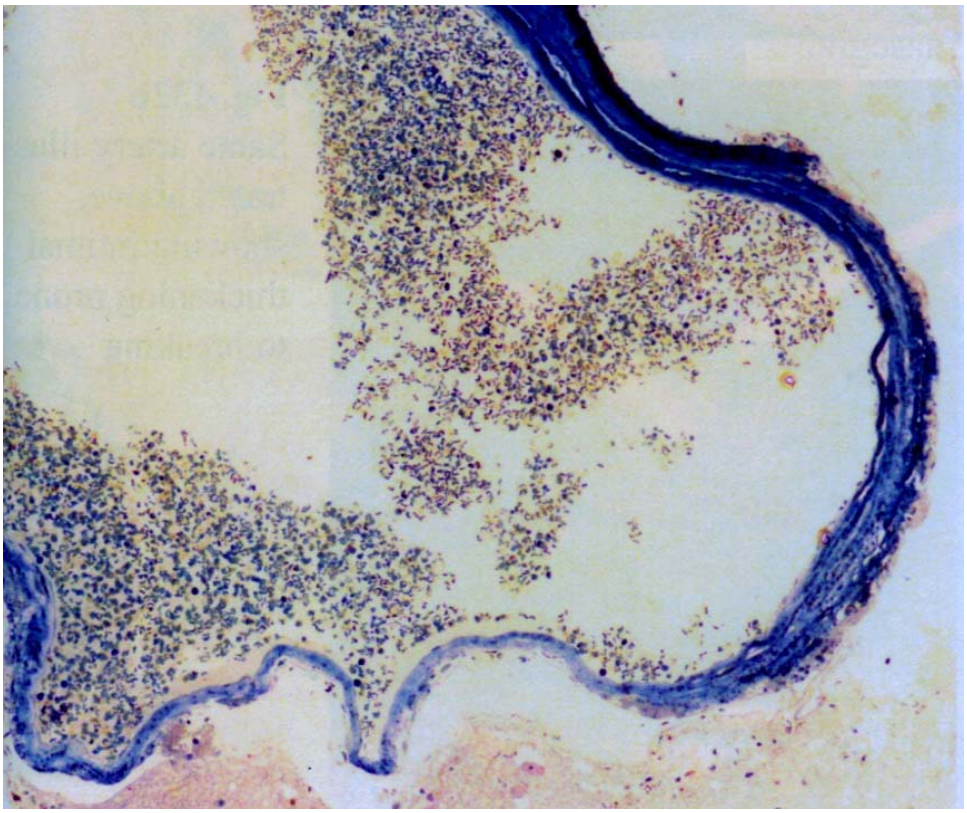

Figure 11. A vascular wall defect with a fibrous thinned wall surrounded by cordocytes and by gliotic parenchyma.

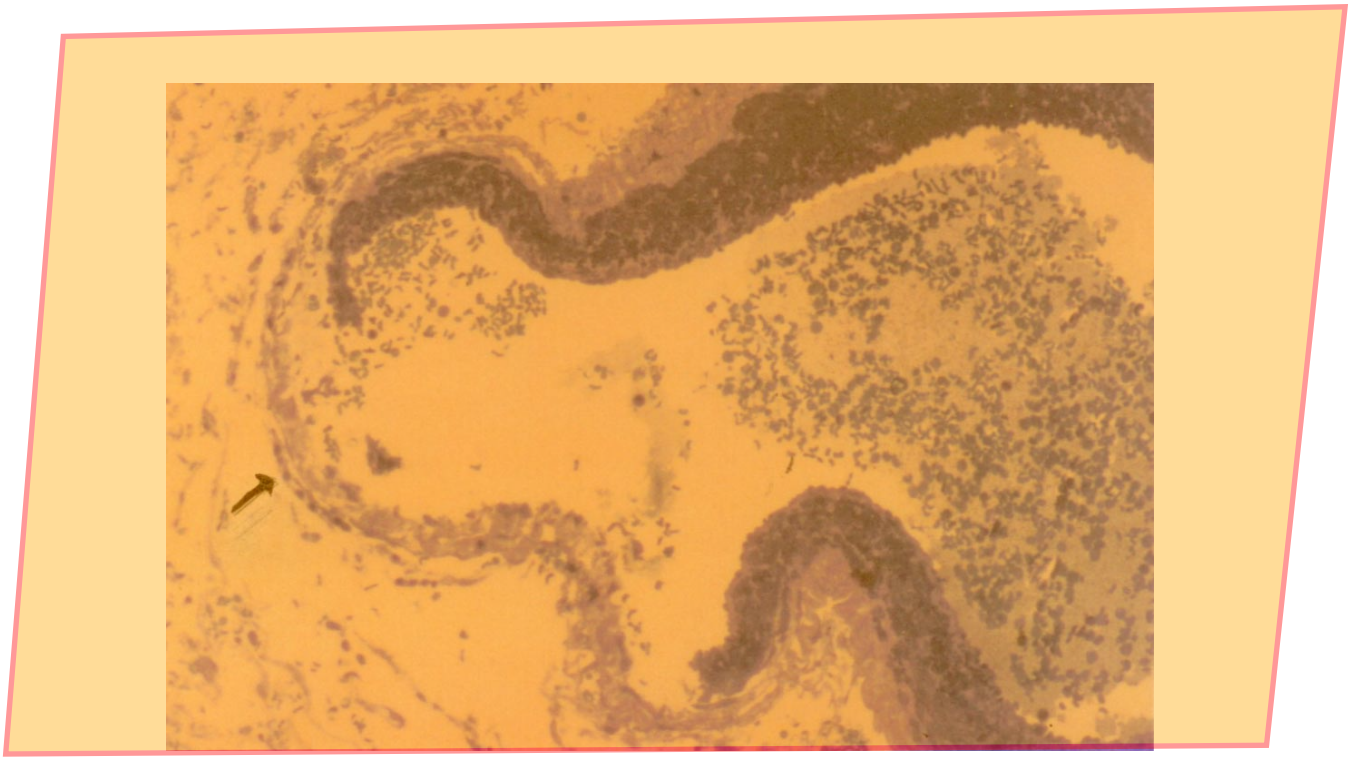

Figure 12. A poorly structured venous wall in which the tunica media is lacking. Here we can see a thick band containing collagen, stem cells, mature cordocytes, which had surrounded numerous stem cells (*OM ×200*).

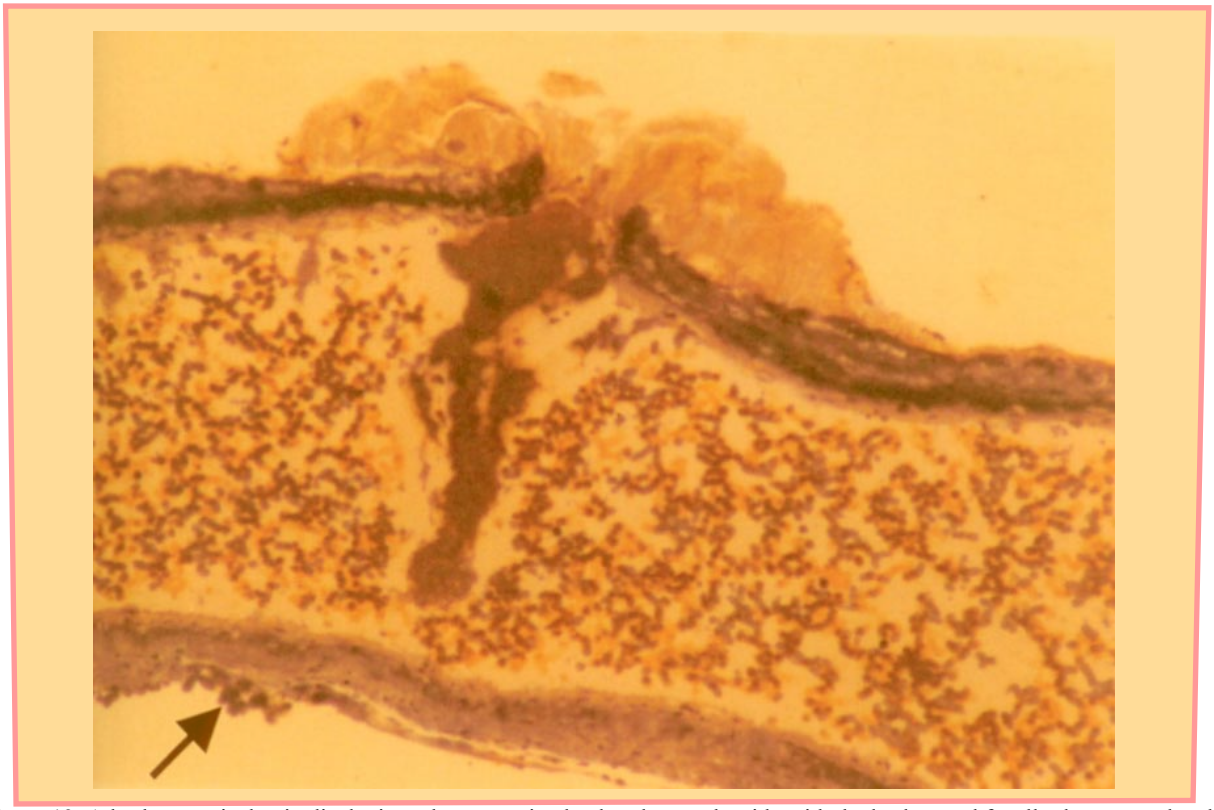

Figure 13. A broken cortical vein displaying a haemostatic platelet plug on the side with the broken and focally degenerated wall. On the opposite side, we can see the proliferation of numerous stem cells in close contact with mature cordocytes (arrow) (*OM ×200*).

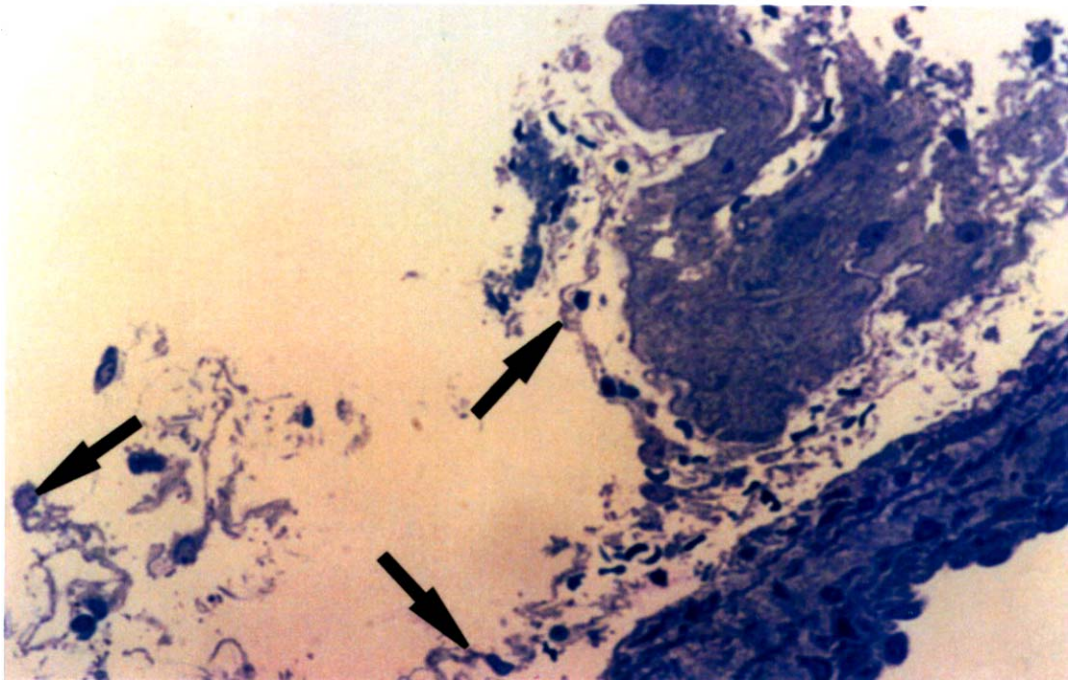

Figure 14. Numerous cordocytes surrounding a cytogenetic focus near the vascular wall (arrows).

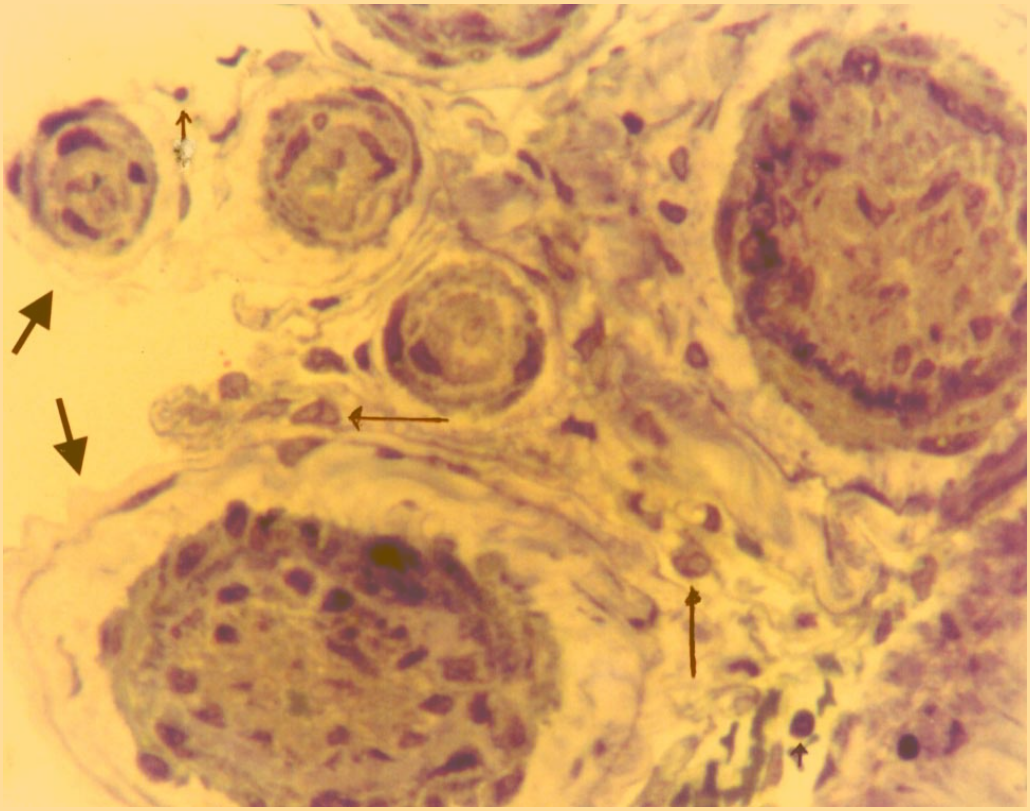

Figure 15. This image shows collateral neoformation vessels (intermediate arrows), stem cells in relation with cordocytes (short arrows), cells in divisions (very long arrows), and a double layer of mature cordocytes disposed around the new vessels (*OM ×400*).

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