Neuraxial healing

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The 2007 multinational medical Nobel to Capecchi, Evans and Smithies ‘for their discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells’ has set agog the promise-mills of medicalese and journalese (Outlook - cover story: Miracle cure) into envisaging an utopia, neo-neurocytogenesis for neuraxial healing not excluded. An epistemologic survey of the current scene may tell us what knockout / knockin stemocytologic technology can do and what it can’t, vis-à-vis neuraxial healing.

The term neuraxis/neuraxial has been chosen with an attempt at eusemantics. Brain-n-spinal-cord, as a phrase, sounds dichotomously too long. The central nervous system (CNS) has the problem of the CNS not being exactly central, being dorso-central, located just beneath the skin for having been derived therefrom. No one can say where the spinal cord ends and the brain begins or vice versa. Elementary embryology tells us that the so-called brain is an expanded neural tube and the so-called spinal cord is the unexpanded version thereof. The term neuraxis - from the lamina-terminalis rostrally to the filum terminale caudally - evocatively encompasses the brain and the cord, without allowing any dichotomy between them. The Dorland’s dictionary, like others, defines neuraxis as the CNS, as also the axon of a nerve cell (!). So much for the semantic lethargy lexicons ail from.

A panoramic dorsal view of the neuraxis shows it to be a gigantic arthropod, that has 40 limbs on either side (12+8+12+5+3) called nerves, 24 of them being cephalopods or head-limbs or the so-called cranial nerves. The body-n-tail limbs are the so-called spinal nerves. The thalidomide-tragedy drove home a point that the so-called limbs/extremities of the human body are mere extensions of the trunk. Likewise, all the nerves are mere, uninterrupted, extremities of the neuraxis, representing its lateral spread. The entire neuraxis, from the tip of the great toe to the frontal lobes, is free from any fiber, for each so-called fiber in the brain and spinal cord as tracts and beyond them as nerves, is part and parcel of the neurone. The entire neuraxis, central and lateral is a huge syncytium, a cytoma, sans any fiber. A single neurone in man or whale may measure six feet or 100 feet in length. Such huge lengths and the highly precise point-to-point connections between any two neurons took away from them the liberty to duplicate assigning them to the class of post-mitotic/perennial/non-duplicating cells as per the classification offered by Leblond and Moorhead (circa 1961). To dream of neuronal-regenesis through stem cell adventurism smacks of Quixotic tilting at the biological windmills.

Neuraxial healing is too involved a process to be viewed lightly. Hence the foregoing preamble.

There are two neoplastic processes that create and sustain life. Embryogenesis is a post-fertilizational neoplastic process wherein very precisely timed new tissue is formed to fashion a Gandhi or Godse, elephant or Einstein. The whole drama is vectorized, each cell knowing where to go and settle or to get lost through programmed apoptosis. The vector or directional element in embryogenetic neoplasm has to be cosmic so as never ever to duplicate any two fingerprints or any two neuraxes.

The other life-sustaining, neoplastic activity is, for want of any better term, called wound healing. Suffice to say that, starting with the work of Le Comte du Nuoy and Carrel over a century ago, all the research on this simplistic process has yielded a cipher. Bullough, of the Postgraduate Medical School, Hammersmith UK, chairing a Listerian symposium on Wound Healing in 1970, summarized the meet on four points:
1. We know nothing about wound healing.
2. Nature has reached the zenith of perfection in wound healing.
3. We can do nothing to accelerate wound healing.
4. Much of what we do decelerates wound healing.

Wound healing, in invertebrates and vertebrates, is the most efficient, highly computerized fill-in-the-void activity that takes care of a shaving scratch to severe injuries, without any supervisory need, save minimalization of whatever the gap. A surgeon’s presiding deity is wound healing that pardons all the forays of the surgical knife, to restore the animal body to as close to status-quo-ante as is divinely possible.
Let us go back to Leblond and Moorhead’s classification of body cells into perennial, expanding and renewing. The perennials are sensory receptors, neurons and muscle cells, the three forming a tandem network. These cells cannot divide normally, cannot divide abnormally and hence cannot cancerate. The expanding cell population comprises blood vessels and fibroblasts, as also parenchymal cells. The expanding cell activity is an on-demand source that goes into action wherever there is a void. Hence the classical regeneration of liver and the routine wound healing at all sites through fibroblasts, their collagenous output, all backed by newly formed blood vessels. The moment the void is bridged, the process goes into a withdrawal to the point of disappearance. An occasional overshoot occurs to form a keloid that as of now remains a mystery. The reparative proliferation through expanding population has barely any vector control save bridging in a gap or restoring the mere cell number of the functioning parenchyma. The renewing cell population comprises the epithelial (skin and mucosa) cells and the hemopoietic marrow cells, both of which ceaselessly divide from womb to tomb. Just as a sample, one may note that the marrow adds 500 million red cells every second; the gut spawns and jettisons a cell numbering equal to that making up the entire body in mere 22 days; the epidermal cover of the skin is renewed every 36 days. The only vector principle the foregoing follow is to provide an epidermal or mucosal integrity that crowns all wound healing.

The word healing is from Greek-holos= complete and is etymologically on par with its sister terms health, whole, holistic (the oft-repeated phrase Holistic healing like Modern medicine, is a fable). The vectorless wound healing in the most evolved vertebrates rarely reaches the holistic promise and is beset with keloids and unseemly scars in the best of hands. That is why till today, a thyroid incision is often a subcervical and Pfannenstiel’s incision a Retronicker one. Bullough’s claim that nature has reached the zenith of perfection in wound healing has to be tempered by the generalization that nature’s very best isn’t good enough for women featuring on Page 3.

The above account should amplify the fact that vector-free, directionless wound healing can hold very little promise for neuraxial restoration to a semblance of status quo-ante. So neuraxial wound healing is pointless as far as the body of the axis is concerned. Its 40 limbs called nerves have the advantage of epineural covers that allow nerve-suturing and nerve-grafting with a sense of direction whereafter you fold your hands and pray. Seddon’s pioneering work on peripheral nerve injury has had the blessing of vectorization that the neuraxial body, with its 10 neuroglial cells per every neurone cannot hope to have. Peripheral nerve repair and replacement is a golden-lettered triumph of surgery that the neuraxial body can only wonder at.

There is an outstanding immunological reason whereby the neuraxis may by itself or through neuroglia, block any neuronal regeneration. It needs to be underscored that during intrauterine immunologic maturation, the entire neuronal population is shielded from the thymus by way of neuroglial/Schwann cell cover. So, whatever the forbidden clones that may be there in the thymus, against one’s own neuraxis, remain undestroyed, so as to be ready to let loose their terror against one’s own neural tissue. One’s thymus treats the neuraxis as not-self as so that the latter must do it’s best to steer clear of the lymphocytes and its other invading allies. Following a neuraxial wound, accidental or intended, neuronal proteins can leak into the wound, travel to the thymus, excite a forbidden clone and kickstart a tragedy of autoimmune encephalomyelitis (better called neuraxitis), an event not rare following vaccination containing neuronal proteins. So one can be bold enough to suggest here and now, that the first trick that the neuroglia do is to disallow any neuronal regeneration that may spill its proteins into the circulation. This small sacrifice is for the greater good of the rest of the neuraxis.

The above danger is precisely but perversely illustrated by an immunologic disaster, rather thoughtlessly called sympathetic ophthalmitis. Injury to the uveal tract in one eye, involving the dilator pupillae and/or the pigmented layer of the iris, both neuroectodermally derived from the optic diverticulum off the developing diencephalon, sets up an auto-immune response that, a few weeks later, ravages the normal eye, to cause bilateral ophthalmitis and even blindness.

Talking in Burnetian terms, a neurone is a Forbidden clone in any wound healing. Future research may reveal that in any neuraxial wound healing, the first that the glial cells do after an injury, is to block loose neuronal ends from exhibiting any growth. The story is fortunately different in peripheral nerve repair blessed with tissue covers that shield the neuronal elements from any proximity to the flowing bloodstream. Medical science’s hope for neuronal regeneration through implantation of stem cells or even embryonically harvested neurones or neuroectodermal cells, must contend with the above FORBIDDEN phenomenon—a sacrifice that the body actively indulges in for the greater good of the balance neuraxis.

The current bandwagon of neoneuronogenesis through marrow stem cells implant into the neuraxial body must reckon with the complex reality of a package deal that the technique must offer. The deal is constrained by the fact that every neurone is an island, shielded from its fellow by spatially but precisely located astrocytes, oligodendrocytes and what have you, who must offer to the neurone a cellular shield of exact shape and layout. The stemcytologists will have to first figure out which stem cell will go which neuroglial way and another...
turns into a neurone. The whole exercise is akin to squaring a circle.

It is time now to conclude on neuraxial wound healing—anatomically, pathologically and functionally. The vasculature and the glial cells of the neuraxis comprise the expanding population that would expectedly go into action to fill in a void. The fibroblasts in the vascular adventitia could do what they do elsewhere, namely to lay down collagen that would span the gap and then contract to reduce the gap to the barest minimum. Nature is unable to treat neuraxial wound healing any different from abdominal wall, heart or kidney. The dead-bits are removed and replaced by progressively contracting scar. Hence the tell-tale appearance of a brain with multiple senile infarcts, almost reminiscent of a nodularly scarred kidney or a cirrhotic liver.

Nature’s saving grace resides in the neuronal surplus that a human brain enjoys. Given that most of us do not use much of our neuronal capacity and that too mostly on sensex, sex and nonsense, one can generalize that 95% of the human neuronal number goes unutilized throughout life. No wonder Carrell compared the brain to a tumor and Koestler called it ‘The unsolicited Gift’. The functional recovery following neuraxial wound healing can be amazing. Wilder Penfield pioneered extensive ablative neuraxial surgery (hemicerebrectomy, hemispherectomy) to relieve children of their epilepsy, some of whom turned into mathematic wizards. Pasteur, suffered dense-total hemiplegia at 47 and then went on to make some epochal discoveries (e.g., levo/dextro-rotation of light) well into his 70s. Joseph Landau, the mathematician, was in coma for over six months, following a car crash and then returned to research and teaching. All told, neuraxial wound healing is nature at her affectionate best, offering a reparative cuisine within the confines of biological constraints evolved over millions of years. If a la Bullough modern medicine knows nothing about wound healing, then it knows even less than nothing about neuraxial wound healing, as evidenced by the alacrity with which every Tom, Dick and Harry are jumping onto the Stem Cell Bandwagon.

It is a widely concealed fact that medical science, in its most sophisticated state, is ailing from what can be called Basic Binary blindness. A human body comprises two basic elements-a sort of binary code of 0 and 1, the former representing a cell and the latter a fiber, the two together comprising the science of cytofibernetics. In the 1960s, Muggleton and Daniell swapped nuclei amongst living cells to prove that the nebulous cytoplasm and not the well-formed nucleus is the boss. Ergo, cytology died that day, realizing that it had been ailing from nucleism, an act of searching a coin under a street lamp, although the coin had been lost elsewhere. A recent symposium on Cell led to a generalization that to claim to know a cell, given the complex array of microscopes, tantamounts to repairing a lady’s wrist watch using a sledge hammer. So cytology, like genetics is tottering on a precipice and waiting for a decent burial.

There is no defined fibrology. The fibers that form the second element of cytofibernetics have their own Clock and Codes that refuse to pay any heed to science. The molecules comprising them are too complicated and cosmic as to yield to medical probing.

The day microscopy was born, half a millennium ago, thanks to von Leeuwenhoeck, we all cried ‘Eureka’ for what started as a roughly ground glass piece and culminated as the Electron Microscope in its elitist form, managed to MAGNIFY everything including our IGNORANCE. Albert Szent-Gyorgyi, the Nobel laureate, chairing a CIBA symposium on (note the title) Submolecular Biology of Cancer was asked a concluding question as to if he could define a cancer cell, to which he humbly replied- ‘I cannot say what is a cancer cell, for I don’t know what is a normal cell’. The stemocytists, ignorant of what is stem and what is cell, are, world over polyannastically promising a cure of this and that through their stem-cell marvel. Modern medicine, having failed to swallow a gnat, is promising to swallow a camel. Neuraxial Healing is too involved a process - allowing you to wonder at it like a child and then urging you to just stop there.