THERAPEUTICS

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NOCICEPTIVE PAIN *VS* NEUROPATHIC PAIN

– A NEW CLASSIFICATION FOR PAIN CONTROL

SUMMARY

Physiological Regulating Medicine (PRM) is the latest integration between Conventional Medicine and Homeopathic Medicine. PRM integrates classic Homeopathy with an innovative therapeutic concept - the restoration of physiological conditions through molecules such as hormones, neuropeptides, interleukins and growth factors in the homeopathic dilution corresponding to the same physiological concentration that is found in the biological environment. The method includes the most current knowledge on Homeopathy, Homotoxicology, the Psycho-Neuro-Endocrine-Immune (PNEI) axis, and nutrition.

Four types of pain can be considered. The physiological type is related to the preservation of life. The nociceptive type presents as pain of an inflammatory origin, in which COX-2 is particularly stimulated by the pro-inflammatory interleukin IL-1ß; this type of pain is therefore modulated by the levels of pro-inflammatory *vs* anti-inflammatory interleukins. Neuropathic pain is the result of damage, compression, or dysfunction of the peripheral nerves, or of the Central Nervous System (CNS); it is a disturbance of the CNS neurotransmitters. The affected neurons generate false informations that are interpreted in the brain as pain. Mixed pain is related to the pain associated with cancer; in this case several factors are involved simultaneously.

- PRM in Pain Control Therapy offers a complete method with excellent therapeutic results, with formulations that can be injected in acupuncture points for the control of inflammation-related pain (nociceptive) as well as neuropathic and mixed pain.

KEY WORDS **PAIN, INFLAMMATION-RELATED PAIN, PHYSIOLOGICAL REGULATING MEDICINE, ACUPUNTURE POINTS, HOMEOPATHY, INTERLEUKINS, PNEI**

Physiological Regulating Medicine (PRM) is the most recent integration between Conventional Medicine and Homeopathic Medicine.
PRM integrates classic Homeopathy and Homotoxicology with a new therapeutic concept - the restoration of physiological conditions through molecules such as hormones, neuropeptides, interleukins and growth factors in the homeopathic preparation and dilution **corresponding to the same physiological concentration that is found in the biological environment.**
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With the phylogenetic development, the **macrophage** is the first cell that is able to produce neurotransmitters, neuropeptides, and hormones, in addition to cytokines; on the other hand, neurons can produce neurotransmitters, neuropeptides, cytokines, and growth factors and express receptors for these molecules (1).

There is also a clear anatomical and functional integration of these systems, which in fact constitute a macrosystem. Psychoneuroendocrine immunology is a new field of investigation characterized by very rapid development and increasing interest among research groups, doctors, and medical schools (Seminar at Loyola University Chicago - Stritch School of Medicine, November 2007; Symposium at University of Miami - Miller School of Medicine, June 2008), since numerous molecular phenomena have been discovered that explain many physiological and pathological states whose mechanisms were unknown (1, 2).
It can therefore be understood that the CNS is connected to the neurotransmitters, neuropeptides, hormones, and of course the cytokines that together form the Psycho-Neuro-Endocrine-Immune (PNEI) axis.

PRM has an innovative framework: it combines the essential experiences of Homeopathic Medicine with those of Allopathic Medicine, integrating elements such as Acupuncture and Mesotherapy (among others) with modern Physiology, thus achieving a superior therapeutic effect.

▶ For this reason, the results of Acupuncture in the treatment of pain can be improved when these aspects are used in combination.

On the other hand, pain and suffering are two sides of the same coin.
When a person is affected by an injury, he/she experiences an unpleasant feeling that is a reflection of individual psychophysical and environmental factors. The duration of the pain is a very important factor in the evaluation of psychophysical effects: acute pain has a rapid onset and is generally associated with defined causes. However, if the pain doesn't comply with the normal or hoped evolution of an acute illness, or the reasonable time period for the healing of an injury, it then becomes

chronic. Chronic pain – on the contrary – causes the patient's physical and psychological destruction and almost always accompanies him/her until death.

Four categories of pain can be identified (3):

1. physiological
2. nociceptive or inflammation-related
3. neuropathic
4. mixed.

PHYSIOLOGICAL PAIN

At the physiological level, pain is acute and it is very important for the preservation of a person's life. While the loss of other sensations (vision, hearing) can be compensated for, insensitivity to pain would expose both men and animals to mortal dangers.

NOCICEPTIVE OR INFLAMMATION-RELATED PAIN

At the nociceptive level, it occurs as peripheral pain that can be somatic or visceral; it is associated with inflammation.

One strategy for pain relief is aimed to the periphery level, at the nociceptors, by using drugs that can inhibit the synthesis of pro-inflammatory and proalgesic prostaglandins. In this respect, non-steroidal anti-inflammatory drugs (NSAIDs) act as the front-line medicines for the control of mild to moderate inflammation-related pain, but the side effects are often particularly strong.
Inflammation is a physiological process in response to a tissue damage.
The cellular injury causes the release of phospholipids (PL) from the cell membrane that are transformed into arachidonic acid (AA) through the action of A2 phospholipases. AA in the presence of the cyclooxygenase enzyme (COX) generates prostaglandins (PGs); these in turn are responsible for vasodilatation, increased blood flow, inflammatory exudates and the sensitization of nerve endings (nociceptors) (FIG. 1), causing the sensation of pain and other signs of inflammation such as heat, redness, and swelling involving a functional limitation. Cytoprotective PGs participate in the protection of the gastrointestinal mucosa by inhibiting acid secretion and increasing the secretion of mucus and bicarbonate, mechanisms responsible for keeping the mucosa intact and preserving the glomerular filtration rate.

In 1971, Vane found the mechanism of action of non-steroidal anti-inflammatory drugs (NSAIDs) **through the inhibition of COX**, whose substrate is AA.
In 1972, Lichtemberger *et* Al. discovered the existence of two isoforms of the COX enzyme (COX1 and COX2) (4, 5).

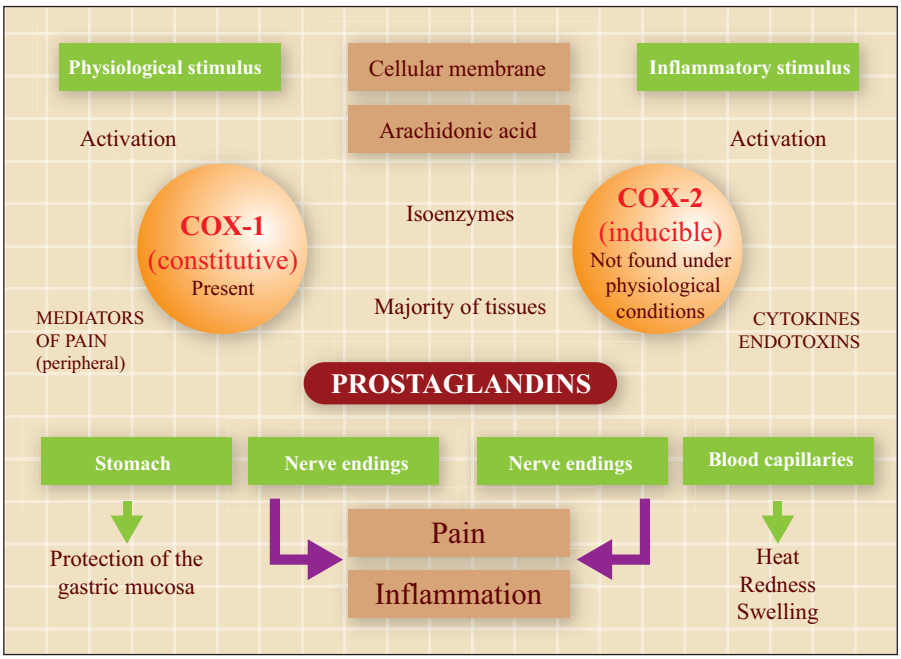

FIG. 1

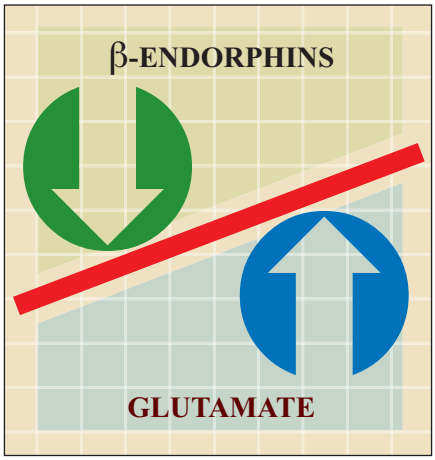

FIG. 2

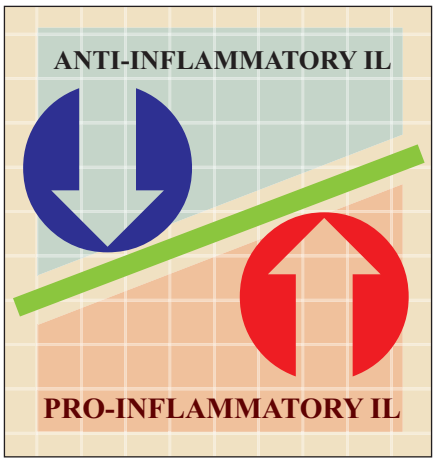

FIG. 3

Most cells in the body contain COX-1 (constitutive) which is expressed in the constituent form; on the other hand, inflamed tissues express COX-2 (inducible) in response to the presence of pro-inflammatory interleukins.
These observations have lead to the hypothesis that COX-2 selective inhibitory NSAIDs can have an anti-inflammatory analgesic effect with fewer side effects and less interference with COX-1. As a consequence, the gastrointestinal tract, kidney, and platelet function show a lower incidence of typical NSAIDs-related injuries, while the inhibition of COX-2 is expressed by a lower production of PGs in inflamed tissues, thus mediating the desired therapeutic effects.
This concept was the starting point for research in selective COX-2 inhibitors (6, 7).

NEUROPATHIC PAIN

Neuropathic pain is an intense, central originated pain, and is the consequence of damage, compression, or dysfunction of the peripheral nerves or of the CNS; it is a disturbance of the neurotransmitters in the CNS. The affected neurons generate false messages that are interpreted as pain in the brain.

It can be caused by:
diabetic neuropathy; infection: herpes zoster injury to the CNS or compression of a peripheral nerve: ischialgia; multiple sclerosis; surgical damage; phantom limb pain.

Treatment is oriented toward the use of *pregabalin*, *gabapentin*, *amitriptyline* and other new drugs, with the aim of modulating pain, especially if associated with diabetic neuropathy and fibromyalgia (10, 11). In these cases, **possible strong side effects** must be taken into account, contrary to the medicines of Physiological Regulating Medicine, in which such a risk does not exist.

Ultimately, the sensation of nociceptive pain is proportional to the intensity of the stimulus, while in neuropathic pain, a small stimulus can provoke a pain of higher intensity.

This type of pain is largely modulated by levels of glutamate, the most excitatory neurotransmitter, and by beta-endorphins with a strong analgesic effect (FIG. 2).

MIXED PAIN

Various factors are included in this group simultaneously; the most indicative example is the pain associated with cancer, which is difficult to control.
The use of analgesics alone or in combination with opiates has been proposed in its treatment (12, 13, 14, 15, 16). In this case, Physiological Regulating Medicine can also be useful; formulations that contain **beta-endorphin**, a potent endogenous analgesic present in *physiological concentrations*, avoid the side effects of other procedures on these patients.

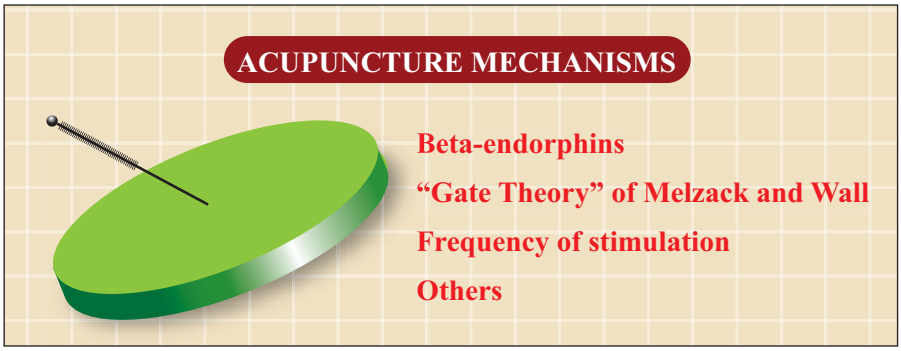

FIG. 4

INNOVATIVE FORMULATIONS FOR PAIN CONTROL

Based on this scientific knowledge, **ten injectable medicines for Pain Control*** have been formulated; they are prepared in a homeopathic form, with the addition of new active ingredients such as the anti-pro-inflammatory interleukins (Anti IL-1α, Anti IL-1ß) (FIG. 3) and beta-endorphin, in **concentrations similar to those found in tissues**.
Of these formulations, nine contain beta-endorphin (all except **GUNA-MUSCLE**) and 8 contain anti-pro-inflammatory interleukins (Anti IL-1α, Anti IL-1ß) (all except **GUNA-MUSCLE** and **GUNA-NEURAL**), so the preparations can modulate nociceptive, neuropathic and mixed pain without undesired effects. By using acupuncture points, a well-known method for its effectiveness in pain relief, different neurophysiological mechanisms are brought into play (17, 18, 19) (FIG. 4).

Finally, if recommendations on acupuncture points are considered in the treatment of pain, and if the best indicated Guna Method formulation is chosen, we are provided with a therapeutic technique that gives excellent results by exploiting different physiological mechanisms for the modulation of pain. The recommendations for treatment consist of **intradermal**, or **subcutaneous injections** of **0.5 ml** into each acupuncture point in the affected area according to the technique of homeopathic mesotherapy (homeosiniatry) with the following advantages: according to personal experience and that of many other colleagues over the last 3 years, it does not have contraindications, does not cause local reactions, does not cause short- or long-term side effects, does not interact with other pharmaceuticals, and in fact optimizes interactions with other PRM or homotoxicologic pharmaceuticals, which can be used in combination (20, 21, 22, 23). For Pain Control, PRM injectable ampoules can be administrated also intra-muscular or orally (indication of the Bystander Reaction).

- It is a personal wish that this article can be useful not only in identifying the origin of pain, but in controlling it with a new, innovative, and very effective method. ■

* Guna-Neck, Guna-Thoracic, Guna-Lumbar, Guna-Shoulder, Guna-Hip, Guna-Handfoot, Guna-Ischial, Guna-Polyarthritis, Guna-Muscle, Guna-Neural, each 2,0 ml (Guna S.p.a. - Milan, Italy).

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