Chronic pain without known cause into the picture

Although a preface often is about the research question and the studied disease this preface is especially about the way in which research started and which research should give an answer to the research questions.
How else can it be understood that a theoretical essay about the menstrual cycle, examining pregnancies and inserting Intra Uterine Devices (IUD) is focused on diagnostic methods in case of chronic pain and possible occurrence of a CRPS (previously called Südeckse dystrophy among others) on spots of chronic pain.

One would suspect otherwise with this summary, yet the research has not been chosen random. It is based on measuring and regulation technical aspects , generating pain, transmission of pain, reaction on pain, pain memory and measuring pain.
There was a search for a common parameter in these processes and for a method to measure and explain this.
There was a search for the parameter in the activity of the autonomous nerve system and its modulating substances, known as "prostaglandins".

Modulation of the autonomous nerve system gives a change in skin temperature. That change can be measured by infrared equipment.

Chronic pain without known substrate (without known cause and without rationalizing deviations) has two ways of appearing:
1. Segmental(usually going with a certain organ and then occurring on the abdominal wall and/or chest wall.
2. Not segmental (mainly occurring on the extremities, arms, legs).

Ad.1: **Segmental pain** is pain going with a certain organ, for instance the characteristic appendicitis pain or cholecystitis (gall bladder) or dysmenorrhea (menstrual pain). That pain is on a certain spot on the belly and can be indicated. Generally this pain is acute so not chronic by definition and not without a substrate.
However, in 1966 a publication appeared by the Dutch gynecologist Kloosterman in which he concluded that chronic abdominal pain in the abdominal wall could be localized without any connection whatsoever with a gynecological problem. This might indicate chronic pain, segmental, without known substrate.
Research by means of infrared detection equipment to this kind of chronic pain could then have something to do with bias by missed diseases in the entrails unless stimulation of the entrails cannot be measured by the equipment.
The still current opinion argues in favor of the latter that a specific division of the autonomous nerve fibers in the abdominal wall is not strictly segmental.
One and the same spot on the skin was to be supplied with nerve fibers from different segments at the same time. A specific reaction from one segment cannot exist as a result of this. The other way around it was not certain whether a by infrared found pain spot could or could not correlate to a specific area in the entrails. That research has not been done previously.
There are also arguments from literature to assume an organ/skin relation indeed. In order to exclude bias first an investigation had to take place whether a correlation can exist between a stimulating situation of an internal organ and the temperature of the skin area specifically belonging to this organ.
Problem: which volunteer wants to have his organs stimulated for the sake of research? The solution was measuring abdominal wall temperature before and after inserting IUD.

If infrared thermography could observe the effects of the insertion then we could speak of a very sensitive measuring system. Then bias can occur in measuring pain because the specificity of the measuring method stays behind the sensitivity. In measuring then too many wrong positive results occur.
For that reason research was set up at two kinds of pregnancies: one with and one without

problems during pregnancy.
Question: are there differences in skin temperature in the specific skin area of the uterus? If so, then infrared thermography measures to physiological level and the problem arises: when can we speak of a deviation in the sense of disease at the found pain spot?

For essential research the choice was made for a describing investigation with intervention. Registration by video thermography of the painful spot followed by intervention and closed by video thermography. The intervention was carried out , double blind and "cross-over" with two types of prostaglandin synthesis inhibitors.
Prostaglandins are and were brought into connection with pain. Both used means were considered pharmacologically equal. Of both means was not known that they could have an influence on the vascular flow and by this on the skin temperature.
On theoretical grounds a difference was assumed in the effective mechanism of these substances in which one was expected to lead to a skin temperature increase and the other to a skin temperature decrease. In the meantime one of both substances became suspicious of having an unwanted serious side effect that by the way rarely occurs. Considering the extent of the usual dose that effect could be a toxic effect as well.
For security reasons intervention was chosen with a dose of 0.2 % of the normal dose of one preparation and 1% of the other preparation.
According to the usual pharmacologically opinions no or hardly any biological effect of the pharmacon may be expected and in no case a difference between both preparations. By this approach the chance was very small that significant improvement of the pain sensation would be found. Looking back perhaps the choice had to be different but the safety situation of the patient was most important.

Ad.2. **Non-segmental pain**.
In researching this area bias as a result of organic suffering is not very likely. This does not have to be considered. But possible bias originated by high sensitivity while the specificity of the measuring method is not known yet, is a potential problem that should be considered.
For that reason a comparable investigation in unilateral occurring pain has been chosen, compared to the not painful other side of the body. Intervention was applied with an existing medicine (pentoxyphylline), by the way not registered as a painkiller but as a perfusion improver to claudicatio intermittens. In the meantime it was known of chronic pain without substrate that the skin temperature in most cases was lower than the surroundings. That might have something to do with a deteriorating perfusion in these areas under influence of the autonomous nerve system. Relative lack of oxygen could cause pain. Improvement of the perfusion could give improvement of the oxygen supply and as a result of that less pain and higher skin temperature.
Purpose of this research was investigating the relation between pain sensation experienced and infrared thermographic images obtained, assuming the expectation that subjective pain sensation should be equally measurable as subjective sound experience.
For possible spin off effects a means was used that was not used as a painkiller but perhaps it would serve that purpose.

These investigations form the base for further theoretical research.

The conclusions from the summary of the results are:
1a.Transmission of organic reactions occurs between organ and skin via viscero cutan reflex orbits.
1b. Abdominal wall pain can be a reaction of a painful process in the matching organ.
2. Increasing skin temperature at IUD insertion cannot be the consequence of direct stimulation of the autonomous nerve system. The a cooling-off should occur. So a mediating substance in the stimulated area must play a role.
3. Differences are observed between pregnant without and pregnant with problems. Infrared thermography registers up till physiological level
4. From abdominal pain research a significant difference in effect only appears to be in the effect between indomethazine and metimazol: the first having a temperature decrease compared to the metimazol.
5. Temperature has decreased in most chronic pain areas, conform the literature.

Pentoxyphylline improves the perfusion and there is a connection between thermographic image and pain sensation experienced.

In this research generating pain, measuring pain, transmission of pain and reaction on pain will be described. The theory is about the memory of pain and the way in which this active maintained pain can change into a serious disease such as CRPS.
CRPS as an expression of an activated measuring and regulating system which is derailed by a small trauma and after that tries to find the final stage of the system like in any other derailing measuring and regulating system.

In medical science _oddly enough- one is not used to think in measuring and regulating systems. Thinking is mainly anatomic/functional terms(structure thinking). But as in the computer world 80% of the failure consists of software failure and only 20% of hardware failure this will not be different in a biological computer system. Yet little attention is given to that.
In 1977 two researchers from Nova Scotia described a few essential characteristics of prostaglandins. Characteristics particularly suitable for biological linking and feedback processes.
Up till now there are no medical articles to be found in which those describes characteristics have been discovered in practical sense.
That is possible when characteristics in the organism are not being used by regulation technical processes but this seems unlikely. There are numerous homeostatic processes controlled in time and quantity. One of the best known: the menstrual cycle. Controlled in time and quantity with various linking moments : ovulation, menstruation, basal temperature curve which has a strong temperature increase at ovulation and an equally strong decrease at menstruation.
Considering the research area two of the theoretical articles are about prostaglandins that are (also) responsible for pain, in linking biological processes. One as an **illustration** for the way of regulation and linking processes by prostaglandins. The same way that can change a chronic pain spot into a strongly passing CRPS.
Another about measuring and regulation techniques in a biological system in which a cold pain spot can change in a hot CRPS.

By this comment I hope to have explained in what way the described research relate to "chronic benign pain" and the now worldwide interesting CRPS.

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