BEE VENOM IN RHEUMATOLOGY — AN EXPERIMENT PERFORMED WITH 1600 CASES

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From 1969, after a 3 weeks stage in Montreal (Canada) at dr. J. SAINE's clinic, we used generally bee venom extracts as local and zonal subcutaneous injections to a great number of patients.

At first we used Porsin's APIVEN, than Rébert and subsequently the lyophilised bee venom extract of Mach (Illertissen—Bavaria). At the beginning, this product was offered by the German Laboratory as sealed vials with increasing concentration. We used than the lyophilised basic extract, which consists of a yellow powder. This product was conditioned into 1.2 cc vials, in a physiological solution (1 mg of dried extract per vial). Actually we have some thousands of such vials, which we can use only on our own responsibility, and on our expenses, according to the French Legislation.

The product that we use now seems to be less efficient than the previous one. We do not know yet if this fact is related to the new sterilization procedure in use — membrane filtration instead of tyndal-lisation (procedure which consists of heatings to 60—80°C, followed by coolings, for some days, for the complete destruction of the microorganisms), or maybe it is the result of a fresh preparation stored at 4°C.

We recommended this treatment only to a limited number of our patients suffering of rheumatism, firstly because our basic activity is the thermal medicine, and secondly, because for many of them this treatment is not helpful, and for some of them it can be even harmful.

Based on an efficient method, which we shall describe here only generally, the avoidance of heavy accidents is possible; we can prove now that this treatment is not death-like even when a serious anaphylactic shock occurs; in a 13 years period we recorded no death cases.

We are but surprised that some medical reports and some articles in the senzation press are writing about some death-like cases, which occured probably because the shock treatment (which occurs rarely — in our group of patients — 1 to 200) was not applied correctly, and in due time.

Present conclusions with regard to the cases that could mostly benefit by bee venom treatment are the following:

- knees pains which appear frequently but preceding an advanced arthrosis;
- chronical periarthritis of the shoulder which are not reactive to cortisone injections;
- epicondylitis tipical disease with tenismen and all those working with heavy instruments; in this case they occur also as a result of the lack of reaction of the local cortisone injections;
- the painful basis of the toes, frequently appeared to women wearing high heels and to those who jog occasionally.

In these cases the efficiency of the treatment is about $80^{\circ}/_{\circ}$.

These general indications could be oftenly added to the cases of the painful affections of the backbone — cervicalgia with or without irradiation to the upper members, lumbalgia with or without sciatic or crural irradiation. In these cases, bee venom can be used only after identification through palpation of some painful areas of the transverse and spinal apophysis, and painful contraction of the paravertebral muscles.

We suppose that these affections are specially connected to an arthrosis of the posteriour side of the vertebrae and not by the predominant alteration to the level of the intervertebral discs, an alteration which requires particular therapeutic treatment. Naturally, not all the painful syndroms of the vertebrae should be treated with bee venom but only those which are not reactive to other treatments.

The efficiency of bee venom treatment in these cases is aprox. 65%. In rheumatic polyarthritis, bee venom is active only in the incipient phase of the disease, but due to its chronical feature, injections must be repeated, a fact that leads to the decrease of their effectiveness.

Finally, we noted that our treatment has no efficiency in coxarthrosis, spondilarthritis with ankylosis, in vertebral osteoporosis of ageing women.

The treatment consists of more or less deep subcutaneous injections, depending on the fat cell infiltration, according to a schedule recommended after clinical examination, with the purpose to discover the painful areas of the joint zone and of the methameric territory. The methameric territory is the zone which originates in the spinal cord and which in fact corresponds to a couple of vertebrae.

Injections must be performed with a fine needle of 2—3 cm length; bee venom extract will be mixed with 1/5 of the xylocaine volume of 1% concentration. Each injections must be preceded by an aspiration, through which we must be sure that no vene was reached; if in the syringe comes blood, the needle must be quickly removed. If when the needle is removed a blood drop appears, we must press the perforated area for 30 seconds. I am more and more convinced that the heavy accidents occured only to patients who are very sensitive (whom we can find knowing that a living bee sting gave them disconfort), but also, and specially by the accumulation in the vene of a high amount of bee venom. The patient must lay down or must stay under control 5—6 minutes after the injection, sometimes even more during the first treatments.

More points are injected, at first every day, then at 2 days intervals, 3 or even 4 days, with an increasing amount of bee venom, amount which can reach 5—6 vials, meaning 5—6 mg/treatment. After this a reaction will occure, which will be called normal. At the beginning during the first seconds after the needle is inside, a light pain senzation appears and some itchings which will las 1 or 2 days.

10 minutes or a quarter of an hour after, a redden swelling occures, oftenly dark redish which will last more days. A light decrease of the blood preasure with 1 or 2 cm Hg will occure, and sometimes feverness, 5—6 hours after the injection.

The intensification of these symptoms (at first itching which can become unbearable, causes wounds and insomnia; an infflamation of the injected area and a deep pain occure) must not lead to the interruption of the treatment, because they lead to the best results. However some patients, impressed and impressive, oftenly influenced by those around them, decide to stop the treatment and this is a pitty.

Nevertheless, we must admit that with some cases, rarely occured, an important decrease of the blood pressure which effects the nervous system occures, with a certain tendancy to syncopa. In these cases, one must immediately apply an intramuscular injection with adrenaline (1—3 mg), followed immediately by an intravenous injection with a soluble corticoid extract. As a result this unpleasant situation dissappears 5 or 10 minutes after. In this case, it is better to renounce repeating the treatment. However, to the patient demand, we continued the treatment without any difficulty. In this special case, the patient almost unable to walk, began to walk almost normally; his decission was foundated.

Other accidents but less dangerous may also occure. The generalized urticaria (itching) occured with 1 case from 50. Unfortunately, it oftenly appears only 30 minutes to 2 hours after the injection, after the patient has already left the Clinic. This fact afrightened the patient and those around him, but this symptom dissappears quickly 1 or 2 hours after; its disappearence (regression) can be accelerated by administering antihistaminics (Phenergan, Polaramine). With a single patient of the 1600 a crisis of astm was noted (a woman); curiously, the crisis appeared only after the second series of treament at 1 year interval after the first one.

No suffocation crises or glotal oedema were noted. This accident, described as rather frequent to living bees stings occures only when the face, the tongue or the neck of the patient is affected, but in our rheumatologic treatments we never prick, these areas.

The shocks, generalized itching, astmal crises, are rare, but they lead to the interruption of treatment and require a desensitiviness in a special cabinet of allergology.

We shall point out now, other spectacular successful cases:

- a 72 years old man, a very active bussiness man, could not drive his car any longer. He suffered also of insomnia for 2 years. After the 3-rd injection a decreasing of about $80^{\circ}/_{\circ}$ of his pains was noted, and the dissappearance of insomnia, so that the man could sleep 48 hours continuously, his wife thinking him in coma. We examined regularly this patient who continues actually his professional activity at the age of 80.
- a 42 years old engineer, suffering of serious sciatica for more than 2 years; insomnia was also noted. His professional activity was seriously comprimised. After the 4-th injection his lumbosciatica dissappeared completely and definitely.
- more recently, a 67 years old woman, with a surgical intervention of osteotomia to both knees, 6 years ago. For 2 years she could not walk, but by the help of a walking stick; after the 3-rd injection she could walk without stick on a 10 fold longer distance than before.

It seems also that in some countries of Eastern Europe, especially in Romania, and in a smaller extend in Germany (West), taking into account the scientific reports to one of APIMONDIA's symposia, bee venom is used in a very large extend.

In France, this method which is applied in a small extend, was interrupted through the dissappearance of APIVEN'70.

It is also true that in the same period, many medicines (drugs) were withdrown from the market, and surprisingly, most of these medi-

cines were already in use and had a good ressistance in time. But their limited sale, due to the financial difficulties of the producing laboratories, did not allow the organization of some research protocols, necessary to continue their manufacturing.

Many scientific studies and animal experiments were performed all over the world and especially in USA. But in these countries the settlement of the administrations have not approved until now to put into practice the treatment with bee venom to human subjects. The lack of some pharmaceutical products, based on bee venom, in USA (a reference country concerning medical researches) represents one of the most important impediments, in using bee venom.

A considerable change in the American medical attitude is necessary as well as that of F.D.A. (Food & Drugs Administration). Some physicians have already spoken about such a change, but it seems that it will not appear soon.

Surprisingly, on the other side of the Atlantic Ocean, the practice of using living bees stings is used almost on a large extend. It is performed by beekeepers, among which many physicians can be found. With the occasion of a recent journey, one of us was invited to a beekeepers' meeting, to which 2 physicians were present too.

The method in their use, was presented.

The effect of bee venom concerning human subjects and rheumatology was not completely and clearly proved. But the simple examination of the area around the bee venom injected point proved that a modification and an acceleration of the local blood circulation which lasted more days, sometimes even, two, three or 4 weeks, occured.

The studies on the experimental arthritis on mice, can not be applied to human subjects whose mechanical problems are much more different than those of the small animal.

It was proved, but only with animals, that high doses of bee venom induce a considerable increase of the blood cortisone level — the cortisone which is normally produced by the organism (VICK and SHIPMAN).

It seems that the therapeutic effect could be seen on one hand through the vaso-motor action and on the other hand through the wellknown anttinflammatory action of cortisone (which level increases also — a fact that must be proved). It seems also that bee venom induces a local immunologic shock which is very intensive and long lasting, and which could interrupt an older morbid process. We must not forget also that some recent scientific reports proved that many arthritic painful phenomena — rheumatisms — depend on the immunologic reaction, even in the case of degenerative rheumatic arthritis and tendinitis. Or, bee venom has a clear effect in the treatment of these diseases. Further researches are still necessary.

We must admit that it is difficult to achieve scientific researches with human subjects in the conditions of suspicion created around bee venom, a product accused of producing heavy accidents, even deathlike ones — so as it is noted by most people and a great number of physicians working in allergology, and surprisingly even by some beekeeper physicians. This problem is therefore difficult but not without solution and the research must be continued.