A Reflection on the Antiinflammatory Drugs for Operative Wounds

— Desirable Development of Type III A.I. Drug —

by

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1. Three Steps associated with Postoperative Treatment

An adequate healing of postoperative wounds, which is the most important aspect of a surgical operation, is still empirical and our knowledge thereof is nothing more than sketchy. Though not a few research literature is available on this subject, it simply deals with this or that phase and fails to grasp the entire picture as a vital defense mechanism.

The present paper is concerned with a reflection of operative wounds associated with an extraction of teeth.

1. Antiinflammatory disturbance

Various types of an antiinflammatory drug which are currently in use are either steroid or non-steroid preparations but since they have been selected as such on the strength of an inhibition of granular formation, a large-scale administration of this kind of drug will mean a retardation of normal granulation in the natural course of healing. In this sense, these drugs are based on a negative reaction. On the other hand, an enzymic drug does not interfere with the granular formation but, at the same time, it has no potent promotive effect of granular masses. Moreover, an anti-granular effect of steroid or non-steroid preparations is still debated.

Yet these three types of antiinflammatory drugs are by no means meaningless: they serve to suppress an excessive manifestation of an inflammation. In other words, these preparations are manufactured on the ground that, by an inhibition of excessive inflammation, the natural healing function is to be promoted. They are mere measures for a peripheral, but by no means central, portion of wound healing physiological mechanism.

With wounds associated with an extraction of tooth or teeth, it is oftener that a postoperative inflammation will take place rather than that of a surgical invasion and, for this reason, the restoration of inflammatory tissues should be positively attempted instead of applying an antiinflammatory drug merely to the peripheral region of a wound.

2. Prevention of an infection

The restoration of inflammatory tissues plays a principal role in the vital defense
reaction such as elimination, encapsulation or organization of a foreign matter, and granular tissues of a wound themselves have a defensive capability against invading bacteria. For instance, granular tissues are rich in blood vessels and, therefore, the blood circulation goes on actively. Other factors come into play for the restoration of tissues. Neutrophil leucocytes, which are highly phagoeytic, are called into a specific locality and thus work against invading bacteria. In the presence of serum protein, there is found antibody globulin that conduces to the attenuation of bacteriological toxicity. The transformation of granulation tissues into fibrinoid can be also looked upon as another manifestation of the vital defense mechanism. The advent of various antibiotics is admittedly a great achievement of 20th century bacteriology but, when viewed in the light of a host-parasite relationship, the possibility of resistant strains is always present and more attention needs to be directed to the promotion of defense mechanism on the part of a host or organ in its entirety.

3. Analgesis

Pains which are symptomatic of an inflammation can be relieved by the systemic administration to a certain extent or by that of a central nervous analgetic. But these have nothing to do with the healing process of inflammatory tissues itself.

The incidence of an inflammatory pain is due to a pain producing substance (PPS) and this pain tends to become alleviated according as the inflammation in question starts its healing process. A possible reasoning may be, i) the production of PPS reduces itself when the healing process starts, ii) PPS may be washed away by an abundant blood stream, iii) PPS will be decomposed in the healing process, or iv) a mediator involved in the healing process work against PPS. Pains attendant upon an extraction of tooth should be regarded in connection with the activation of a vital defense mechanism toward the repair of inflammatory tissues rather than with the administration of a local analgesic.

2. Dry Socket Complaint

A surgical operation is performed, of course, for bringing about a cure but an attendant medication for multiple wounds in general and many dry socket complaints in particular seems insufficient to cope with the situation effectively. This sad state of affairs is undoubtedly due to our lack of proper understanding of the restorative mechanism of inflammatory tissues, which is an integrated function of wound healing or mesodermal tissues. The incidence of a dry socket is regarded as a result of poor skill in the extraction of tooth or teeth and, on the basis of 30 million teeth assumed to be extracted in Japan every year, a proportion of 0.1% (300,000 teeth) results in some kind of dry socket complaints for which there is no adequate medicative measure.

3. Development of New A.I. Drug Urged

In order that a new light or better understanding of the problem may be brought about, it is necessary that one should re-examine our previous knowledge regarding an inflammatory mechanism and antiinflammatory drugs used for it.
The thought of an epiphenomenon appears to be strongly associated with an inflammation, for the material affection which causes an inflammation is accidental. For this reason, it is mistakenly assumed that once an inflammation is repressed it has been cured. As the matter of fact, one should always keep in mind that physiologically the healing mechanism which is an integrated function of mesodermal tissues is at work. As long as this function is in operation, an inflammation will implicitly be cured in the passage of time. Seen in this light, various types of antiinflammatory drugs currently in use are to be classified as follows.

a. **Type 1 A.I. drugs**

Those steroid and non-steroid preparations which undergo the first screening in the form of inhibiting the granulation are known as the Type 1 A.I. drugs. A large dosage of this kind of drug is known to delay the healing process of a wound. Administered internally in a large quantity, they may cause the ulceration of digestive ducts. These drugs were originally developed as a cure for the rheumatism.

b. **Type 11 A.I. drugs**

Those drugs including the derivatives of salicylic acid and aspirin (acetylsalicylic acid) which are not concerned with the granulation mechanism come under this category.

Some enzymic agents are being now studied but it is yet not clear whether they will definitely inhibit granulations or not.

c. **Type 111 A.I. drug**

Granulations which will form themselves through the encapsulation subcutaneously are pathologically interpreted to be granulomata. Regarded as a physiological response, however, they are nothing but a repair action of the inflammatory granulations and find expression as a curative process of wound. Though undeveloped at this stage of our investigation, a type 111 antiinflammatory drug will be such that is screened not only as promoting the granulation process instead of inhibiting it, but also as interfering with the formation of edema.

Fig. 1 A schematic presentation of the action mechanism of type 111 A.I. drug
(Through the administration of this kind of drug, the usual length of inflammatory conditions b can be much reduced as in a)
4. Conclusions

Our knowledge of chemical mediators that control the initial stage of an inflammation, i.e., an exudation, has been much advanced and there are known as many as twenty-odd kinds of this kind of chemical mediator. Many substances which work in opposition to these chemical mediators are discovered but an inflammation as a process cannot be fully explained away by these substances.

Moreover, the healing process of a wound which is the final stage in an inflammatory condition or its end has not been studied as it should.

In his previous study[1], the author gave his suggestions for the solution of the problem, in particular by discovering a chemical mediator which controls the integrating function of mesodermal tissues that manifests itself in the repair of an inflammatory condition. It is believed that this substance will open the way for an antiinflammatory drug which will be screened in terms of its promotion of granular activity and, at the same time, its anti-edematic effect. In view of the prevailing situation that wounds, particularly those associated with a dental extraction, are left to a natural healing process, it will be all the more effective if this process should be physiologically enhanced: it is still kept within bounds of an assistance rendered by Great Nature.

In current practice, a drug of systemic effect is administered to a disease finding expression locally in the form of a dental extractive wound, in the belief that it will prove itself locally effective. However, a systemic drug to cope with a localized lesion may be said to be fairly inefficient. It would be ideal if a drug can be realized which will be locally effective in terms of a local analgesic, antiinflammatory and promotive of a local lesion. If this objective is to be realized, it will be nothing else than the desired development of type III antiinflammatory drugs, referred to in the present paper.

References