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THERAPEUTIC AGENT FOR TREATMENT OF BODILY LESIONS.

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The present invention relates to surgery and therapeutics, and has for its object to provide a means and treatment for preventing the development of peritonitis and the formation of undesirable adhesions following surgical operations, and for the promotion of normal repair of injured or diseased body tissues. It comprises both a new mode of treating serous surfaces exposed to possible injury by operations involving entrance into the abdominal cavity or other serous cavities, and of treating lesions occurring in consequence of such operations or otherwise, and also a new agent which I have discovered and made available for such treatment, for the purposes and object above set forth.

It is a fact well known to physicians and surgeons that operations involving entrance into the abdominal cavity or the pleural cavity cause grave danger of abnormal adhesions occurring in the healing process, not only between the wound necessarily made in the course of the operation and adjacent surfaces, but also between other parts which are accidentally injured by contact with the operator's hands or the instruments and materials used in the performance of the operation; and danger of peritonitis, also, in abdominal operations. It is not necessary in this specification to recite the numerous lesions which may occur in the course of surgical operations in the cavities of the body above mentioned, or the adhesions which may take place in consequence thereof, or the disorders, functional and otherwise, liable to follow from the occurrence of adhesions or peritonitis; all these things being well known and understood by those skilled in the profession to which this specification is addressed.

I have discovered that when amniotic fluid (by which term I include unmodified amniotic fluid, as well as the more desirable product of amniotic fluid obtained by treating amniotic fluid to remove or neutralize objectionable or potentially harmful ingredients thereof) is placed in the abdominal cavity during or following a surgical operation, the occurrence of objectionable adhesions, at least of a permanent character, is largely or mainly prevented, and the healing of internal lesions is promoted. As, in the nature of things, the processes occurring after closing of the external wound are incapable of minute and exact observation, it is impossible to say whether formation of adhesions is wholly prevented from the beginning, or whether initial adhesions occur to some extent and are subsequently digested by the action or influence of the amniotic fluid so that they eventually disappear. I have concluded, as the result of my experience, that the action of this fluid is to stimulate the normal peritoneal reaction against infection. When bacterial invasion or trauma of the normal peritoneum occurs, a defensive reaction takes place which consists first in the pouring forth of a serous transudate, which in turn deposits a white plastic exudate (fibrin) on all peritoneal surfaces exposed to attack. This fibrinous deposit lessens the rate of absorption of toxic substances and assists the loops of bowel to adhere lightly to each other, thus localizing the process. Through the meshes of this loose fibrinous coating the phagocytes are able to carry on their attack against the infection. After destruction of the invading bacteria by the phagocytes, the action referred to as resolution, or clearing away of the effects of the conflict and the restoration, wholly or in part, of the tissues to normal takes place. The agents chiefly involved in accomplishing this second half of the cycle are proteolytic enzymes given off by the white blood cells, known as proteases. A delay in resolution will permit the fibrinous exudate to organize into fibrous bands and cause firm unabsorbable adhesions. Post-operative adhesions have occurred to a large extent in clean cases, where there was no infection present to give the necessary initial stimulus for a protective plastic exudate. Slightly eroded surfaces were permitted to come into direct contact, and, in the absence of strong primary response on the part of the peritoneum, resolution was feeble or delayed and firm adhesions resulted. A reaction like that caused by infection, which ultimately results in the resolution of fibrin, is stimulated by amniotic fluid, in clean as well as infected cases, but without actual infection or harm. My experience has demonstrated that the result of treatment with amniotic fluid is the healing of wounds and other lesions usually with complete absence of evidence indicating the presence of adhesions. I have used this treatment in a large number of operations, a considerable

proportion of which were subsequent operations upon the same patients in the same region. In a large majority of the cases, with but trifling exceptions, where a second operation has given opportunity to examine internally the abdominal or pleural cavity in which the amniotic fluid treatment had been used in a previous operation, I have found a complete absence of adhesions; and in all other cases where the same treatment was used there has been a complete absence of symptoms or other evidence indicating the presence of adhesions or the remote effects of peritonitis. In all of the operations to which I have reference here, in which my amniotic fluid treatment was used, the circumstances were such as those in which adhesions or peritonitis commonly occur. This discovery and treatment constitute one phase of my invention. In addition to the operations above referred to, I have caused numerous experiments with amniotic fluid to be performed on animals in the abdominal cavity.

The technic of the above described treatment is not precise or rigid, but may be carried out with wide variation as to the time and mode of introducing the fluid and as to the quantity of fluid used. For instance, I may use as small an amount of the fluid as one ounce or less or a greater amount up to many ounces. The fluid may be poured or injected into the cavity from any suitable sterile container. It may be so introduced at any time convenient to the operator. It need not even be administered in the course of the operation, but may be injected afterwards as a treatment subsequent to the operation, to destroy adhesions already in course of being formed or prevent the onset of peritonitis. It is important, however, for the success of the treatment that the fluid be free from contamination, or admixture of any substances liable to cause inflammation or other ills.

The second phase of my invention comprises the modifications and derivatives of amniotic fluid containing the principle of such fluid by which normal healing of body tissues is stimulated, and with components or ingredients of natural amniotic fluid which possess possibilities of harm to the human organism, or which otherwise contaminate the essential principle, substantially removed or neutralized. It also includes modifications or amniotic fluid prepared by adding ingredients for its preservation or asepsis, or for enhancing its action on the patient, whether or not it is also modified by the removal of any ingredients or parts of its original content. I may use for my purposes amniotic fluid derived from any mammals (including human beings, if feasible), preferably obtaining it from animals which are large enough to furnish it in substantial quantities. One important and plentiful source is cows slaughtered when in a sufficiently advanced state of pregnancy. In preparation, the fluid is drawn from the animal in a manner such as to avoid contamination, and is preferably then filtered to remove microorganisms and other foreign matter. The well-known Berkefeld filter, or one of similar type, is a suitable means for this purpose. After filtering, and while still fresh, the substance is safe to use. But to preserve it against decomposition, I may sterilize it by heat, or add suitable harmless preservative agents. But whether or not so sterilized, or fortified by preservatives, the amniotic fluid prepared for the treatment hereinbefore set forth is within my claim to protection for that substance.

The term "prevent", as used generically in this specification and in the claims with reference to adhesions and peritonitis means not merely their initial prevention, but includes also their ultimate prevention, by reduction of incipient peritonitis or digestion or destruction of incipient adhesions, so that permanent adhesion of an abnormal sort is prevented. I have used the term "abnormal" in this specification with reference to adhesions, as meaning those between organs or internal parts in the body which are not normally joined by adhesion, but become so as the undesired effect of a surgical operation. In the broad sense, the term "lesions" used herein includes peritonitis.

The foregoing description is not exhaustive of the uses which the therapeutic principle of amniotic fluid is adapted to serve. With increased clinical and experimental experience, it has been found to have curative value in other conditions and circumstances. My claim to protection is therefore not limited as to the parts of the body to which the agent and treatment may be applied.

As yet the chemistry of amniotic fluid, and particularly the active principle thereof, and the chemistry of its action in the repair of lesions, are but little known. It is certain, however, that the unmodified fluid as taken from the animal is not best suited to be placed in the internal cavities or applied elsewhere to lesions of the human organism; for the unmodified fluid contains ingredients which are obnoxious and potentially or actually harmful, and the removal or neutralization of which is desirable in the preparation of a substance which may be used with reasonable safety for the purposes herein explained.

What I claim and desire to secure by Letters Patent is:

1. A therapeutic agent for use in promoting the healing of animal body tissues comprising amniotic fluid.

2. A therapeutic agent for use in promoting the healing of animal body tissues comprising the product of amniotic fluid resulting from substantial removal or neutralization of ingredients thereof potentially harmful to the living organism.

3. A therapeutic agent for use in the prevention of undesirable adhesions of animal body tissues comprising amniotic fluid.

4. A therapeutic agent for use in the prevention of undesirable adhesions of animal body tissues comprising the product of amniotic fluid resulting from substantial removal or neutralization of ingredients thereof potentially harmful to the living organism.

5. A therapeutic agent for use in preventing development of peritonitis comprising amniotic fluid.

6. A therapeutic agent for use in preventing development of peritonitis comprising the product of amniotic fluid resulting from substantial removal or neutralization of ingredients thereof potentially harmful to the living organism.

In testimony whereof I have affixed my signature.

HERBERT L. JOHNSON.