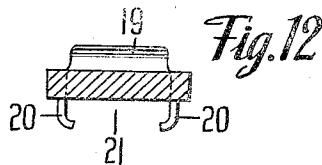
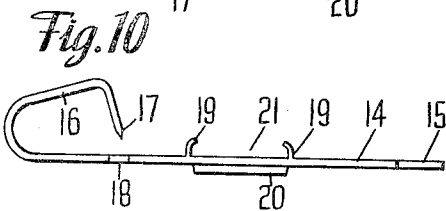
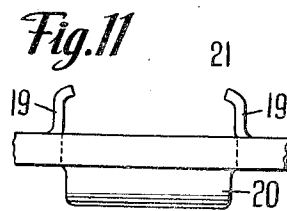
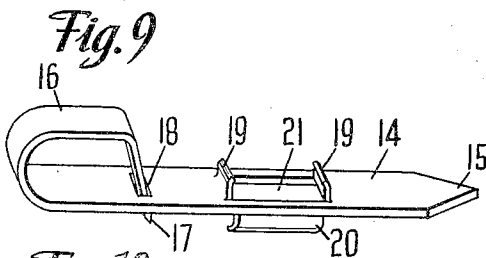
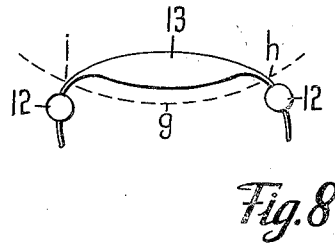
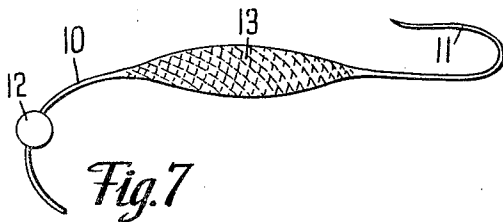
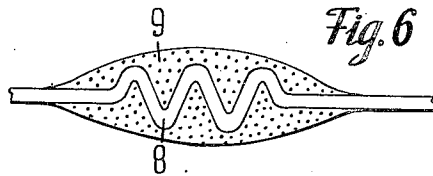
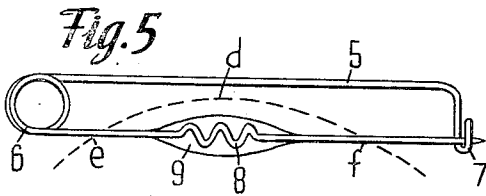
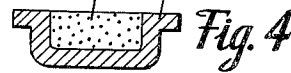
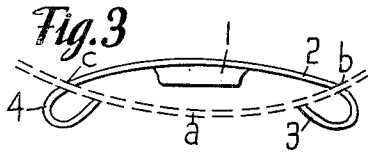
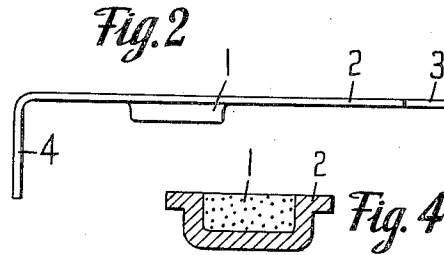
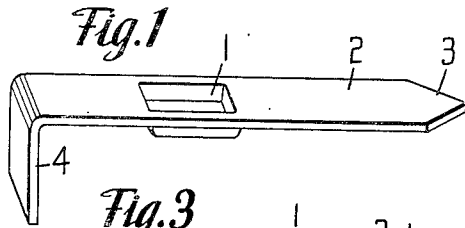


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J. W. LEE ET AL
SUBCUTANEOUS MEDICATION

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SUBCUTANEOUS MEDICATION

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7 Claims. (Cl. 128—260)

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The present invention broadly relates to the subcutaneous administration of medicaments.

Particularly our invention relates to a device for and a method of implanting medicaments subcutaneously in such a manner that the medicament comes in direct contact with body tissues and after remaining in place for a period of time any residual medicament can be readily removed.

More specifically, the invention relates to a device for implanting hormones or hormone-like substances subcutaneously in poultry, said device having a means for removing any residual hormone material after a period of time.

In the field of drug therapy, it is a well established principle that the subcutaneous route of administration produces a most desirable type of response. In some cases, i. e., when it is desired to obtain continued medication over a period of time, it is usually necessary to give repeated subcutaneous injections at frequent intervals, especially when the medicament is in a liquid form. It has been determined that when solid medicaments in the form of fused pellets or compressed tablets are implanted subcutaneously the rate of absorption by the body is such that a continuous and desirable type of therapeutic action is produced. There are, however, certain disadvantages which result from the subcutaneous administration of pellets or tablets. One of these disadvantages is that in some instances, the rate of absorption is such that toxic symptoms are produced and it is extremely difficult to locate and remove the medicament before serious consequences result. Another disadvantage is that when medication is desired for a prolonged period of time, there is a tendency for the pellet to be walled off by body tissues in such a manner that drug absorption is seriously hindered. In the treatment of domestic animals for improving their flesh quality by pellet implantation, it is necessary to discard the portion of the animal in which the implantation was made in order to avoid possible harm from consumption of the meat. Still another disadvantage of the ordinary pellet implantation technique is that a special trocar or similar instrument is required for making the implant or an operative procedure must be employed.

It is an advantage of the present invention that a device and means for the subcutaneous administration of medicaments is provided which avoids the disadvantages enumerated above.

Another advantage of our invention is that a device is provided which has means for maintaining a medicament in direct contact with

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body tissues after subcutaneous administration and in such a manner that the medicament can be withdrawn at any time desired to avoid toxic manifestations of the drug or for any other reason.

It is also an advantage of our invention that a unitary device comprising a medicament holder and a medicament is provided which can be readily implanted subcutaneously, held in position and removed at any desired time.

It is an especial advantage of our invention that a device and method is provided for the subcutaneous administration of hormone-like materials to poultry whereby the hormone effect can be maintained for any desired period of time and after which time any residual material is easily removed.

The present invention is particularly well suited for the subcutaneous administration of hormones and hormone-like materials. In this connection, it is suited for the administration of any of the naturally occurring hormone materials or any of the synthetic organic compounds having a hormone-like action. Included among such hormone materials are estrone, estradiol, progesterone, testosterone, gonadotropic hormones, lactogenic hormones, diethylstilbestrol, hexestrol, 2,4 - di(P - hydroxyphenyl) - 3-ethylhexane and the like.

The present invention can also be used for the subcutaneous administration of chemotherapeutic agents including the various sulfonamides, penicillin, streptomycin and the like. Similarly, the present invention can be used for the subcutaneous administration of arsenicals, organic bismuth compounds and other antilueticals.

It is evident from the foregoing that our invention is adapted for the subcutaneous administration of any medicament wherein a continuous therapeutic effect is desired and wherein for any reason the medicament might need to be removed.

In order that the invention may be clearly understood, reference is made to the accompanying drawings, in which:

Figure 1 is a perspective view of one form of our device;

Figure 2 is a side view of the device of Figure 1;

Figure 3 is a plan view of the device of Figure 1 secured to the skin as when in use;

Figure 4 is a cross section of the medicament retaining trough 1 of the device of Figure 1;

Figure 5 is a plan view of another form of our device secured to the skin as when in use;

Figure 6 is a detailed view of the medicament retaining means of the device of Figure 5;

Figure 7 is a perspective view of one other form of our invention;

Figure 8 is a plan view of the device of Figure 7 secured to the skin as when in use;

Figure 9 is a perspective view of still another modification of our device;

Figure 10 is a side view of the device of Figure 9, with the fastening means raised;

Figure 11 is a detailed view of the medicament retaining means of the device of Figure 9;

Figure 12 is a cross-sectional view of the medicament retaining means of the device of Figure 9.

The device shown in Figure 1 is composed of a body 2 which is made of metal, plastic or other rigid or semi-rigid substance. The body 2 has the trough or receptacle 1 positioned about mid-way between the extreme ends of the device. The walls of the trough may be inclined slightly inwardly if desired. One end 3 of the device is pointed so that it can be used for piercing the skin when introducing the device. Both ends can be pointed if desired. At the opposite end 4, provision is made for making a bend to act as a stop when inserting the device and to hold the device in position after the insertion has been made. The side view of the device in Figure 2 shows the trough 1, or drug receptacle, more clearly. In Figure 3, the device is shown fastened in an operative position as occurs in actual use. The point 3 was inserted through the skin *a* at the point *c* and brought out through the skin *a* at point *b*. The end 4 and the point 3 were then bent back against the skin *a* to hold the device in position. In Figure 4, a cross sectional view of the trough 1 is shown with the medicament contained therein. The medicament can very easily be introduced into the trough in a molten or fused condition and allowed to solidify. It is seen that the trough is relatively shallow and that the surface of the medicament in the trough is rather large. When the device is in an operative position as shown in Figure 3, the entire top surface of the medicament is exposed to body tissues and fluids and provides an excellent absorption area. The device illustrated by Figs. 5 and 6 is a modification of our invention wherein the medicament is molded onto one arm of a safety pin device. In use, the point of the safety pin is inserted through the skin *d* at the point *e* and out again at the point *f*. The safety pin 5 is provided with spring tension means 6 and the clasp 7, for locking the pin in position. The pointed arm of the pin 5 has a bent or irregular portion 8 around which the medicament 9 is molded. It is readily seen that in an operative position, the entire surface area of the oblong shaped medicament is exposed to tissues for absorption and that the irregular area 8 will permit any residual material to be removed along with the safety pin device. The medicament is molded in such a shape that it will readily pass through the opening made in the skin by the pointed arm of the pin 5. It must also have a consistency such that it will not break or crumble easily.

A third modification of our invention is illustrated by Figs. 7 and 8. The device shown in Fig. 7 is preferably composed of woven cloth, glass, plastic or similar material in such a manner that a relatively wide surface area 13 is provided and having cord-like ends 10 and 11. The woven area 13 is porous in nature so that a melted or fused medicament may be applied thereto and after solidification the medicament will be readily retained. The end portions 10 and 11 are such

that either can be threaded into the eye of a needle (not shown), drawn through the skin *g* at the point *i* and out again at the point *h*. A lead shot 12 with a slit therein or similar clamping device is then placed on each of the ends in such a manner that the device is held in position. In lieu of clamping means thine cord-like ends can simply be tied together. After any desired period of time one of the clamps 12 can be removed and the device withdrawn by pulling on the opposite end. In operative position, as shown in Fig. 8, it is seen that the drug absorbed and/or held by the portion 13 presents a large surface area for absorption and that the residual drug will be withdrawn along with the device.

Still another modification of our invention is illustrated by the drawings of Figs. 9, 10, 11 and 12. The device of Fig. 9 shows a body member 14 which may be formed of metal, plastic, or other semi-rigid material. The device has a pointed end 15 for piercing the skin, and an opening 18 through which the pointed end 17 can be introduced and locked by applying pressure at the point 16. The Fig. 9 shows the device in a locked position as would be the case when in an operative position. The side view of Fig. 10 shows the device in an unlocked position prior to introduction. The holder 14 is provided with means for retaining a medicament in tablet form. This drug retaining means comprises two tabs 20 which run longitudinally of the holder and two tabs 19 which are crosswise of the holder 14. The Fig. 11 shows an enlarged, more detailed view of the drug retaining means. Fig. 12 is a cross sectional view through the drug retaining means, showing the tabs 20 more clearly. In order to load the device with the drug, a compressed or fused tablet of the drug having a shape roughly corresponding to the shape of the drug retainer 21 is placed in the retaining member with the tabs 20 bent in slightly to support the tablet. The tab members 19 are then bent over to clamp the top side of the tablet. The tabs 19 and 20 therefore, serve to hold the medicament tablet and yet expose a considerable portion of both the upper and lower surfaces to the body tissues for absorption when in an inserted position.

In practicing the present invention, it will be readily seen that all of our devices are designed to hold a solid medicament underneath the skin of an animal in such a manner that a relatively large area of the medicament is exposed directly to the body tissues and that means are provided for withdrawing the holding device together with any unabsorbed medicament at any given time. Many of the medicaments used subcutaneously are solid substances at body temperatures. When these solid substances are not injured by heat, they may be melted and either poured directly into the drug retaining means of our holders or molded onto the holders or molded in a satisfactory form for inserting into our holders. Some solid drugs injured by heat may be mixed with auxiliary solid substances having relatively low melting points such as the waxes, higher fatty alcohols and the like liquefied by heat and used as indicated above. Suitable auxiliary substances include beeswax, cholesterol, cetyl alcohol, lanolin, polyvinyl alcohol, polyethyleneglycols and the like or mixtures thereof. Similarly, liquid medicaments may be mixed with solid inert diluting material such as the waxes, solid alcohols and these mixtures employed for producing a solid product suitable for subcutaneous use.

In Poultry Science, vol. 24, March 1945, begin-

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ning with page 128, there is an article by F. W. Lorenz, entitled "The Influence of Diethylstilbestrol on Fat Deposition and Meat Quality in Chickens." Lorenz in this article indicates that while stilbestrol pellets produce a very desirable effect upon the quality of poultry meat, there are some problems that should be solved. For example, he states on page 130:

"A problem not solved previously (Lorenz, 1943) was raised by the presence of pellet residues at killing time. Such residues represent a wastage of active material, and they would be objectionable if inadvertently ingested by the consumer. This danger may be minimized by placing the pellet in a part of the bird not usually eaten—i. e., high in the neck—but the only completely satisfactory solution to the problem would be a pellet that is completely dissolved before the bird is killed."

On page 132, he describes a method whereby he proposed to solve the problem:

"The problem, apparently, is to produce a pellet that will maintain a high rate of absorption throughout the treatment period and yet be completely absorbed at the end of the period. The dilemma arises from the necessity of maintaining a large surface area in order to have rapid absorption. An attempt was made to resolve this difficulty by coating sugar pills with the fused diethylstilbestrol."

As previously pointed out, our invention is especially well suited for the administration of hormone-like materials subcutaneously to poultry. We have carried out a number of comparative experiments wherein fused pellets representing 15 mgms. of diethylstilbestrol were implanted subcutaneously in the necks of 8 week old male chickens as described by Lorenz. At the same time a pellet holding device such as shown in Fig. 1, having 15 mgms. of diethylstilbestrol in the trough 1, was inserted in the neck of 8 week old male chickens and fastened in accordance with the illustration (Fig. 3). In the case of the diethylstilbestrol pellets, it was evident from the appearance of the birds that they were showing typical effects of the drug. When the pellets were removed at the end of 2, 3, and 4 weeks, there was considerable residue and in practically all cases, the pellets were surrounded with tissue material. The chickens carrying our holding device with diethylstilbestrol likewise showed typical diethylstilbestrol effects and when the holder together with diethylstilbestrol was removed at the end of 2, 3, and 4 weeks, there was less tissue surrounding the diethylstilbestrol material than was the case with the pellets. The rate of absorption, as determined by actual weight, was greater when the diethylstilbestrol was used in conjunction with our holder than when used as a simple fused pellet. Similar experiments were conducted wherein the diethylstilbestrol was mixed with equal amounts of cetyl alcohol to facilitate the production of pellets and the introduction of the material into the holding device. In these instances also a typical diethylstilbestrol effect was obtained and the material in the holding device showed a more constant and greater rate of absorption than did the pellets when used alone. The pellets when used alone were difficult to locate and in many cases had migrated to the lower neck region after having been inserted in the upper neck region and when located required a surgical operation for their removal.

In actual practice, our device can be very satisfactorily employed for the administration of

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diethylstilbestrol to poultry. The holding device, with the desired amount of diethylstilbestrol, may be inserted subcutaneously in the neck of the fowl, clamped in position and allowed to remain for a period of from two to four weeks. If further treatment is desired, it is only necessary to insert a new holder at the time the other is removed. In order to avoid the possibility of the consumer ingesting diethylstilbestrol that may be stored in the various organs or tissues of the fowl, it is usually desirable to remove the diethylstilbestrol and holder a few days before the bird is to be killed or marketed. In this way, the drug would be eliminated from the organs or tissues before being consumed for food.

It is apparent from the foregoing that our invention can be varied to a considerable extent without departing from the spirit thereof. The invention is, therefore, to be broadly construed in accordance with the appended claims.

What we desire to claim is:

1. A device for the subcutaneous implantation of medicaments comprising a body having means for retaining a solid medicament with a relatively large proportion of the medicaments surface being exposed, a sharpened end on said body adapted for introducing the medicament retaining portion of the body subcutaneously, means for fastening the body in position after introduction and means for withdrawing the body.

2. A device for the subcutaneous implantation of medicaments comprising a body having a trough for retaining a solid medicament with the upper surface exposed, means for introducing the trough portion of the body subcutaneously, means for fastening the body in position after introduction and means for withdrawing the body.

3. A device for the subcutaneous implantation of medicaments comprising a rigid body having a trough for retaining a solid medicament with the upper surface exposed, a sharpened end adapted for introducing the medicament trough subcutaneously, the ends of said body adapted to be bent and clamp the skin after introduction.

4. An article of manufacture comprising the device of claim 1 and a solid medicament attached thereto.

5. An article of manufacture comprising the device of claim 3 and a solid medicament attached thereto.

6. An article of manufacture comprising the device of claim 1 and a solid form of diethylstilbestrol attached thereto.

7. An article of manufacture comprising the device of claim 3 and a solid form of diethylstilbestrol attached thereto.

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