United States Patent Office 3,574,829 Patented Apr. 13, 1971

3,574,829

METHOD OF IMPROVING THE CONCEPTION RATE IN EWES

Jack F. Wagner and Edward L. Veenhuizen, Greenfield, Ind., assignors to Eli Lilly and Company, Indianapolis, Ind.

No Drawing. Continuation-in-part of application Ser. No. 541,086, Apr. 8, 1966. This application Aug. 6, 1968, Ser. No. 750,453

Int. Cl. A61k *17/00, 17/06*

U.S. Cl. 424—100 8 Claims

ABSTRACT OF THE DISCLOSURE

The conception rate in ewes is improved by the administration of a gonadotropin after onset of estrus and insemination.

CROSS-REFERENCE

This application is a continuation-in-part application of our co-pending application Ser. No. 541,086, filed Apr. 8, 1966.

BACKGROUND OF THE INVENTION

Heretofore, sex hormones such as the progestational agents, including progesterone, chlormadinone (6-chloro-Δ^6-17-acetoxy progesterone), and the like, or the estrogenic hormones, including estradiol, estratriol, estrone and the like, have been employed to synchronize estrus in female mammals. With the increased use of artificial insemination, the synchronization of estrus in female domestic animals, particularly sows, cows and ewes, has received a great deal of attention since it is most desirable in actual practice to have all females in the group come into estrus during a one- or two-day period so that the technician in charge of the artificial insemination program need not be in attendance every day during an estrus cycle of the particular species.

In addition to the broad problem of achieving estrus synchronization in a group of female mammals, there is a special problem with regard to induction of estrus in female sheep. In many breeds of sheep, the ewes undergo a period of reproductive quiescence during the late winter, spring and summer months. Ewes in such a physiological state are referred to as anestrus. Thus, with ewes, there is a double problem of finding a hormonal drug to induce reproductive activity and then to find the same or a different hormonal drug to improve the fertility at the time of the induced estrus.

In general, when it is desired to synchronize estrus in a large group of female mammals, it has been common to administer a particular progestational agent to all members of the group for a predetermined number of days. After progestational treatment is stopped, estrus begins a certain number of days later, depending upon the particular species involved. When estrus is seen to begin, the cycling females are bred, either by artificial insemination or by letting in the males of the species. After a first synchronized breeding period, it is a common practice to take all of the females who did not conceive at the first service and breed them again during the next estrus period, which will be synchronized naturally (not by drugs) since a group of females (mammals) will usually remain synchronized for 2 to 3 breeding periods following an initial synchronization using a progestin. It is, of course, an object of any breeding program, including the type outlined above, to achieve the highest possible conception rate after two cycles. However, normally with sheep, conception rates following two synchronized breeding periods will be in the range of 70 to 80 percent.

It is an object of this invention to provide a method for increasing the pregnancy rate and number of live births in ewes by a hormonal treatment initiated after the onset of estrus.

DESCRIPTION OF THE INVENTION

In fulfillment of the above and other objects, this invention provides a process for increasing the pregnancy rate and percent of live births in ewes by administering a gonadotropin to said ewe after the onset of estrus. While we prefer to administer the gonadotropin to the ewe also after insemination or impregnation, it is permissible to administer the hormone before the ewes are bred provided, of course, that insemination occurs while the ova produced during ovulation are still fertile.

We have found, surprisingly, that treatment of a group of ewes after ovulation and breeding with a gonadotropin greatly increases both the conception rate in the group as a whole and also the number of live births, as compared to the number of live births in a group of ewes receiving no gonadotropin after the onset of estrus. While it has been a common practice to use gonadotropins to induce follicular growth and ovulation in female mammals, gonadotropins have not heretofore been used to increase conception rates after estrus and ovulation in ewes. The term gonadotropin as used herein includes, among other preparations, pregnant mares serum (PMS), lutenizing homone (LH), follicle stimulating hormone (FSH), and human chorionic gonadotropin (HCG).

In carrying out the process of this invention, ewes are administered a gonadotropin within 1–16 days following estrus and breeding. Thus, our invention comprises the administration of a gonadotropin to an ovulating female mammal after the onset of estrus and during the estrus cycle, said female being bred within a few hours after the onset of standing estrus. More particularly, our invention finds its most beneficial use in an estrus synchronization program specifically employing ewes as the female mammal to be so treated. In such a program, a group of cycling ewes is synchronized by treatment for 14 to 16 days with a progestational agent such as chlormadinone acetate. The drug is then withdrawn, the ewes coming into estrus during the next five days. As soon as signs of estrus show, each ewe is artificially or naturally inseminated. One to 16 days later, during which time about 70 to 90 percent of the ewes have come into heat, and have been bred, a gonadotropin such as PMS or HCG or a combination thereof is administered to each member of the group. The conception rate of those ewes receiving the gonadotropins is increased 12 to 26 percent by this treatment and the number of lambs per ewe lambing is increased 18 to 50 percent. This same regimen is employed in the anestrus non-cycling ewe, except that prior to the administration of PMS or HCG to increase conception rate and to increase the number of lambs born per pregnant ewe, an earlier treatment with a progestine plus PMS must be used to induce follicular growth and initiate the estrus cycle. In general, the gonadotropins, not being orally active, are administered by injection.

The following experiments will more fully explain the nature of our invention:

Experiment I

A group of 73 anestrus ewes were treated with chlormadinone acetate for 16 days. Each ewe then received an injection of PMS to induce estrus and ovulation. All of the ewes coming into heat after the PMS injection were inseminated by fertile rams. Twenty-seven of the ewes were then administered PMS 16 days after first coming into heat. The control group of 46 did not receive PMS after breeding. Sixty-three percent of the ewes in the treated group lambed, whereas only 50 percent of the

ewes in the control group lambed, a difference in conception rate in favor of the process of our invention of 26 percent. The treated group had 1.9 live lambs born per pregnant ewe, while the control group only had 1.7 live lambs per pregnant ewe.

The over-all results of this experiment are as follows:

TABLE 1

Group	No. of ewes	No. of lambs	Lambing rate,[1] percent	Over-all difference, percent
Treatment	27	32	118	+39
Control	46	39	85	

[1] Percent of treated ewes.

In another similar experiment, a control group of 69 anestrus ewes, which did not receive any PMS after induced ovulation and estrus, yielded only 1.4 live lambs per pregnant ewe and only 48 percent of the ewes conceived. In a similar group of 22 ewes treated according to the process of this invention, 59 percent of the ewes lambed and 1.9 live lambs were born per pregnant ewe. The over-all results of this experiment are as follows:

TABLE 2

Group	No. of ewes	No. of lambs	Lambing rate,[1] percent	Over-all difference, percent
Treatment	22	25	114	+70
Control	69	46	67	

[1] Percent of treated ewes.

Experiment II

In this experiment a group of 178 cycling ewes were treated as follows: 126 were synchronized by the administration of a progestin (chlormadinone) for a 16-day period, after which the entire group was treated with PMS or HCG at 24–96 hours, after estrus, ovulation and breeding. The control group of 52 ewes were synchronized by the same means with chlormadinone, but the ewes in this group did not receive any PMS or HCG following estrus, ovulation and breeding. In this experiment, 50.0 percent of the ewes treated with PMS or HCG lambed, but only 42.3 percent of the control ewes lambed (a difference of 18%). The over-all results of this experiment are as follows:

TABLE 3

Group	No. of ewes	No. of lambs	Lambing rate,[1] percent	Over-all difference, percent
Treatment	126	89	70.6	+22
Control	52	30	57.7	

[1] Percent of treated ewes.

It can be seen from the above experiments that not only does the gonadotropin treatment program involving the process of this invention give a 18–26 percent higher conception rate, but also it increases the number of live births per pregnant ewe by a substantial factor (22% to 70%).

The increased birth rate brought about by the process of this invention is not readily explicable by present day theories of hormonal treatment. By either method—the double breed cycle with gonadotropic injection or the one without—the same number of females come into estrus. Thus, the improved results cannot be attributed to an increased number coming into estrus and thus ready to conceive. The treatment must, therefore, either increase the conception rate or decrease the fetal death rate or both, by a mechanism that has not been fully explained.

We claim:

1. A method of increasing the pregnancy rate and percent of live births in ewes which comprises administering a gonadotropin by injection to an ewe after said ewe comes into estrus and is inseminated.

2. The process of claim 1 in which the gonadotropin is administered from 1–16 days after onset of estrus.

3. The process of claim 1 in which the gonadotropin is pregnant mares serum.

4. The process of claim 1 in which the gonadotropin is human chorionic gonadotropin.

5. The process of claim 1 in which the gonadotropin is follicle stimulating hormone.

6. The process of claim 1 in which the gonadotropin is lutenizing hormone.

7. The process of claim 1 in which the ewe is bred within a few hours after the onset of estrus.

8. In an estrus synchronization program for breeding ewes, the improvement which comprises administering a gonadotropin by injection to each of said ewes from 1–16 days following ovulation and insemination.

References Cited

Pincus et al.: The Hormones, vol. III, 1955, Academic Press, New York, N.Y., pp. 337–342.

SAM ROSEN, Primary Examiner

U.S. Cl. X.R.

128—1; 424—105, 108