consider the close agreement in space between the VGP paths to be far more significant than the partial discrepancy in time between the paths.

The presence of the same feature of the geomagnetic field in independently dated paleomagnetic and archeomagnetic records indicates that correlation of paleomagnetic and archeomagnetic records is feasible when certain conditions are met for both types of records. For lake sediments, the minimum conditions require the collection of overlapping cores that can be dated independently and correlated precisely as well as the measurement of closely spaced paleomagnetic samples that can be shown to contain a stable magnetic signal in which the geomagnetic field has been accurately recorded. For archeomagnetic studies, there must be sufficient sites to provide a record of accurate directions from many samples extending over several hundred years. In addition, during the time interval of interest, there must be some distinct feature in the VGP path of the geomagnetic field. These conditions imply that it is possible to correlate only between features in paleomagnetic and archeomagnetic VGP paths and that, in general, it is not yet possible to determine the age of an undated archeological site or an undated lava flow from a single paleomagnetic direction associated with the site or the flow.

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13. The difference in VGP between the moving window centered at A.D. 1000 and the one centered at A.D. 1025 is 8.9°. This difference corresponds to a rate of change of VGP position of 0.36° per year, which is 30 times greater than the average rate for the Holocene and 6 times greater than the fastest observed rate (R. Thompson, *ibid.*, p. 103). Furthermore, this difference in VGP is greater than the sum of the cone of 95 percent confidence of the pole position for A.D. 1000, which is 4.4°, and that of the pole position for A.D. 1025, which is 3.2° (*9*). Thus the cones do not overlap even though the pole position for A.D. 1000 is determined from sites dated between A.D. 950 and 1050 and that for A.D. 1025 is determined from sites dated between A.D. 1000 and 1050.
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19 December 1983; accepted 10 February 1984

Initiation of Angiogenesis by Human Follicular Fluid

Abstract. *Angiogenesis was observed and measured after injection of human follicular fluid into rabbit corneas. Undiluted human follicular fluid stimulated angiogenesis in every case, with new blood vessels visible 3 days after injection and extending 2.0 millimeters from the corneal scleral limbus into the injection site by day 15. Stimulation of angiogenesis was lost by heating or diluting the follicular fluid but was retained after charcoal stripping or dialysis. Human follicular fluid contains an angiogenic factor that may be associated with perifollicular neovascularization during folliculogenesis.*

Angiogenesis plays a major role in a variety of important biological processes, including wound healing, collateral circulation, tumor growth, and embryonic development. Angiogenesis also occurs during maturation of the preovulatory follicle and subsequent formation of the corpus luteum, suggesting that the follicle complex may produce an angiogenic factor. Here we report the presence of an angiogenic factor in human follicular fluid (hFF).

Human follicular fluid was pooled from follicles (> 16 mm; $N = 30$) in 12 spontaneously cycling women 16 days after the onset of menses. The women had been treated with clomiphene citrate (days 5 to 9), luteinizing and follicle-stimulating hormones (150 IU/day; days 10 to 14), and human chorionic gonadotropin (hCG) (5000 IU; day 16). Each hFF sample was mixed with an equal volume of a solution containing 10 percent Hydron, 60 percent ethanol, and 1 percent polyethylene glycol. The hFF was sterile-filtered and serially diluted (1:0, 1:2, 1:3, 1:4, 1:9, and 1:27) with phosphate-buffered saline (0.05*M*; *p*H 7.4) for dose-response studies. The supernatant (600*g* for 30 minutes) of hFF treated in 10 percent dextran-coated charcoal (24 hours at 4°C) and the retentate of dialyzed (molecular weight cutoff, 8000) or heated (62°C) hFF were also tested (20 μl).

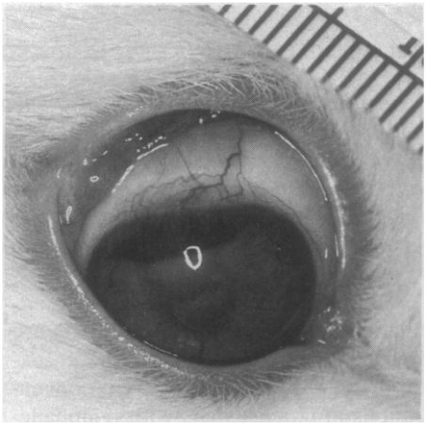

Fig. 1. Angiogenesis 12 days after injection of hFF into the cornea of a rabbit eye. Vascularization extends across the sclera and 2 mm into the cornea.

The effects of the hFF-Hydron solution on angiogenesis were assessed in 44 New Zealand White female rabbits (1.5 to 2 kg) anesthetized with ketamine hydrochloride (20 mg/kg, intravenously). A 20-μl portion of the solution was introduced into the right cornea by aseptically creating a pocket 2 mm proximal to the superior limbus (*1*). To evaluate the effects of hCG at concentrations typically found in follicular fluid after hCG treatment, 20 μl of a solution of hCG (1 mIU/ml) and Hydron was similarly injected into the cornea of three New Zealand White female rabbits. The left cornea of each animal was injected with Hydron and saline as a control.

Corneas were evaluated daily for 15 days. Sustained growth of well-defined new capillaries from the limbus toward or into the corneal implant was considered a positive angiogenic response (Fig. 1). Responses were graded qualitatively as follows: 0, no angiogenesis; 1, plexus of blood vessels seen at the limbus; 2, intracorneal vessels present; 3, intracorneal vessels extending more than 1.0 mm from the limbus toward the injection site;

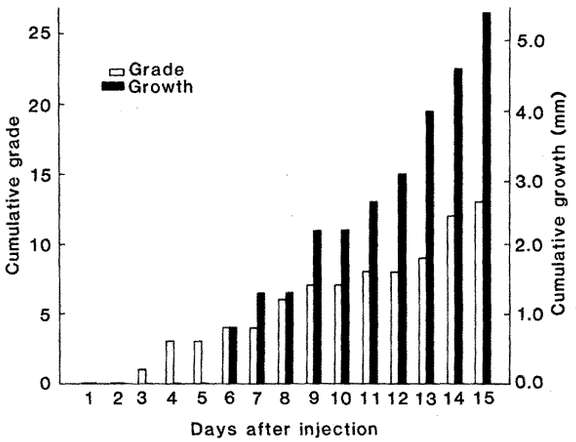

Fig. 2. Cumulative growth of new blood vessels after injection of hFF into rabbit corneas (N = 8).

4, vessels extending more than 2.0 mm; 5, vessels extending more than 3.0 mm; and 6, vessels extending more than 4.0 mm. Measurements of vessel growth in millimeters per day were also obtained. Eyes that demonstrated angiogenesis were removed, fixed, and stained with hematoxylin and eosin for microscopic evaluation.

Undiluted hFF stimulated angiogenesis in eight of eight rabbits (Fig. 2). The invasion of blood vessels was macroscopically evident 3 days after injection and by day 15 extended 2.0 mm into the injection site from the closest part of the corneal-scleral limbus. Two- and four-fold dilutions of hFF stimulated angiogenesis 5 and 3 days after injection, respectively, in two of four rabbits, with the vessels seen at 3 days extending 1.0 mm into the injection site by day 15.

Dialyzed hFF induced angiogenesis in two of three rabbits, with vessels extending up to 1.0 mm into the injection site by day 15. Charcoal-treated hFF produced angiogenesis in three of three rabbits, with a plexus of blood vessels growing more than 4.0 mm by day 15. In contrast, intracorneal injection of heated hFF did not result in corneal vascularization.

None of 20 control rabbits injected with Hydron and saline and three rabbits treated with hCG and Hydron showed any angiogenic activity. Histological examination of sections prepared 3 weeks after the injections did not reveal any foreign bodies or marked inflammatory reaction in the injection site.

During the follicular phase of the human menstrual cycle a single follicle usually matures and ovulates in response to the midcycle surge of serum gonadotropins. The question arises as to why only a single follicle develops to maturity while others undergo atresia in the same gonadotropin environment.

Basset (*2*) described the appearance of perifollicular blood vessels during growth and regression of rat ovarian follicles. From the endothelial walls of these vessels angiogenic sprouts began to grow into the granulosa layer, and this was associated with a rapid increase in capillary permeability. Jakob *et al.* (*3*) showed that the rat corpus luteum produced a vigorous stimulation of capillary growth. Koos and LeMaire (*4*) described the induction by rat follicles and corpora lutea of gonadotropin-responsive angiogenesis in the chorioallantoic membrane of the chick embryo. Gospodarowicz and Thakral (*5*) found that explants of rabbit corpora lutea stimulated angiogenesis when placed into a rabbit cornea. Taken together, these results suggest that a signal for angiogenesis accompanies follicular development and formation of the corpus luteum in these species. Recent evidence by diZerega and Hodgen (*6*) and Zeleznik *et al.* (*7*) demonstrated an increasing density of blood vessels in the complex of the dominant follicle in primates. This increase in perifollicular vascularization may result in preferential gonadotropin delivery and thus in selection and maintenance of the dominant follicle.

The cornea provides a naturally transparent, avascular substratum in which neovascularization can be continuously monitored (*8, 9*). Using the corneal implant assay we found that hFF contains an angiogenic factor that may be involved in neovascularization. Three days after injection of hFF, new blood vessels were visible; by day 6 these extended more than 1 mm into the cornea. Thereafter vessel growth continued progressively. We conclude that developing follicles produce an angiogenic factor and that this selective vascularization may be important during preovulatory folliculogenesis.

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10. Supported in part by grant HD-401 and a USC Faculty Research and Innovation Fund award.
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18 November 1983; accepted 6 February 1984

Rectal Insemination Modifies Immune Responses in Rabbits

Abstract. *Weekly deposition of pooled rabbit semen into the rectum in healthy male rabbits resulted in the appearance of immune complexes and antibodies to sperm and to peripheral blood lymphocyte antigens. It also led to a decreased ability to mount a humoral immune response to T lymphocyte–dependent antigens, keyhole limpet hemocyanin, and sheep red blood cells. These findings suggest that repeated rectal deposition of semen may compromise some aspects of the immune system.*

Antibodies to spermatozoa and to circulating immune complexes (CIC's) are present in apparently healthy homosexual men (*1, 2*) and at increased concentrations in homosexuals with lymphadenopathy or acquired immunodeficiency syndrome (AIDS) (*2, 3*). The etiology of AIDS is not clear; however, the fact that a large proportion of AIDS cases have been found in highly sexually active homosexual men suggests that the syndrome may have some relation to circulating antibodies evoked as a result of semen deposition in the alimentary canal. Human seminal fluid apparently contains components that potentially can suppress the immune response (*4, 5*), and syngeneic mouse spermatozoa in-