pegmatites. Another serious difficulty was in the preservation of kyanite, for any metamorphic pressure-temperature cycle of rocks must make a considerable excursion through the sillimanite field at elevated temperatures in order for the rock to return to the surface.

The present determination removes both difficulties. The kyanite field now dominates the geologic portion of the pressure-temperature plane, which fact is intuitively more satisfactory in explaining the predominance in nature of the kyanite polymorph. Reasonable pressures of deep metamorphism (3 to 5 kbar) require that the temperature be no higher than 450° to 550°C to prevent inversion to sillimanite. If a temperature of 500°C is reached in the aureole of a granite body intruded at a depth of 8 km, for instance, kyanite will change to sillimanite. If temperatures remain fairly high until the rock has risen by natural causes so that it is closer to the earth's surface, the kyanite-sillimanite line would not be recrossed at temperatures higher than 200° to 300°C when cooling occurs. The very slow sillimanite-andalusite inversion, especially where water is absent, might prevent inversion to andalusite. Hence the sillimanite could be preserved. The occurrence of kyanite in metamorphic rocks is easier to explain, in that a geothermal gradient of 30°C/km lies entirely within the kyanite field until a temperature of 600°C is reached. Kyanite, once created, might remain ever after in its own field of stability.

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1 February 1966

Gonadotropin-Induced Anomalies of the Zona Pellucida of the Baboon Ovum

Abstract. *Vesiculation and other anomalies were observed in the zona pellucida about the ovum of female baboons* (Papio anubis) *that had received treatment with Pergonal and human chorionic gonadotropin; and in some instances the zona pellucida was absent.*

The mature ovum is surrounded by a thick homogeneous membrane, the zona pellucida, which is believed to be a secretion product of adjacent follicular cells (*1*). The function of the zona is protective, and during the course of fertilization it is a barrier that must be penetrated by the spermatozoa.

Formation and constitution of the zone pellucida in maturing follicles of the baboon (*Papio anubis*) appear to encounter interference in animals that have been treated with Pergonal (*2*) (trade name for human postmenopausal gonadotropin) and human chorionic gonadotropin. These gonadotropins are currently finding wide usage in the treatment of infertile women and produce a condition of superovulation that has led to a high incidence of multiple births (*3*).

We studied ovarian sections of seven untreated animals and compared the data with that of ovaries obtained from five animals, in two groups, whose regimen of treatment was as follows.

Group 1: Starting on the 5th day of the menstrual cycle, we administered 75 international units of Pergonal intramuscularly to three animals for 8 days. Human chorionic gonadotropin (2000 units) was also administered intramuscularly on each of days 6 and 7, and 2000 units were injected intravenously on the 8th day in order to produce a sudden surge of ovarian stimulation (*4*).

Group 2: The two animals in this group received 150 international units of Pergonal intramuscularly, the treatment being started on the 5th day of the menstrual cycle and continued for 5 days. A reduced dose of 75 units per day was given for an additional 3 days. This was complemented by a dose of 2000 units of human chorionic gonadotropin administered intramuscularly on days 6 and 7 and intravenously on day 8. Ovariectomy was performed after various periods of time following intiation of treatment. Histologic preparations were stained with hematoxylin and eosin, and the first 25 follicles (secondary and tertiary) that were viewed and found to contain ova were examined for the presence and condition of the zona pellucida. Findings are given in Table 1.

Ovaries of 80 percent of the treated animals showed a high incidence of defective development of the zona pellucida. This was indicated by a variety of anomalies that included vesiculation, hypotrophy, and absence of this structure. The effect was particularly marked in the tertiary follicles. Slides of the

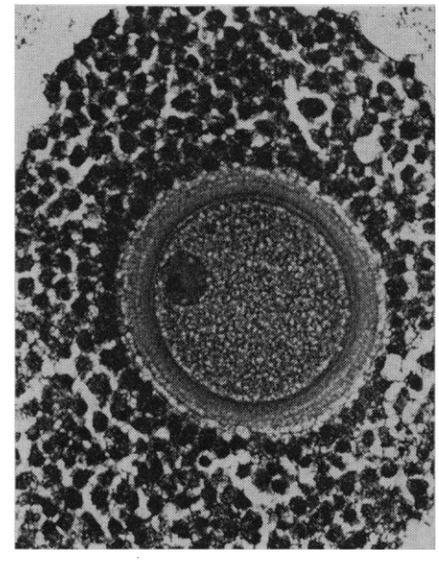

Fig. 1. Ovum of untreated animal with normal zona pellucida.

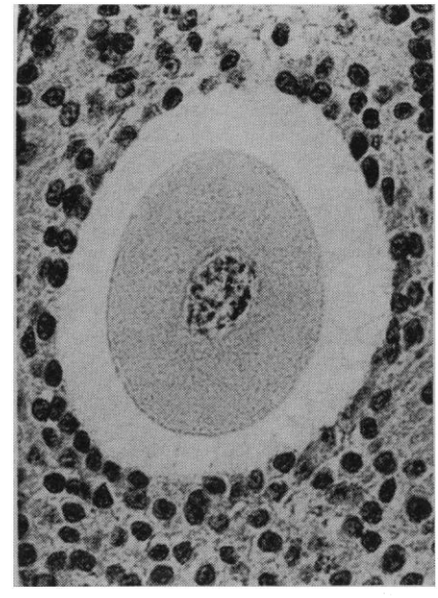

Fig. 2. Ovum of treated animal showing vesiculation of the zona pellucida.

Table 1. Effect of gonadotropin treatment on the zona pellucida.

Animal No.	Ovary	Ovariectomy (day after treatment)	Dose schedule	Zona pellucida		
				Normal (%)	Defective (%)	Absent (%)
C-1	Left	0	Untreated	96		4
C-2	Left	0	Untreated	100		
C-3	Left	0	Untreated	100		
C-4	Left	0	Untreated	100		
C-5	Left	0	Untreated	96		4
C-6	Left	0	Untreated	96	4	
C-7	Left	0	Untreated	96	4	
X-1	Left	3	Group 1	0	72	28
	Right	9	Group 1	0	60	40
X-2	Left	6	Group 1	12	88	0
	Right	9	Group 1	24	76	0
X-3	Left	13	Group 1	12	68	20
X-4	Left	9	Group 2	16	48	36
	Right	13	Group 2	12	76	12
X-5	Left	12	Group 2	4	76	20
	Right	12	Group 2	0	76	24

experimental group were studied without reference to the animal records. There is an appreciable agreement on tabulation of the results obtained from any one pair of ovaries even though the ovariectomies were performed after two different periods of time after treatment. There are some individual differences in response to these compounds among the several treated animals, as demonstrated by animal X-2, which appears to be refractile.

Treatment with compounds such as Pergonal may incite a number of mechanisms and produce a variety of factors that may lead to the observed defects of the zona pellucida. These factors, obviously, are biochemical in nature and their action and interaction produce morphological discrepancies that in turn may greatly modify the normal physiological function of the ovum.

Since the zona pellucida is believed to function as a protective membrane, its absence may facilitate the transport of nutritive materials to the developing ovum, thus accelerating its maturation. Also, since it is a barrier that spermatozoa must penetrate to accomplish fertilization, its absence removes any possible function of sperm selectivity that may be exercised by the zona pellucida. Either of these factors may in part account for the high fertility encountered in women treated with such compounds. Whether this could connote undesirable situations that may express themselves genetically cannot be immediately ascertained.

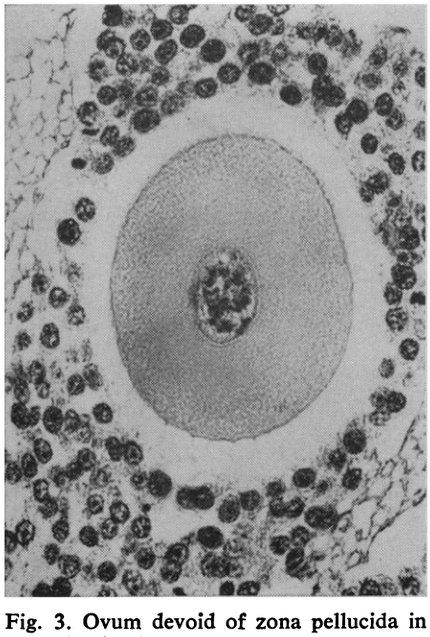

Fig. 3. Ovum devoid of zona pellucida in treated animal.

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6 December 1965

Osteolytic Sterol in Human Breast Cancer

Abstract. *Eleven of twelve human breast cancers contained a lipid which increased urinary ^{45}Ca and ^{40}Ca excretion of ^{45}Ca-labeled, parathyroidectomized rats receiving a low Ca diet. The lipid has mobility on thin-layer chromatography and gas-liquid chromatography close to, but not identical with, that of 7-dehydrocholesterol. Authentic 7-dehydrocholesterol has osteolytic activity similar to that of the extracted sterol. Fluorescence and Lieberman-Burchard reactions of the extracted sterol are similar to those of 7-dehydrocholesterol. The lipid was found by thin-layer chromatography in the extracts which had osteolytic activity. Neither the lipid nor osteolytic activity was found in extracts of tissue from two normal human breasts.*

A number of host responses to many kinds of tumors of nonendocrine tissues result from ectopic elaboration of humors by the cancers. All of those so far identified are peptides: ACTH, parathyroid hormone, chorionic gonadotrophin, erythropoietin, and substances with the activities of antidiuretic hormone or thyrotrophin (*1*). In some cases of carcinoma of the lung, kidney, pancreas, and colon (*2*), parathyroid hormone has been identified immunologically; it accounts for the chemical syndrome of hypercalcemia and hypophosphatemia. In most cases, however, the hypercalcemia of malignancy is not accompanied by hypophosphatemia, but by normal or slightly elevated concentrations of phosphate in serum (*3*). Since breast cancer is the most common malignancy producing hypercalcemia (*4*) and since it is not associated with hypophosphatemia (*3*), we studied extracts of 12 human breast cancers, removed at operation (*5*), for osteolytic activity. We now report the presence of an osteolytic sterol in 11 of these tumors.

To identify extracts containing osteolytic activity, we measured their effect on the urinary ^{45}Ca and ^{40}Ca excretion of parathyroidectomized, labeled female rats. Female Sprague-Dawley rats were parathyroidectomized by electrocautery at body weight 60 to 75 g and injected subcutaneously with 10 μc of $^{45}CaCl_2$ (*6*). Starting 1 week after operation the labeled animals were fed a diet low in calcium and low in vitamin D (*7*). Each gram of diet contains 0.067 mg of Ca, 2.2 mg of phosphate, and 1.5 ng (0.06