

Table II. Effects of reserpine on growth and development of DMBA induced mammary tumors in female rats

Group and treatment ^{aa}	Total No. of rats	Average No. of palpable tumors/rat					Average total weight of tumors/rat (g)
		Initial	10 days after treatment	25 days after treatment	50 days after treatment	Change (%)	
1. Controls, intact	16	3.3 ± 0.5 ^{bb}	3.9 ± 0.6 ^a	5.3 ± 0.8 ^d	6.9 ± 1.0 ^g	+109	12.0 ± 3.8 ^j
2. Reserpine (10 µg), intact	16	3.3 ± 0.7	5.2 ± 1.1 ^b	7.1 ± 1.3 ^e	10.6 ± 1.8 ^h	+221	15.5 ± 3.4
3. Controls, ovariectomized	19	4.1 ± 0.6	2.6 ± 0.5 ^c	1.4 ± 0.4 ^f	1.3 ± 0.4 ⁱ	-68	1.9 ± 1.2 ^k
4. Reserpine (10 µg), ovariectomized	16	4.0 ± 0.7	2.4 ± 0.4	1.6 ± 0.4	1.3 ± 0.4	-68	1.4 ± 0.7
5. Reserpine (100 µg), ovariectomized	13	4.3 ± 0.6	3.6 ± 0.5	1.4 ± 0.3	-	-	-

^{aa} DMBA was administered at 55 days of age. The rats were treated with reserpine and/or ovariectomized approximately 75 days after DMBA treatment. ^{bb} S.E. of the mean. ^{a,c,d,f,g,i,j,k} = *P* 0.001. ^{a,b} = *P* 0.02. ^{d,e,g,h} = *P* 0.05.

existing rat MT^{7,8}. Reserpine, however, failed to significantly influence MT development in ovariectomized rats. This may be due, at least in part, to inadequate prolactin secretion by these rats. Recent studies in our laboratories have demonstrated that reserpine may or may not have a significant effect on blood prolactin levels in ovariectomized rats⁹, depending upon the dose and time schedule of administration.

The lower dose of reserpine administered either before or after MT appearance had no effect on body weight. The higher dose of reserpine given before MT appearance decreased body weight for a period after treatment but most rats recovered by the time the experiments were terminated. The temporary loss in body weight may have been partly responsible for the decreased incidence of MT observed in these rats, since losses in body weight are often associated with decreased tumor development¹⁰. The higher dose of reserpine administered to ovariectomized MT-bearing rats for 25 days markedly reduced body weights, and as a result this treatment was not continued for 50 days or administered to intact-MT bearing rats.

LACASSAGNE and DUPLAN¹¹ reported that mice of the C₃H strain, treated with reserpine, developed spontaneous MT earlier than the controls. These results are in accord with the study of Boor et al.¹² which demonstrated that long term injections of prolactin in mice resulted in enhanced mammary tumorigenesis. By contrast, CRANSTON¹³ reported that several central nervous system depressants, including reserpine, had no significant effect on growth of spontaneous MT in mice. DUKOR et al.¹⁴ reported that the maximum tolerated dose of reserpine given to mice bearing spontaneous MT had a slight inhibitory effect which could be correlated with the degree of body weight loss. The probable explanation for these contrasting results is that the mouse MT are not generally

hormone responsive in later stages of development, although they are initially hormone dependent¹⁵. On the other hand, carcinogen-induced rat MT are hormone dependent initially and generally remain hormone responsive in later stages of development, since either hypophysectomy or ovariectomy before or after MT appearance results in decreased incidence and growth, respectively, of MT¹⁶.

Résumé. Si l'on injecte de la réserpine à des rates avant de les avoir traitées au carcinogène, leurs tumeurs mammaires diminuent très nettement. En revanche, si l'injection de réserpine s'opère chez des rates déjà atteintes de ces tumeurs, la croissance de ces dernières en est sensiblement stimulée.

C. W. WELSCH and J. MEITES

*Departments of Anatomy and Physiology,
Michigan State University,
East Lansing (Michigan 48823, USA), 16 March 1970.*

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Extranuclear ³H-Thymidine Incorporation in Subcortical Cytoplasmic Organelles of Primary Oocytes in the Japanese Quail (*Coturnix coturnix japonica*)

In the present work, laying Japanese quails were injected i.p. with 1 mCi of thymidine 6-³H (specific radioactivity: 14 Ci/mM, 1 mCi/ml). 1½ h later, the animals were killed by decapitation, their abdomens opened and the intrafollicular peduncular oocytes removed from the ovaries by the cutting off their pedicle. These oocytes were then fixed in acetic acid-alcohol (1:3) for 1 h at

4°C, thereafter for 2 h at room temperature. After dehydration, the oocytes were embedded in paraffin and sectioned at 8 µ. After deparaffination and rehydration, the acid-soluble precursors were extracted by treatment of the sections with 3% perchloric acid at 4°C for 20 min. The slides were coated with nuclear emulsion L4 (Ilford, Great Britain) by the dipping method. After 28 days

exposure in the dark at 12 °C and subsequent photographic development, the sections were stained with Groat's iron haematoxylin and eosin.

In the Japanese quail, the peduncular intrafollicular oocytes have a diameter ranging from 1 to 18 mm, after fixation in acid alcohol. Yellow yolk formation is found when their diameter is approximately 4 mm or more. The younger oocytes are white. In those with a diameter

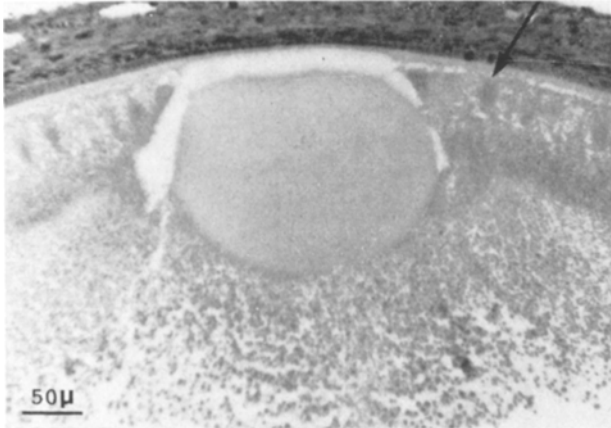


Fig. 1. Low power view of the germinal vesicle and the subcortical cytoplasmic masses (one of which is indicated by an arrow) in a quail oocyte of 5.5 mm diameter. A few little spheres occupy a central position in the nucleus. Some distortion of the nucleus is apparent, due to fixation.

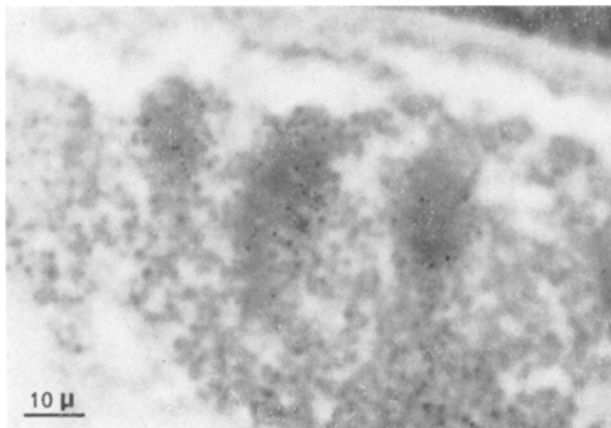


Fig. 2. High power view of 3 distinctly labelled subcortical masses.

of 4 to 8 mm the germinal vesicle is located in, or has already wholly penetrated, the cortex of the ooplasm. In this subcortical ooplasm which is filled with very fine yolk vacuoles, and at various distances from the germinal vesicle, irregular shaped masses are found, pressed in between adjacent yolk vacuoles (Figure 1).

These masses stain darker than the surrounding cytoplasm and are distinctly labelled (Figure 2). The cross-sectional area of most of these masses is usually far greater than that of a typical adjacent follicle cell. No radioactive grains are found over the germinal vesicle or other parts of the ooplasm. Some of the follicle and theca cells around the oocytes are densely labelled. In oocytes with a diameter less than 3 mm, the nucleus is still located beneath the compact cortical layer and no subcortical cytoplasmic masses are visible. In the oocytes with a diameter greater than 8 mm (usually in a laying quail, only 3 are to be found) these subcortical masses are absent. Seeing that in regularly laying quails, oviposition occurs approximately every day, the subcortical ^3H -thymidine-incorporating masses must still be present in each egg 3 or 4 days before ovulation. Since no other structure in the oocyte is found labelled after the $1\frac{1}{2}$ h ^3H -thymidine pulse, presumably the labelled cytoplasmic organelles incorporate thymidine $6\text{-}^3\text{H}$ in situ. If the ^3H -thymidine-incorporating structures contain DNA, then we have here an example of extranuclear DNA synthesis. Its possible role in vitellogenesis and/or early embryonic development of the quail is being studied. In the light of the investigations of BRACHET^{1,2} in amphibian eggs, and the recent work of BOND³ and BELL⁴, it would seem probable that these structures might possess an informative function.

Résumé. Après une injection intrapéritonéale de thymidine ^3H à la caille japonaise pondeuse, nous avons trouvé une incorporation de ce précurseur dans des organites cytoplasmiques subcorticaux des oocytes, quelques jours avant leur ovulation.

M. CALLEBAUT⁵

*Laboratorium voor Anatomie en Embryologie,
Rijksuniversitair Centrum, 2020 Antwerpen (Belgium),
17 March 1970.*

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Abstossung von Tumoren unter Einwirkung von anorganischem Diphosphat

Beim Aal der deutschen Küstengebiete werden Hauttumoren immer häufiger; sie finden sich je nach Ort und Jahreszeit bereits bei über 15% des Bestandes. Es handelt sich hier um epidermale Papillome, die von einem bindegewebigen Stroma getragen werden. Während der Tumorgenese beginnen hochdifferenzierte Epidermiszellen (Kolbenzellen, Schleimzellen) zu degenerieren und werden schliesslich weitgehend oder völlig eliminiert. Der Tumor

besteht somit fast ausschliesslich aus indifferenten Epidermiszellen (Basalzellen, intermediäre Zellen, Deckzellen). Invasives Wachstum ist nur selten zu beobachten.

Von der Mehrzahl der Untersucher werden eine Verminderung des oxydativen und eine Verstärkung des glykolytischen Energiestoffwechsels als Charakteristikum aller Tumoren angesehen – das gilt auch für die Tumoren minimaler Abweichung¹. Das Ausmass dieser Stoffwech-