Chromosomal examinations were performed for original and metastatic tumor cells, and in vitro cell lines established from the former. The degree of differentiation of tissues from those tumors was different presumably by the influence of chemotherapy. The morphology of in vitro cell line appeared to be neuroblast, lacking any premature cells. Cells produced neither tumors nor colonies by transplantations on athymic mice and soft agar cultures, though those had been immortalized. Those showed overt aneuploidy, and the origin of yolk sac tumor has been confirmed by analyses of polymorphisms. Chromosomal polymorphisms observed in tumors were identical to the ones of the host lymphocytes, suggesting the parthenogenetic origin of a germ cell before termination of first meiosis. Karyotypes from three kinds of cells contained similar chromosomal abnormalities. Trisomy of chromosome 1 was consistently observed in those cells, suggesting that this associated characteristically with yolk sac tumorigenesis. However, chromosomal changes reflecting tumor cell differentiation failed to be explored.

45. Genetic Study on Mechanism of Origin of Ovarian Solid Teratomas

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In order to investigate the relationship between the mechanism of origin and malignant potentiality of ovarian solid teratomas, six cases of these tumors were analyzed for chromosome Q- and R-heteromorphisms, HLA antigens and polymorphisms of phosphoglucomutase-1 and esterase D and their stage, histologic grade (Norris et al.) and prognosis were examined in each case.

Four tumors were homozygous for chromosome heteromorphisms found to be heterozygous in their host and either homozygous or heterozygous for HLA and enzyme markers and therefore originated from a failure of meiosis II or duplication of a haploid ovum. Of these four cases, three were in stage Ia and grade 1 or 2 and one was in stage Ia and grade 3. All four had an uneventful postoperative course. Two tumors were heterozygous for chromosome heteromorphisms, HLA antigens and enzyme polymorphisms which were identical to those of their host. They, therefore, originated from a premeiotic cell or failure of meiosis I. Of these two cases, one being in stage Ia and grade 3 experienced a recurrent tumor and the other being in stage IIc and grade 3 died.

These observations show that ovarian solid teratomas originate from a germ cell in different ways and tumors arising from a germ cell before meiosis I have a high propensity for malignancy.

46. Influence of Steroid Hormone Application on a Transplantable Tumor Tissue Originated from Primary Epithelial Cancer in Rat Ovary

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To observe the influence if hormonal impacts on ovarian epithelial tumor, estrogen or progesterone was applied to rats with transplantable cancer. The tumor line was obtained from a primary ovarian adenocarcinoma in rat, which had been induced by local application of 7, 12 dimethylbenz(a)anthracene. The resulting changes of the tumor tissue were as follows:

1) Both steroid hormones could affect the development of the tumor tissue to be promote. The lifespan of the hormone-treated rats decreased to 21.5 days in estrogen group and 23.5 days in progesterone group (control: 34.1 days).

2) Histologic changes of the tumor tissue were evident in estrogen group increasing the cellular pleomorphism. Prominent nuclear mitoses were noted in the tumor tissues of both two groups.

3) These acquired characteristics by the hormonal stimulation remained in the tumor tissues obtained from the following five generations.

On the bases of this experimental result, recommendations were made for a more serious consideration for the role of steroid hormones playing on the epithelial carcinogenesis in the human ovary.

47. Re-evaluation of Upper Limit of Normal Prolactin Level in Women

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To re-evaluate the range of prolactin level in women with normoprolactinemia, blood samples of 10 normal females with normal cycles were drawn daily for thoughout one menstrual cycle. Prolactin was measured by RIA kit provided by Daiichi Radioisotope Co. The marked daily change of prolactin levels was not found, but slightly lower level was observed in menstrual phase than in follicular and luteal phase. Prolactin levels through cycle showed log-normal distribution, of which mean, 95% confidence limits (M + 2SD) and 68% confidence limits (M + SD) were 12.2, 25, 15 ng/ml, respectively.

If 15 ng/ml is considered as the upper limit of normoprolactinemia, 75% of the occulted hyperprolactinemic women were exempted from the normoprolactinemia.

These concludes that 1) prolactin level less than 15 ng/ml is a normoprolactinemia. 2) 15-25 ng/ml is a borderline case. 3) more than 25 ng/ml is a hyperprolactinemia.

48. Studies on the Upper Limit of Normal Prolactin (PRL) Level and the Normal PRL Responsiveness to TRH in Regularly Ovulating Women

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Serum PRL level were measured throughout the menstrual cycles in 90 women, having normal menstrual cycles without sterility, galactorrhea, luteal insufficiency and medication. And the normal PRL responsiveness to TRH (500 μg) was studied in the follicular phase. PRL levels were higher ($p<0.01$) in the ovulatory phase (15.8 ± 6.1 ng/ml, n=16, mean ± SD) than in the follicular phase (10.5 ± 4.5, n=150) and the luteal phase (10.4 ± 4.7, n=100). In all samples except for those in the ovulatory phase, PRL levels were 10.5 ± 4.5. The peak PRL levels after TRH stimulation were 89.5 ± 35.5 (n=90) and there was a good correlation (n=90, r=0.27, $p<0.05$) between the basal PRL levels and the peak PRL levels.

From these results, the conclusions are as follows. (1) It is reasonable that the upper limit of normal PRL levels in regularly ovulating women is determined to be 20 ng/ml, which is lower than those of previous reports. (2) The upper limit of the peak PRL levels after the TRH stimulation should be 160 ng/ml, and the positive correlation was shown between the basal PRL levels and the peak PRL levels.

49. Estrogen Feedback and Effect of Sulpiride-induced Hyperprolactinemia in Postmenopausal Women

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Estrogen feedback and the effect of sulpiride-induced hyperprolactinema on gonadotropin release was studied in postmenopausal women. The age of the volunteers ranged between 50 and 85. Twelve normal postmenopausal women (the control group) were administered ethinyl estradiol (EE) 40 μg/day, by mouth throughout the study. After four weeks, EE 200 μg/day was added orally to each subject for four days. On the other hand, twelve sulpiride-induced hyperprolactinemic postmenopausal women (the sulpiride group) were administered sulpiride 150 mg/day by mouth throughout the study and EE was given in the same manner as in the control group.

The administration of sulpiride 150 mg/day resulted in hyperprolactinemia throughout the study. In the both groups, the administration of EE 40 μg/day resulted in a gradual decline in both LH and FSH levels as seen in the normal premenopausal women and the additional administration of EE 200 μg/day for 4 days elicited a positive response in the serum LH levels. Especially, the serum LH levels elevated markedly (200% or over) in about a half of the subjects of the both groups.

The results suggest that negative and positive estrogen feedback is preserved in postmenopausal women and estrogen feedback is not disturbed by sulpiride-induced hyperprolactinemia.

50. Evaluation of GnRH Administration on Prolactin Response to Thyrotropin-releasing Hormone in Normal Women

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