Animal studies in which certain susceptible strains and species are used and the dosage, excessive and continuous, cannot be transferred exactly to human expectancy. Nevertheless, a warning is there and a so-altered endocrine environment in human tissues might result in an abnormal expression or potentiation of growth.

Recommendations

1. The more extensive use of dogs and nonhuman primates in the animal testing of these drugs.
2. To test the presently approved contraceptive pills, if this has not been done, for mammary effects in dogs.
3. Encourage research in long-term administration of estrogens and other sex hormones in low and intermediate doses to nonhuman primates.
4. Continue the study groups on contraceptive pills in order to obtain more long-term data. Assure that the patients in those study groups are regularly and adequately examined and tested and that abnormal findings are immediately reported.
5. Continue the warning that the contraceptive pills are contraindicated in the presence of genital or breast malignancy and to extend this contraindication to any suspicion of genital or breast malignancy.
6. To establish at least two long-term study groups: one on the contraceptive pills and at least one control group. The minimum number in each group should be 20,000 women and the term of study for each group no less than 10 years. These studies must be within a reasonably stable population and geographic area. These are the minimum number required to ascertain a 2x change of genital and breast cancer incidence rates with 5 percent acceptable risk rate.

Table I.—*Cervical carcinoma—Initial screening* [1]

		Number of women	Number of cancers	Rate per thousand	In situ	Invasive cancers
2	Mayo Clinic, Rochester, Minn	139, 503	987	7. 1	897 (6. 4)	90 (0. 7)
3	Ohio State University, Columbus, Ohio	113, 758	388	3. 4	213 (1. 9)	175 (1. 5)
4	Memphis, Tenn	108, 136	724	6. 7	393 (3. 6)	331 (3. 1)
5	Wisconsin State Laboratory, Madison	65, 163	548	8. 4	195 (3. 0)	353 (5. 4)
6	Mecklenburg County, N.C	48, 697	412	8. 5	290 (6. 0)	122 (2. 5)
7	San Diego, Calif	33, 746	336	10. 0	259 (7. 7)	77 (2. 3)
9	Honolulu, Hawaii	24, 182	134	5. 5	51 (2. 1)	83 (3. 4)
10	Strang Clinic	19, 462	48	2. 5	46 (2. 4)	2 (0. 1)
12	Floyd County, Ga	17, 761	84	4. 8	56 (3. 2)	28 (1. 6)
11	Los Angeles, Calif	19, 192	145	7. 6	97 (5. 1)	48 (2. 5)
14	Puerto Rico	8, 435	119	14. 1	67 (7. 9)	52 (6. 2)
8	Metropolitan Hospital, N.Y.—Sedlis	27, 226	123	4. 5	71 (2. 6)	52 (1. 9)
15	Tijuana, Mexico	2, 161	51	23. 6	25 (11. 6)	26 (12. 0)
13	Kansas—Hellwig	10, 197	96	9. 4	52 (5. 1)	44 (4. 3)
1	Vancouver, British Columbia	322, 352	2, 156	6. 7	1, 228 (3. 8)	928 (2. 9)
	Total	959, 971	6, 351	6. 6	3, 940 (4. 0)	2, 411 (2. 6)

[1] Adapted from Day, E, table 4, p. 1193, Clinl. Obst. and Gynec., 4: 1183–1198, 1961, with additions.