Dienestrol*

Another Synthetic Estrogen of Clinical Value

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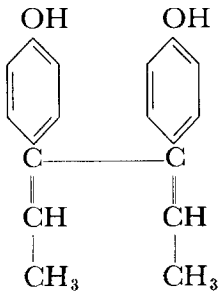
An opportunity to study the clinical usefulness of dienestrol was afforded us* in November, 1944, following brief reports of favorable results in British journals.[1,2] This synthetic estrogen is a hexadiene and it differs from the stilbestrol derivatives and from the other synthetic estrogenic materials on the American market at present. Its chemical and physical properties were recorded in 1938 and 1939 by Dodds et al.[3,4] Emmens[5] found in 1938 that its oral activity in mice was higher in relation to its subcutaneous dose than in any other estrogen yet tested. Barnes,[1] using it to inhibit lactation in women, considered that dienestrol was effective in dosage about one-tenth that of stilbestrol. Because of this known high potency per mg. the original supplies were in tablets of 0.1 mg.

The formula of dienestrol:



Our observations were made on a group of twenty-one women out-patients suffering from the complaints well known as characteristic of the climacteric syndrome. Only two had had no prior experience with estrogenic therapy. Most of them had been under observation for variable periods of time and had used one or more estrogens, natural or synthetic. Their success with other estrogens had been variable, usually satisfactory when the dose had been maintained at an adequate level. Three had had definite nausea and emesis when using barely adequate doses of diethylstilbestrol. Consequently, both clinician and patient had a basis for comparing the results following dienestrol and other estrogens. Exact dose comparisons were not made because this would have required prolonged periods of use of each substance at the minimum effective level if fair relative statements were to be made. Microscopic study of stained vaginal smears was made throughout, and the usual changes toward cornification of shed epithelial cells indicated estrogenic activity as compared with pre-treatment conditions.

The important data are presented in tabular form relating, however, to only thirteen women since eight were unable to report to the clinic regularly enough to justify conclusions about the effectiveness of the therapy. Excellent or completely satisfying results were reported by five women with doses ranging from 0.1 to 0.6 mg. daily. Seven patients secured good results but relief of

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symptoms was not complete; doses varied from 0.1 to 0.5 mg. daily in this group. It is likely that some of this latter group would have had excellent results if circumstances had allowed us to follow them after slightly higher doses, as we did in some of the first five mentioned. An unsatisfactory result occurred in only one case and this woman preferred to discontinue trial of dienestrol at only 0.3 mg. daily.

It will be noted that in most of these women the menopause began spontaneously. The only apparent difference in results in this connection was seen in the two women whose climacteric syndromes followed irradiation and who had adequate trial of dienestrol. They secured less complete relief from the treatment than did most of our patients. In both cases there is reason to believe that the irradiation was not thorough enough to cause complete inactivation of the ovaries, a circumstance which has repeatedly seemed to cause a syndrome difficult to relieve.

Our twenty-one patients reported no nausea, emesis, nor other unpleasant side reactions from dienestrol in dosage up to 0.5 mg. twice daily, but usually not over 0.5 mg. daily. As mentioned, three patients had had nausea and emesis following diethylstilbestrol in minimum effective dosage. On the other hand, the use of dienestrol has not been followed by the spontaneous reports of well-being which were made following use of some of the natural estrogens.[6] Based on an admittedly small series, we think dienestrol is the most satisfactory synthetic estrogen with which we have had experience.

Since 0.1 mg. dienestrol secured acceptable results in only three cases and 0.2 mg. would have secured such results in six of the twelve favorable results, we suggest that the initial trial dose be 0.2 mg. and that the minimum tablet might well be this size. Similarly, since three of the twelve required 0.5 or 0.6 mg. per day, a 0.5 mg. tablet would be a convenient and probably economical size.

SUMMARY

Clinical trials of dienestrol for relief of climacteric symptoms in thirteen women indicate that doses of 0.2 to 0.5 mg. daily are adequate, dependable and tolerated without unpleasant side effects.

MENOPAUSE

Patient	Age	Spontaneous	Surgical	Radiation	Dienestrol mg./day	Results	
						Excellent	Good
Ac....	55	#			0.2		#
An....	49		#	#	0.6	#	
Er.....	29			#	0.3		#
Ha....	47	#			0.3	#	
Ke....	36	#			0.5		#
Ko....	54		#		0.3		#
Na....	53		#		0.2	#	
Re....	50	#			0.5		#
Sc.....	56	#			0.1		#
Sm....	38	#			0.2	#	
Sw....	49	#			0.1		#
Va....	31	#[a]			0.1	#	
We....	39			#	0.3		

[a] Irregular menses, climacteric symptoms.

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