

# J. Stevenson

## Progestins—Are They All the Same?

## PROGESTOGENS

- 19 nor-testosterone derivatives
  - norgestrel
  - norethisterone acetate
- C-21 steroids
  - medroxyprogesterone acetate
  - dydrogesterone

## PROGESTINS: RECEPTOR EFFECTS

19 nor-testosterone derivatives

Progestogen	E	A-E	AND	A-A	GLU	A-M
norethisterone	(+)	+	+	-	-	-
levonorgestrel	-	+	+	-	-	-
norgestimate	-	+	+	-	-	-
desogestrel	-	+	+	-	-	-
gestodene	-	+	+	-	(+)	+
dienogest	-	+	-	+	-	-

## PROGESTINS: RECEPTOR EFFECTS

progesterone derivatives

Progestogen	EST	A-E	AND	A-A	GLU	A-M
progesterone	-	+	-	(+)	(+)	+
medroxyprogesterone	-	+	(+)	-	+	-
dydrogesterone	-	+	-	-	-	(+)
chlormadinone acetate	-	+	-	+	+	-
medrogestone	-	+	-	(+)	-	-
cyproterone acetate	-	+	-	+	+	-
drospirenone	-	+	-	+	-	+

## PROGESTOGEN EFFECTS

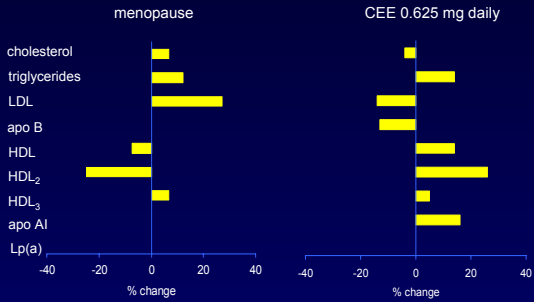
Depending on the type of progestogen:

- endometrial effects - similar
- bone effects - similar
- metabolic effects - *differ*
- vascular effects - *differ*
- side-effects - *differ*

## METABOLIC EFFECTS

- lipids and lipoproteins
- glucose and insulin metabolism

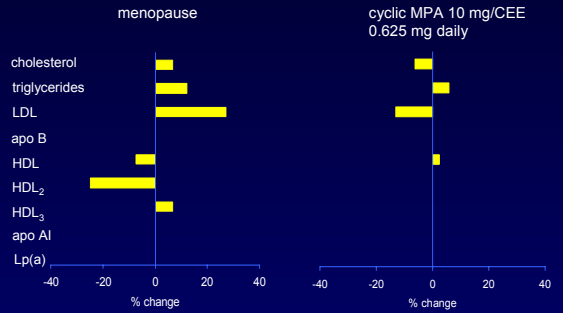
## CEE AND LIPIDS



Stevenson et al. Atherosclerosis 1993; 98: 83-90

Lobo R. J Clin Endocrinol Metab 1991; 73: 925-30

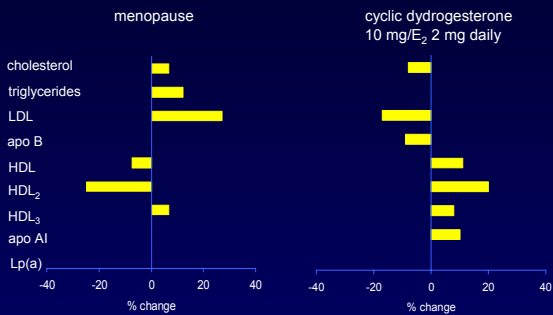
## MPA/CEE & LIPIDS



Stevenson et al. Atherosclerosis 1993; 98: 83-90

PEPI J Am Med Assoc 1995; 273: 199-208

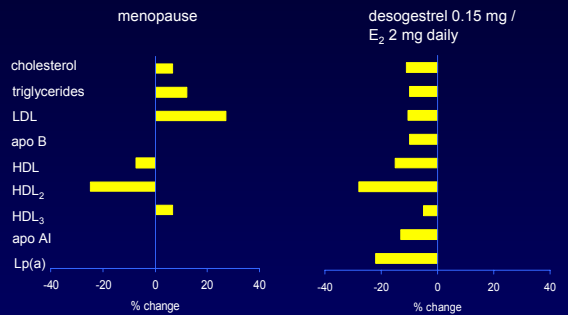
## DYDROGESTERONE/ E<sub>2</sub> & LIPIDS



Stevenson et al. Atherosclerosis 1993; 98: 83-90

Crook et al. Br J Obstet Gynaecol 1997; 104: 298-304

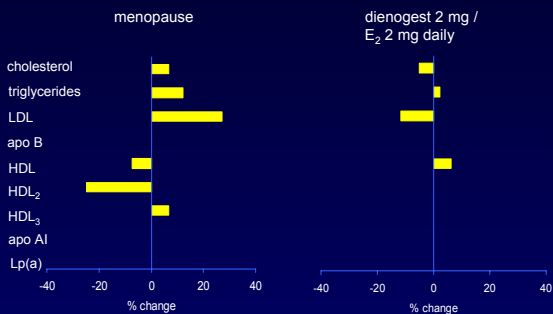
## DESOGESTREL/E<sub>2</sub> & LIPIDS



Stevenson et al. Atherosclerosis 1993; 98: 83-90

Marsh et al. Obstet Gynecol 1994; 83: 19-23

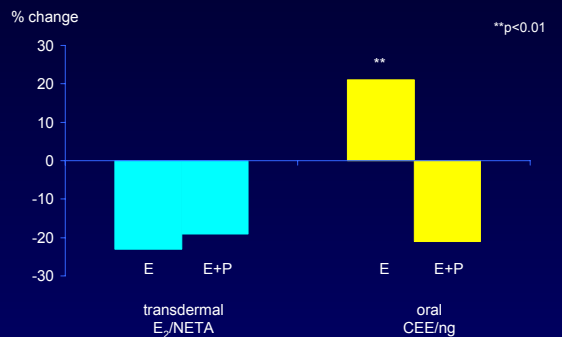
## DIENOGEST/E<sub>2</sub> & LIPIDS



Stevenson et al. Atherosclerosis 1993; 98: 83-90

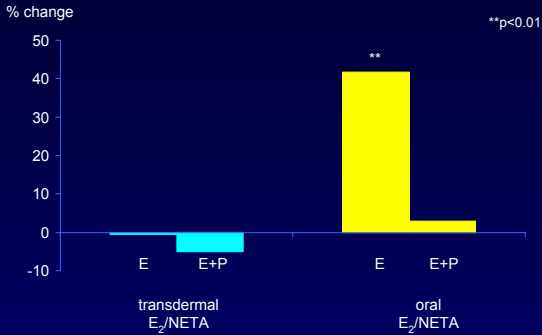
Graeser et al. Climacteric 2002; 4: 332-342

## HRT: INSULIN SENSITIVITY



Godsland et al. Metabolism 1993; 42: 846-53

## HRT: INSULIN SENSITIVITY

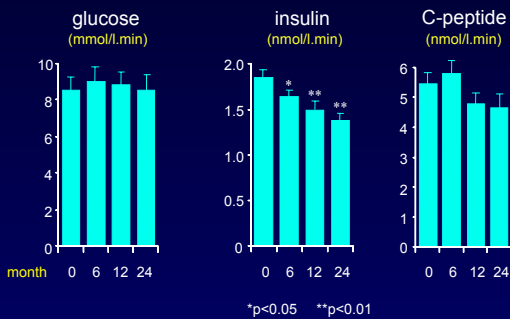


Spencer et al. Metabolism 2000; 49: 742-47

## PROGESTINS - ARE THEY ALL THE SAME?

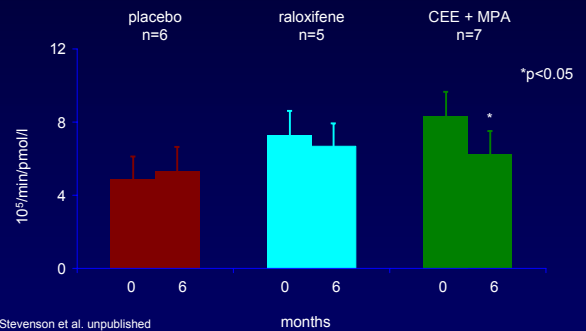
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## E<sub>2</sub> / DYDROGESTERONE



Crook et al. Br J Obstet Gynaecol 1997; 104:298-304

## CCHRT: INSULIN SENSITIVITY



Stevenson et al. unpublished

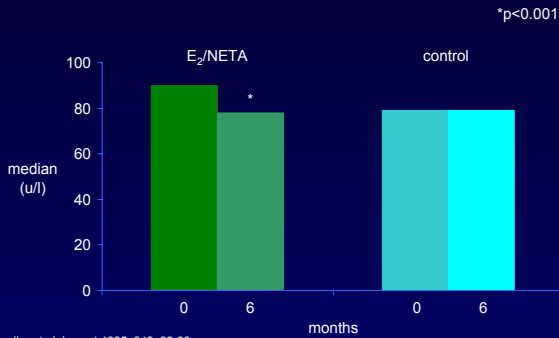
## PROGESTOGEN & GLUCOSE / INSULIN

- oral androgenic progestogens increase insulin resistance
- transdermal NETA little effect on insulin
- MPA adverse effect on glucose / insulin
- progesterone / dydrogesterone little adverse effect on glucose / insulin

## PROGESTINS: VASCULAR EFFECTS

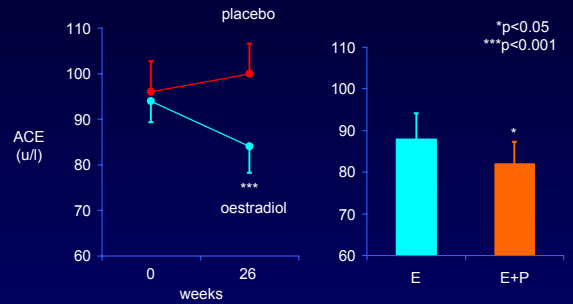
- MPA reverses oestrogenic benefit to vascular endothelial function
  - Miyagawa et al. Nature Medicine 1997; 3:324-327
- NETA has small reversal effect (20%)
  - Hillard et al. Fertil Steril 1992;58:959-63

## HRT & ACE ACTIVITY



Proudler et al. Lancet 1995; 346: 89-90

## PROGESTOGENS & ACE



Proudler et al. Clin Endocr 2003; 58: 30-35

## SIDE-EFFECTS

### C-19 progestogens

- physical symptoms
  - backache, bloating, acne, breast tenderness

### C-21 progestogens

- psychological symptoms
  - irritability, depression, anxiety
- not invariable - tailor to individual

## PROGESTINS: CONCLUSIONS

- effects of various progestogens are different
  - type of progestogen used may be critical for correct management
- side-effects of various progestogens are different
  - tailoring of HRT essential for continuance

## HRT: CONCLUSIONS

- different forms of HRT have different metabolic effects
- metabolic effects have their major impact on the cardiovascular system
- different HRT regimens may have different cardiovascular effects