

# Physiological dose reverse rhythm testosterone treatment abolishes the development of permanent gynaecomastia in adolescent boys with 47,XXY Klinefelter syndrome (KS)

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## Gynaecomastia as a feature of KS

- Reports of incidence 40-60% (30-40% non-KS boys )
- Different natural history from non-KS as usually do not resolve spontaneously
- Persistent ?due to low testosterone/obesity/increased aromatase activity
- Major psychological morbidity

## Reasons to treat KS boys with testosterone

### *Biochemical hypogonadism*

Low testosterone: often not before puberty stage G4

### *Clinical hypogonadism*

Slow virilisation including micropenis

Poor muscle development/tone

High BMI

**Gynaecomastia?: but when to start?**

## Patients: from UCLH Klinefelter syndrome clinic

Local and national referrals

Currently over 50 patients; 29 over 11yr at time of study

## Methods

Prospective evaluation of gynaecomastia in 29 boys over 11yr

Recording of Tanner puberty stage & breast stage

Measurement of breast disc diameter by palpation

Started routine physiological testosterone replacement schedule **but in reverse rhythm** ie taken in morning using testosterone undecanoate (oral) 40mg od or Tostran (transdermal) 20mg od but NOT SUSTANON im due to adverse pharmacokinetics

## Results

8/29 developed gynaecomastia. Only one had a high BMI

All offered physiological testosterone replacement

2 failed to comply: gynaecomastia did not resolve

3 testosterone undecanoate TU (Restandol) 40mg om

3 transdermal testosterone (Tostran) 20mg om

Age onset (yr)	G stage	TV (ml)	B stage	Disc (cm)	BMI SDS	Age offset (yr)	Time (yr)
12.9	2-4	3-6	2-3	2.1	0.6	13.6	0.8
11.4-14.2				1-3	-1.33 to +3.0	12.5-15.9	0.2-1.7

## Conclusions

**Reverse rhythm testosterone, using a morning administration regimen started at the onset of gynaecomastia and then given continuously in physiological dose increments, abolishes the development of permanent gynaecomastia in adolescent boys with KS**