

Comparison of Gender Specific Clinical Laboratory Reference Ranges in Transgender Patients

*Tiffany K Roberts-Wilson PhD, Colleen Kraft MD, Vin Tangpricha
MD PhD, Alan Wu PhD, and Corinne Fantz PhD*

AACC SES Audioconference
April 27th, 2011

How did we get into this?



Sean Delonas New York Post April 6th, 2008

Partitioning of reference ranges: How do we know what's normal?

- What is “normal” for one population, may not be for another.
- Analytes partitioned by sex
 - Creatinine (GFR)
ALT
 - Hemoglobin
 - Etc.

Must have population specific reference ranges.

- Allows for more accurate identification of patients in need of follow-up testing and care.
 - Reduces risk of hospitalizing a healthy individual.
 - Reduces risk of missing an individual in need of care.

What about transgender patients?

- Which reference range should be used?
 - Natal Sex or Identified Sex?
- What is the effect of hormone therapy?

Treatment Guidelines

- Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline
- Released
 - September 2009
 - The Endocrine Society and the Journal of Clinical Endocrinology and Metabolism

Hormone Therapy: Fundamentals

- Hormone treatments are one of the easiest parts
- FTM – Testosterone up to normal male dose
 - Dose that masculinizes and stops menses is enough
- MTF – More difficult because must suppress testosterone production to get best results
 - Anti-androgen(s s) – Spironolactone most common in US
 - Estrogens

Hormonal Therapy: MTF

- Estrogens at high dose
 - 3-5x normal female replacement doses
 - Partially to feminize
 - Partially to better suppress testosterone
- Anti-androgen
 - Spironolactone and others
 - Orchiectomy
- Results variable
 - Age at starting is important
 - Genetics play a big role

The special case of Transgender Girls



Hormones: MTF - Estrogens

- Oral - \$
 - \$\$\$ Premarin 1.25 – 10mg/d (usu. 5mg)
 - \$ Estradiol 1-5mg/d (usu. 2-4mg)
 - \$\$ Ethinyl Estradiol (OCPs) – drug interactions (PIs, P-450, etc.)
- IM – Delestrogen \$\$
 - 10-40mg q2weeks (usu. 20mg)
 - Can't easily “stop” in an emergency when patient immobilized
- Transdermal – Estradiol patch \$\$\$
 - 0.1-0.3mg/d (1-3 patches/week – overlapped)
 - Probably the safest for transwomen predisposed to thromboembolic and CV dz (age>40, smoking, FH, etc.)



Hormones: MTF - Estrogens

- Beneficial effects
 - Breast growth
 - Suppress androgen production
 - Change of body habitus
 - Softening of skin
- Contraindications/Precautions
 - Same as cisgender women
 - Individual risk/benefit (MTF get greater mental health benefits than menopausal cisgender women)

Other Hormones

- Anti-androgens
 - Spironolactone 50-300mg/d (\$)
- Progestins
 - Usually requested for breast growth based on anecdotal evidence – decrease total estrogen!

Hormones: MTF - Efficacy

- What is adequate treatment?
 - PT outcomes – breast growth (peak 2-3yrs), changes in skin, hair, fat/muscle, libido
 - The FLOOR – testosterone levels (female range)
 - The ROOF – prolactin level

Hormones: Adverse Effects

- Estrogen
 - Thromboembolic disease
 - Hepatotoxicity (especially ORAL)
 - Prolactinoma (dose too high)
 - Decreased glucose tolerance
 - Lipid profile
 - Gallbladder disease
 - Worsening migraine/seizure control
 - Breast cancer
 - Mood
 - Decreased libido
- Spironolactone
 - Hyperkalemia
 - Decreased H/H

Monitoring Patients on Hormone Therapy

- Routine monitoring for adverse effects
 - Lipid profile
 - Cholesterol, triglycerides, HDL and LDL often have gender-specific ranges
 - Blood glucose and HgbA_{1C}
 - Liver enzymes
 - ALT and AST frequently have gender-specific ranges
 - Renal Panel
 - Creatinine frequently has gender-specific ranges
 - CBC
 - Hemoglobin and hematocrit often have gender-specific ranges
 - Prolactin
 - Usually has gender specific ranges

Monitoring Patients on Hormone Therapy

- Recommend evaluating and setting a baseline for medical conditions that can be exacerbated by therapy prior to initiation of treatment.
- BUT - are changes from baseline really ADVERSE? Or could they be an acceptable response to hormone therapy?

Study Goal

- Identify consistent changes in measurand levels with hormone therapy.
 - could indicate that changes from pre-therapeutic levels should be considered indicative of potential adverse effects

OR

- may be a part of the desired physiological changes induced by the therapy

Study Design

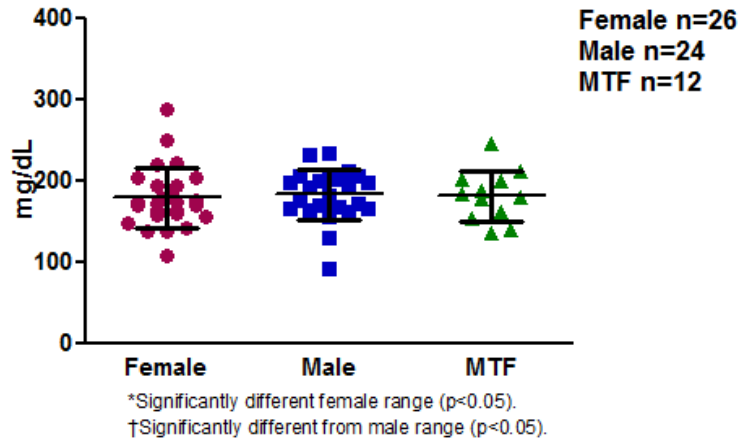
- Obtained IRB approval from Emory University
- 29 self-identified male to female transgender patients
 - On hormone therapy for ≥ 6 months
 - 5 post-SRS
 - 4 post-orchietomy
 - 16 on spironolactone
 - 2 on progesterone
 - all on various doses of estrogen (oral, IM, patch)
 - Ages 21-65, median age of 49

Study Design

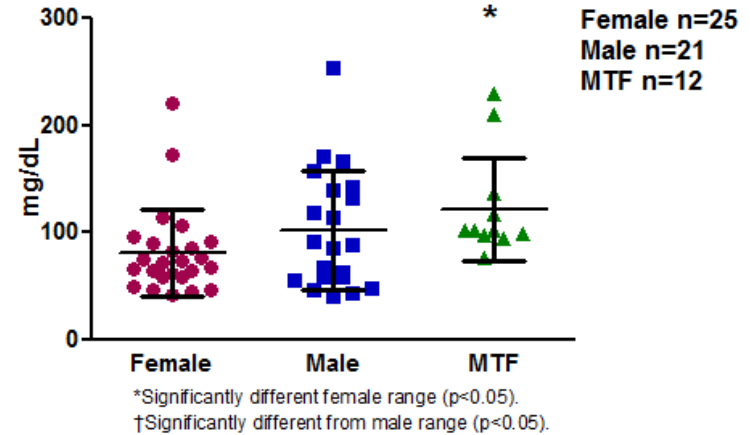
- Laboratory data abstracted from the medical record
- Values were compared to values from 26 female and 24 male patients previously drawn for reference range verification studies.
- Data was analyzed using StatisPro software from Analyze-it[®] and CLSI and Prism5.0 from GraphPad Software

Preliminary Data – Lipid Profile

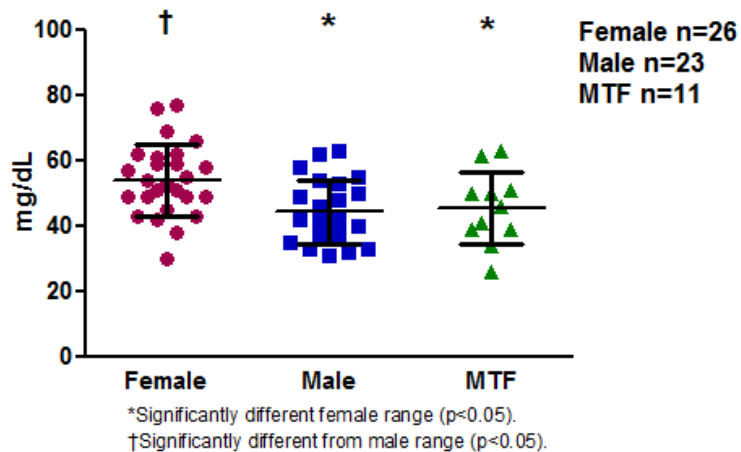
Cholesterol



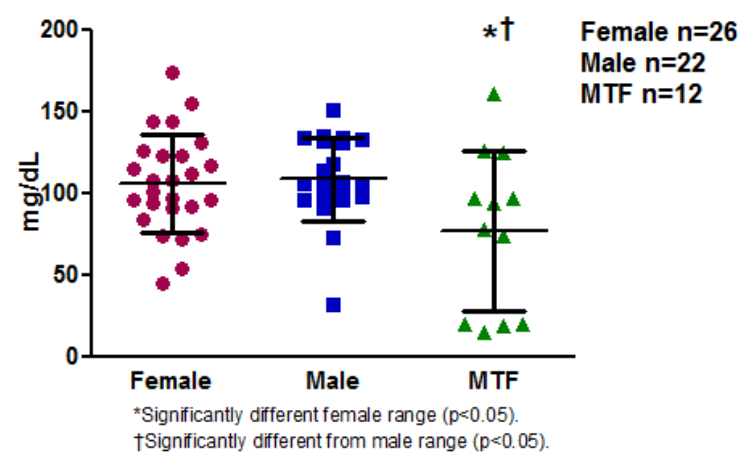
Triglycerides



HDL



LDL

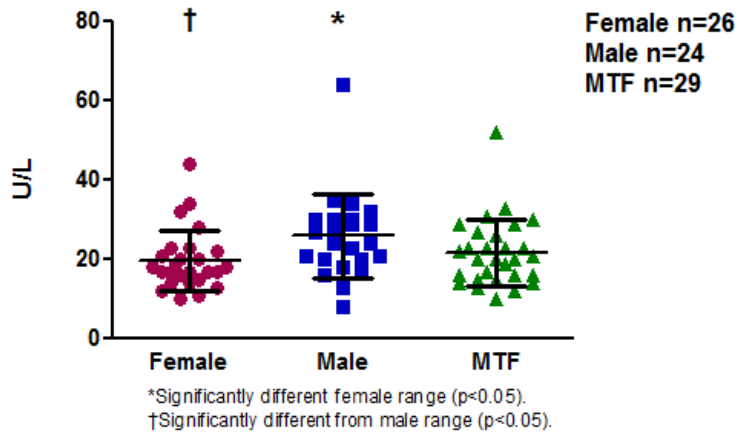


Summary

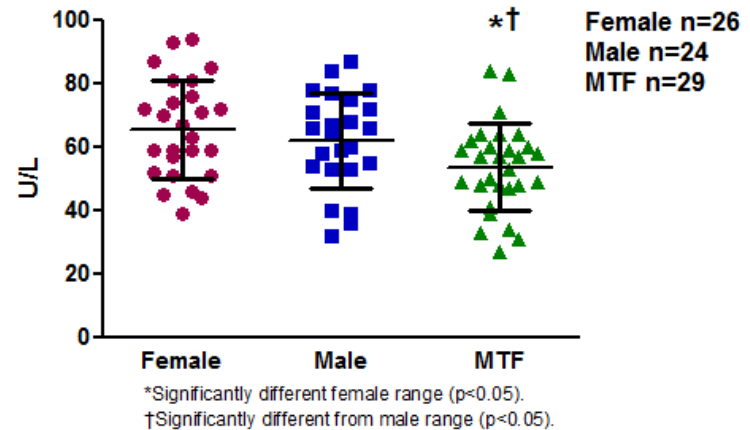
- Lipid Panel
 - Total cholesterol is no different
 - Triglycerides and HDL are the same as natal sex
 - LDL is lower than both natal and identified sex

Preliminary Data – Liver Enzymes

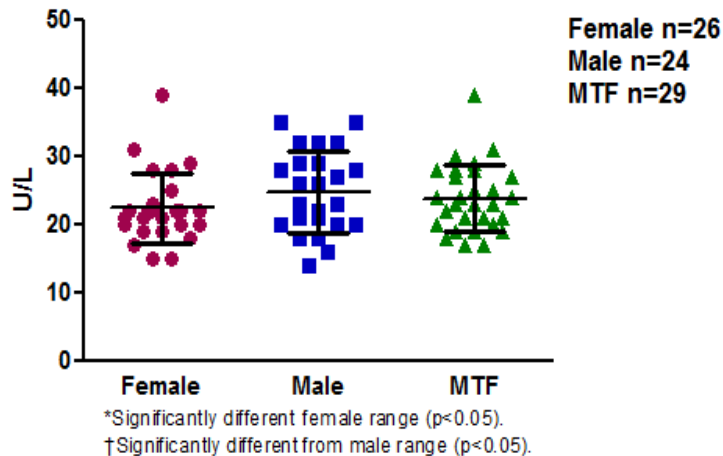
Alanine Aminotransferase (ALT)



Alkaline Phosphatase (ALP)



Aspartate Aminotransferase (AST)

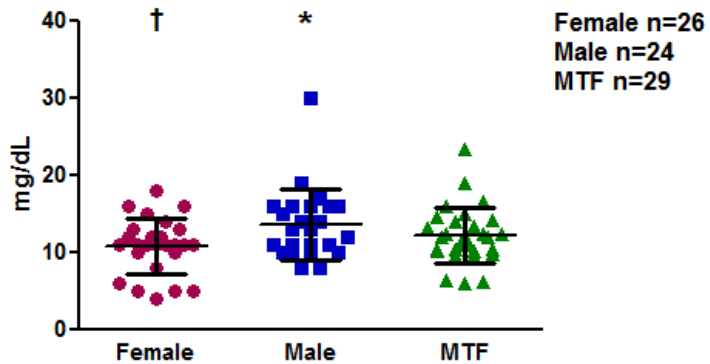


Summary

- Lipid Panel
 - Total cholesterol is no different
 - Triglycerides and HDL are the same as natal sex
 - LDL is lower than both natal and identified sex
- Liver Enzymes
 - ALT and AST are not different
 - ALP is lower than both natal and identified sex

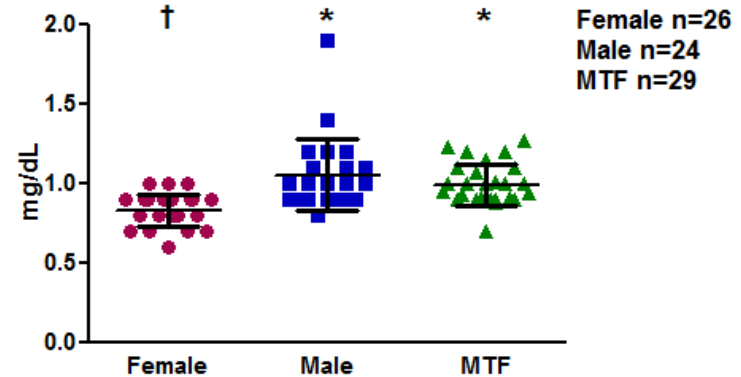
Preliminary Data – Renal Panel

Blood Urea Nitrogen (BUN)



*Significantly different female range ($p < 0.05$).
†Significantly different from male range ($p < 0.05$).

Creatinine



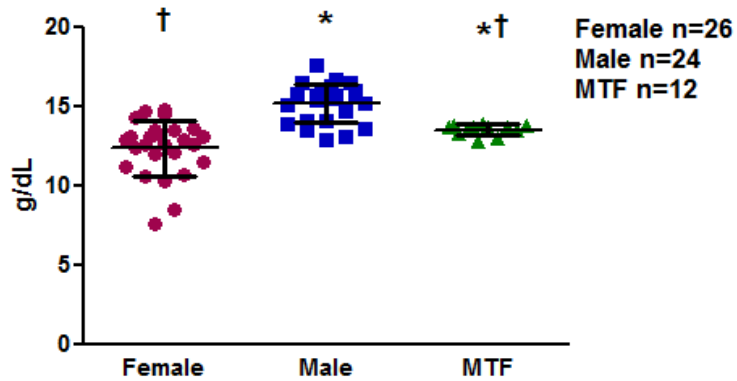
*Significantly different female range ($p < 0.05$).
†Significantly different from male range ($p < 0.05$).

Summary

- Lipid Panel
 - Total cholesterol is no different
 - Triglycerides and HDL are the same as natal sex
 - LDL is lower than both natal and identified sex
- Liver Enzymes
 - ALT and AST are not different
 - ALP is lower than both natal and identified sex
- Renal Panel
 - BUN is not different
 - Creatinine is the same as natal sex

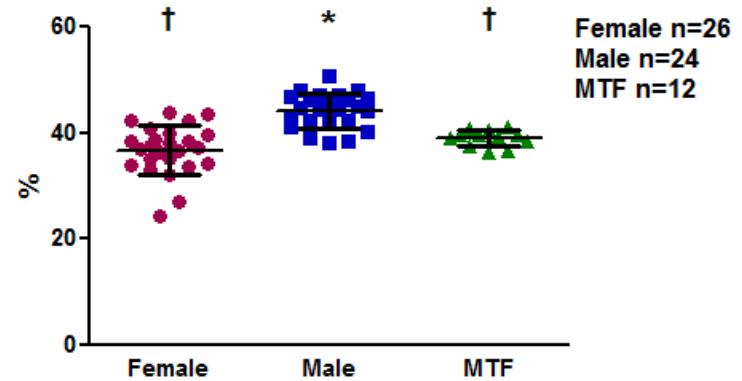
Preliminary Data -- Hematology

Hemoglobin (Hgb)



*Significantly different female range ($p < 0.05$).
†Significantly different from male range ($p < 0.05$).

Hematocrit (HCT)



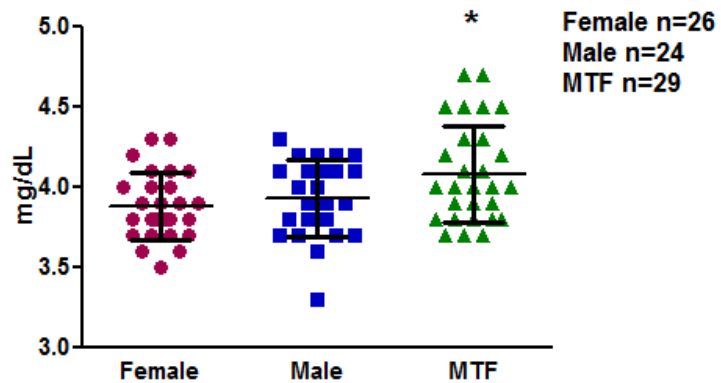
*Significantly different female range ($p < 0.05$).
†Significantly different from male range ($p < 0.05$).

Summary

- Lipid Panel
 - Total cholesterol is no different
 - Triglycerides and HDL are the same as natal sex
 - LDL is lower than both natal and identified sex
- Liver Enzymes
 - ALT and AST are not different
 - ALP is lower than both natal and identified sex
- Renal Panel
 - BUN is not different
 - Creatinine is the same as natal sex
- Hematology
 - Hematocrit is the same as identified sex
 - Hemoglobin is intermediate between natal and identified sex, but significantly different than both

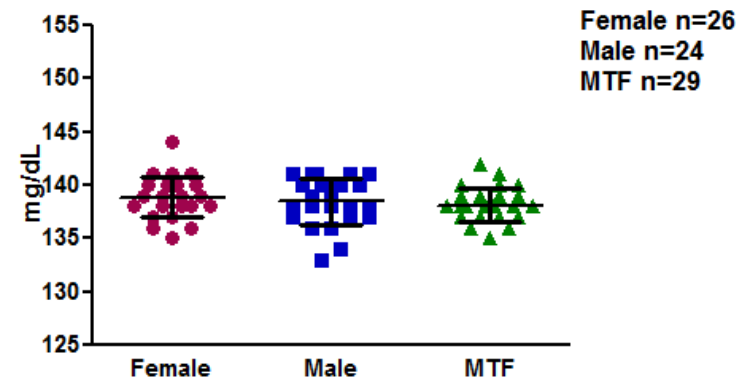
Preliminary Data -- Electrolytes

Potassium (K)



*Significantly different female range ($p < 0.05$).
†Significantly different from male range ($p < 0.05$).

Sodium (Na)



*Significantly different female range ($p < 0.05$).
†Significantly different from male range ($p < 0.05$).

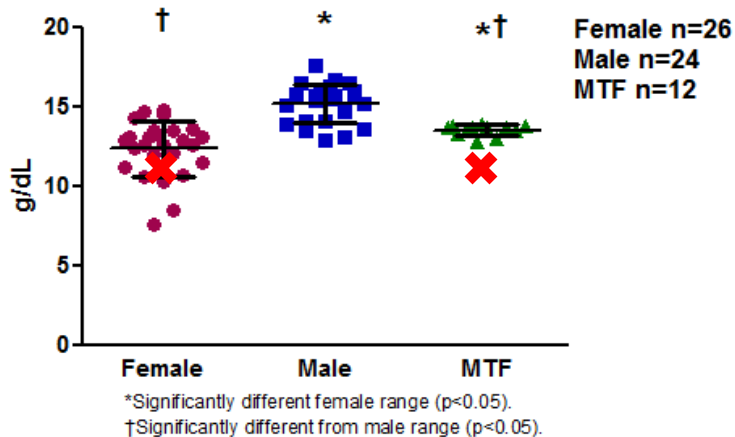
Summary

- Lipid Panel
 - Total cholesterol is no different
 - Triglycerides and HDL are the same as natal sex
 - LDL is lower than both natal and identified sex
- Liver Enzymes
 - ALT and AST are not different
 - ALP is lower than both natal and identified sex
- Renal Panel
 - BUN is not different
 - Creatinine is the same as natal sex
- Hematology
 - Hematocrit is the same as identified sex
 - Hemoglobin is intermediate between natal and identified sex, but significantly different than both
- Electrolytes
 - Sodium is not different
 - Potassium is significantly higher than identified sex and, though not significant, is also trending higher than natal sex ($p=0.056$).

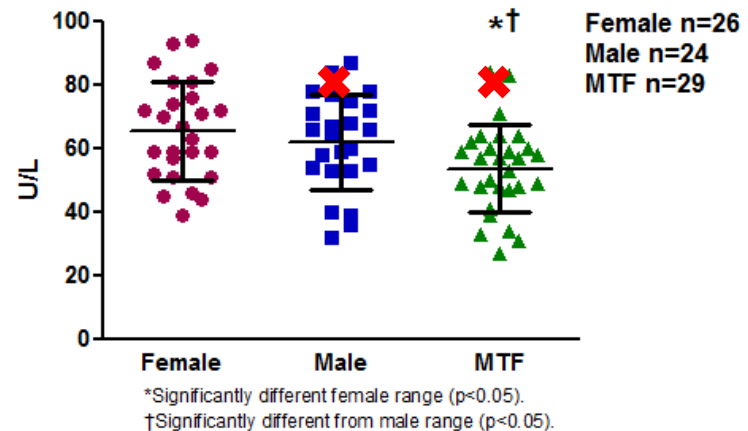
Conclusions: How should transgender patients be classified?

- No one knows!
- These data suggest that MTF patients do not fit neatly into either the male or female categories.
 - Can't just add "T" as an option on in-take forms without understanding what it means.

Hemoglobin (Hgb)



Alkaline Phosphatase (ALP)



Conclusions: How should transgender patients be classified?

- Reference ranges for male and female patients have been established based on measurements taken from hundreds of individuals.
- Our data indicates that similar studies need to be done for MTF and FTM patients.

Acknowledgements

- Vin Tangpricha MD PhD
- Colleen Kraft MD
- Corinne Fantz PhD
- Alan Wu PhD



EMORY
UNIVERSITY
SCHOOL OF
MEDICINE