Acne and Rosacea Update
Maui Derm NP+PA FALL 2017

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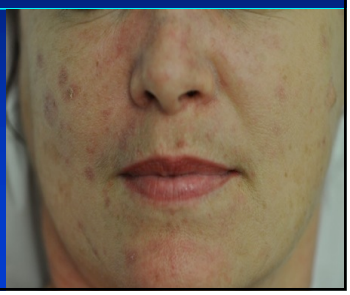
Case Study

- 32 yr. old female w/ chronic mild - moderate papulopustular acne on the central and lower face
- On BPO wash only – normal menses; no hormonal therapy
- She admits to picking
- She has "sensitive" skin



What Do We Really Understand About the Nature of Acne in the Adult Female?

DOI: 10.1111/jdv.12757 JEADV

374 FEMALE PATIENTS WITH ACNE

ORIGINAL ARTICLE

Large-scale international study enhances understanding of an emerging acne population: adult females

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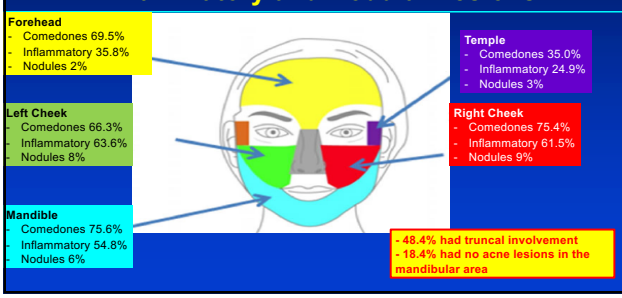
Distribution of Comedones, Inflammatory and Nodular Lesions



Study Conclusions

- Two distinct presentations:
  - ~90% similar to adolescent acne
  - ~10% mild, inflammatory/nodular acne localized to mandibular region
- Most women do not have hormonal abnormalities
- Acne is typically found in active, working women in their 20's to 40's

What Does the Study Results Suggest Us in Terms of Treatment??

- Treat their underlying disease as though they are a teenage acne patient
- ***Maintenance program (long term):***
  - Topical retinoid
  - Retinoid/BPO
  - Retinoid/topical antibiotic combo
  - BPO-combo

What About Hormonal Manipulation ?

- Oral Contraceptives
- Spironolactone

Acne Combination Therapy
Establishes Synergy Among Agents

	Decreases Sebum Production	Normalizes Keratinization or Is Keratinolytic	Decreases *P acnes*	Decreases Inflammation
Topical Therapy				
Antibiotics			♦	♦
Retinoids		♦		♦
Benzoyl peroxide		♦	♦	♦
Azelaic Acid		♦	♦	
Oral Therapy				
Antibiotics			♦	♦
Isotretinoin	♦	♦	♦	♦
Estrogens/ Antiandrogens	♦			
Spironolactone	♦			

Excess Androgens in Women

- Excess production of androgens from the ovary may also cause acne
- Should be excluded in females with:
  - acne that is persistent
  - of late onset
  - associated with hirsutism [1]
- Serological investigation in these women has revealed high circulating levels of free testosterone and DHEAS and a low concentration of sex hormone-binding globulin.[2,3]

[1] Beylot C, Doutre MS, Beylot-Barry M. Oral contraceptives and cyproterone acetate in female acne treatment. *Dermatology* 81, 70–74 (1998).
[2] Lucky AW, McGuire J, Rosenfield RL *et al.* Plasma androgens in women with acne vulgaris. *J. Invest. Dermatol.* 81, 70–74 (1983).
[3] Vexiau P, Husson C, Chivot M *et al.* Androgen excess in women with acne alone compared with acne and/or hirsutism. *J. Invest. Dermatol.* 94, 279–283 (1990).

SPIRONOLACTONE

- MOA: Is a K+ sparing diuretic that inhibits actions on both the androgen receptor and 5α-reductase (T -> 5-DHT)
- Reduces sebum production by 30–75% depending on the dose.[1 – 4]
- Used "OFF LABEL" for acne….not FDA approved
- Dosing: 50–100 mg daily (bid dosing with meals)…..Most often started at 100 mg/d
- Women with sporadic outbreaks can be successfully managed with as little as 25 mg daily[4]

[1]Muhlemann MF, Carter GD, Cream JJ *et al.* Oral spironalactone: an effective treatment for acne vulgaris in women. *Br. J. Dermatol.* 115, 227–232 (1986).
[2]Goodfellow A, Alaghband-Zadeh J, Carter C *et al.* Oral spironalactone improves acne vulgaris and reduces sebum excretion. *Br. J. Dermatol.* 111, 209–214 (1984).
[3]Lubbos H, Rose LI. Adverse effects of spironalactone therapy in women with acne. *Arch. Dermatol.* 134, 1162–1163 (1998).
[4]Thiboutot D. Acne: hormonal concepts and therapy. *Clin. Dermatol.* 22, 419–428 (2004).

SPIRONALACTONE

- Little data despite widespread use
- Cochrane analysis: "effectiveness indeterminate"
- Study of 85 women with acne, 93% demonstrated at least partial improvement in their acne, with 66% showing a marked improvement or complete clearance [1]
- Similar to other hormonal therapies: response is slow and it may take up to 3 months of continuous treatment before any benefit is observed [2]

[1]Shaw JC. Low dose adjunctive spironalactone in the treatment of acne in a retrospective analysis of 85 patients consecutively treated patients. *J. Am. Acad. Dermatol.* 43, 498–502 (2000).
[2]Marcoux D, Thiboutot D. Hormonal therapy for acne. *J. Cutan. Med. Surg.* 1(Suppl. 1), 52–56 (1996).

SPIRONOLACTONE: SIDE EFFECTS

- Usually dose dependent (>100 mg/d)
- Menstrual irregularities, potential hyperkalemia, breast tenderness, fatigue, headache, fluid retention and, rarely, melasma
- Potential for feminization effects:
  - Males: spironolactone should NOT be prescribed
  - Females: should be advised to avoid pregnancy owing to potential abnormalities to the male fetus.
- ***Hyperkalemia:*** baseline laboratory for kidney function; avoid K+ containing sports drinks

You recommend starting spironolactone but the patient reads on the internet and asks:

What about:

Hyperkalemia?
Cancer?

Is serum K+ monitoring in young healthy women on *Spironolactone* necessary?

- **Study Population:**
  - 974 healthy young women taking spironolactone for acne
  - 1165 healthy young women not taking spironolactone
- **Exclusion criteria**
  - cardiovascular disease, renal failure, and the use of medications that affect the renin-angiotensin-aldosterone system.
- There were 13 abnormal serum potassium measurements (6 erroneous/7 no action taken) in ***1802 measurements obtained among young women receiving spironolactone therapy***
  - **Yielding a hyperkalemia rate of 0.72%, equivalent to the 0.76%baseline rate of hyperkalemia in this population.**

Plovanich M; Weng QY; Mostaghimi A.*JAMA Dermatol.* 2015;151(9):941-944.

TAKE HOME POINT

- Get a baseline K+ level/renal function
- K+ monitoring in healthy females **NOT** necessary
- Avoid sports drinks containing K+
- "Healthy" = no disease in exclusion criteria

SPIRONOLACTONE: WARNING

- Aldactone® spironolactone tablets, USP WARNING Aldactone has been shown to be a ***tumorigen*** in chronic toxicity studies in rats (see Precautions).
- Aldactone should be used only in those conditions described under Indications and Usage. Unnecessary use of this drug should be avoid

Aldactone: PDR Safety Data in Rats

- 18-month study using doses of about 50, 150 and 500 mg/kg/day, there were statistically significant increases in benign adenomas of the thyroid and testes and, in male rats, a dose-related increase in proliferative changes in the liver (including hepatocytomegaly and hyperplastic nodules)
- 24-month study in which the same strain of rat was administered doses of about 10, 30, 100 and 150 mg Aldactone/kg/day, the range of proliferative effects included significant increases in hepatocellular adenomas and testicular interstitial cell tumors in males, and significant increases in thyroid follicular cell adenomas and carcinomas in both sexes.

2013 Danish study: Spironolactone and Uterine/Breast/Ovarian Cancer

- Danish database was used to study the association of breast, uterine and ovarian cancer with use of spironolactone and furosemide (comparator drug)
  - Women > 20 years old (2.3 million women)
- Increased use of both drugs in the year before cancer diagnosis: Rx was linked to cancer symptoms or hypertension
- Overall conclusion is that use of spironolactone ***does not increase*** the risk of these cancers

Biggar *et al.* Cancer epidemiology 2013:37:870-875

Start Her On

- **Spironolactone 100 mg/d**

PLUS

1. A ***topical retinoid*** 2x/week and increase gradually (over months) as tolerated OR ***BPO/Abx*** combo
2. Gentle skin care
3. Cotton gloves for pickers

What About Treating More Aggressive Acne?

Optimal use of oral antibiotic therapy for the treatment of adult acne

- United States guidelines recommend ***oral antibiotic*** duration be limited ***to 3 to 6 months*** for acne.
- ***Topical retinoids*** are recommended in combination with and as maintenance therapy after antibiotics.

Straight C et al. J Am Acad Dermatol 2015;72:822-7

STUDIES: Combination Oral Antibiotic and Topical Retinoid

- Minocycline + Tazarotene
- Doxycycline + Adapalene
- Doxycycline + Adapalene/BPO

Leyden J. et al. Arch Dermatol. 2006 May;142(5):605-12. Thiboutot DM, et al Arch Dermatol. 2006 May;142(5):597-602. Thiboutot DM, et al Skinmed. 2005 May-Jun;4(3):138-46. Tan J, et al J Drugs Dermatol. 2012 Feb;11(2):174-80.

Moderate-Severe Acne: Take Home Point:

- Start patient on an oral antibiotic + topical retinoid for 1 – 3 months
  - Preferably use a ”cycline” i.e. tetracycline, doxycycline or minocycline
- Discontinue the oral antibiotic in 1-3 months and continue the use topical retinoid

ACNE AND PREGNANCY

Case Report

Management of severe acne during pregnancy: A case report and review of the literature☆,☆☆

S.Z. Awan, MD, J. Lu, MD *

International Journal of Women's Dermatology 3 (2017) 145–150

CLINICAL REVIEW

Treatment of Acne in Pregnancy

Anna L. Chien, MD, Ji Qi, BA, Barbara Rainer, MD, Dana L. Sachs, MD, and Yolanda R. Helfrich, MD

CLINICAL REVIEW Treatment of Acne in Pregnancy Anna L. Chien, MD, Ji Qi, BA, Barbara Rainer, MD, Dana L. Sachs, MD, and Yolanda R. Helfrich, MD
JABFM March–April 2016 Vol. 29 No. 2 254-262 http://www.jabfm.org

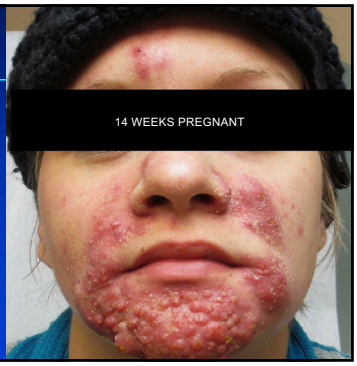
Severe Acne During Pregnancy

30 yo WF primigravid – 14 week pregnant

Presents w/ painful acne 6-7 x weeks

Treatment at time of initial visit: she was on oral erythromycin after failing oral amoxicillin and cephalexin

Hx of acne as teen controlled w/ adapalene, PO minocycline and oral contraceptives ALL of which were D/C's 6 weeks before conception



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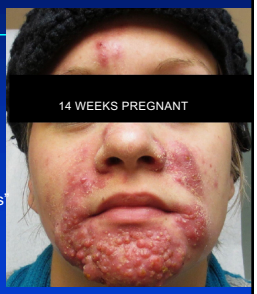
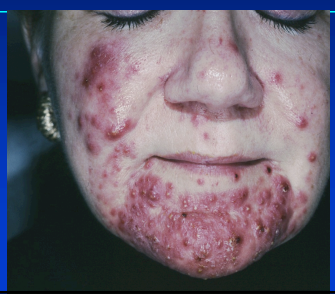
Severe Acne During Pregnancy

- **Differential Dx:**
  - ***Acne conglobata:***
    - Long hx of acne
    - Truncal involvcement
    - Lack of "trigger induced flares
  - ***Pyoderma faciale:***
    - Facial distribution c/w PF
    - Trigger induced flushing: "Rosacea fulminans"
    - No preceding hx acne
    - Lack truncal involvement
    - Lack of comedones
    - Demographics



Plewig G. Pyoderma faciale. A review and report of 20 additional cases: Is it rosacea? Arch Dermatol 1982;128(12):1611–7.

A Different Case of: Pyoderma Faciale



FDA GUIDELINES ON PREGNANCY AND LACTATION

- 2014: FDA first approved **Pregnancy and Lactation Labeling Rule (PLLR)** as a replacement for the lettered pregnancy categories (Pregnancy Category A, B, C, D, X)
- June 2015, lettered categories were replaced with a complete analyses of the risks and benefits of each newly approved medication.
- **PLLR**:
  - Each recommendation contains a synopsis of the existing data during pregnancy and lactation.
  - Lists adverse effects were observed during animal studies or human cases
  - Discusses whether the drug in question crosses the placenta or is secreted into breast milk
  - Whether a pregnancy registry exists for a particular drug
  - ***References to the old categories may be made.***
- **SUMMARY:** The PLLR is designed, when consulting with an individual regarding risk/benefit of a drug to facilitate the communication regarding a "patient based" decision

Therapeutic Options: TOPICALS

- **TOPICALS**: First Line Agents for Mild-Moderate Acne in Pregnancy
  - ***Topical clindamycin (Category B)****....rare reports of C. Difficile (?? Clinicially significant)*
  - ***Topical erythromycin (Category B)***
- ***Benzoyl peroxide (BPO) (Category C)***
  - Strong keratolytic, comedolytic, and antibacterial properties
  - Issue of Category C: risk of congenital malformations is theoretically small
  - Most experts agree on its safety during pregnancy
- ***BPO/Clindamycin Combination:*** superior to each case individually and may decrease the risk of antibiotic resistance
- ***Azelaic acid: Category B***
  - Bacteriostatic broad antimicrobial effects (mechanism unknown)
  - Used in acne, rosacea, perioral dermatitis → good for "overlap cases"
  - Well documented safety profile during pregnancy

Therapeutic Options: TOPICALS…Cont'd

- ***Topical retinoids:*** adapalene, tretinoin, tazaretene
  - Systemic retinoids absolutely contraindicated → concern extrapolated to topicals
  - Animal studies: → equivocal teratogenicity with "supra-therapeutic" doses of topical tretinoin BUT none with adapalene; tazarotene (Category X) has 6% absorption → contraindicated
  - Case reports on safety/teratogenecity conflicting →: **NOT recommended**
- ***Sodium sulfacetamide: (Category C)***
  - Inhibits bacterial dihydropteroate synthetase → decreases folic acid formation. Despite this,
  - No reports of congenital anomalies have been linked to sulfacetamide OR the combination of sulfacetamide/sulfur
  - **Not contraindicated during pregnancy**

Therapeutic Options: TOPICALS…Cont'd

- ***Topical Dapsone***
  - "New"….lacks decades of safety data
  - No link to congenital malformations
  - Only recommended when benefits clearly outweigh risks
- ***Topical Salicylic acid***
  - Strong keratolytic agent
  - Deemed safe when used in a "limited scope for short periods of time"

Therapeutic Options: SYSTEMIC

- **Beta-lactams:** first-line agents.
  - Penicillins and cephalosporins: compatible with pregnancy and show efficacy in the treatment of acne
  - Amoxicillin: (Category B) aminopenicillin and has shown good efficacy
    - Increased risk for cleft lip and palate after third-trimester
    - Often been used during pregnancy for a variety of conditions
    - Most studies support its safety
- **Macrolides:** recommended the next indicated class of antibiotics when macrolides fail
  - Erythromycin base or ethylsuccinate is recommended over erythromycin estolate due to the non-negligible risk of maternal hepatotoxicity
  - Azithromycin: effective; compatible with pregnancy

Therapeutic Options: SYSTEMIC

- **Oral metronidazole:**
  - Rarely used to treat uncomplicated acne
  - Common treatment for perioral dermatitis.
  - Excellent record of safety during pregnancy
  - Frequently used as the treatment of choice for several common non-dermatologic infections during pregnancy
  - In patients resistant to standard oral antibiotics, metronidazole may be a safe and reasonable next step.
- **Oral retinoids: Isotretinoin……Category X**
  - clear causal link to congenital malformations and are absolutely contraindicated during pregnancy
- **Spironolactone:**
  - Commonly used to treat adult acne due to its anti-androgenic effects
  - Contraindicated during pregnancy due to the risk of feminization of the male fetus

Therapeutic Options: SYSTEMIC

- **Tetracyclines:**
  - Contraindicated after 15 weeks of gestation due to deposition fetal teeth and bones with subsequent malformations
  - Avoid during pregnancy unless the benefits clearly outweigh the risks.
- **Trimethoprim:**
  - 1st trimester use associated with an increased risk of spontaneous abortion
  - Avoid during pregnancy unless the benefits clearly outweigh the risks.
- **Fluoroquinolones:**
  - Associated with tendinopathy and chondrotoxicity in animals; teninopathy in adverse event self-reporting databases
  - No clear fetal risk has been established, amounts of fluoroquinolones cross the placenta
  - Avoid during pregnancy: theoretical risk of fetal cartilage damage and the relative benignity of acne.

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Therapeutic Options: SYSTEMIC

- **Oral prednisone:**
  - May be linked to cases of cleft palate
  - High doses should generally be coordinated with an obstetrician. Our patient presented with a rare case of severe acne
  - Acne that is refractory to multiple modalities, prednisone may be used in low-to-moderate doses in controlled courses.
  - *Safer alternatives exist and we do not advocate the routine use of corticosteroid medications during pregnancy unless the benefits clearly outweigh the risks.*
- Intralesional steroids:
  - Effective in treating individual acne nodules
  - Generally 2.5 mg/cc Triamcinalone suspension used
  - Risk of depressed scar with too high a concentration or amount
  - Monitor cumulative amount injected

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Therapeutic Options: Energy Devices

- ***In refractory cases, alternative methods of treatment may be considered.***
- **Narrowband ultraviolet B (NB-UVB) phototherapy:**
  - Anti-inflammatory properties that have been shown to be effective in the treatment of acne during pregnancy
  - Excellent safety record during pregnancy
  - Risk: decrease in serum folate levels with as few as 18 sessions of NB-UVB – check serum levels and supplement
  - Short-term treatment during pregnancy is likely safe and the highest risk with folate deficiency occurs in the early stages of pregnancy. Still, experts recommend caution

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Therapeutic Options: Energy Devices

- **Photodynamic Therapy (PDT) Category C**
  - Animal reproductive studies are not available.
  - Efficacious in controlled studies
  - Painful and requires multiple session in a dermatology office
  - Lack of insurance coverage
- **Pulsed dye, KTP (potassium titanyl phosphate), NdYAG (neodymium-doped yttrium aluminum garnet)**
  - Demonstrate efficacy for the treatment of acne with excellent overall safety in general population
  - Shallow depth of penetration conceptually poses little risk to the fetus
  - Effects of a painful stimulus in the late stages of pregnancy are unclear
  - Actual reports of use during pregnancy are limited and make it difficult to establish clear safety guidelines

1. Hongcharu W, Taylor CR, Chang Y, Aghassi D, Suthamjariya K, Anderson RR. Topical ALA-photodynamic therapy for the treatment of acne vulgaris. J Invest Dermatol 2000;115:183–92.
2. de Leeuw J, van der Beek N, Bjerring P, Neumann HAM. Photodynamic therapy of acne vulgaris using 5-aminolevulinic acid 0.5% liposomal spray and intense pulsed light in combination with topical keratolytic agents. J Eur Acad Dermatol Venereol 2010; 24:460 –9

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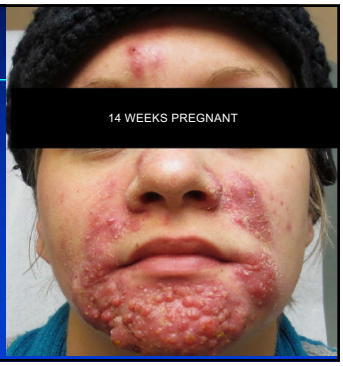
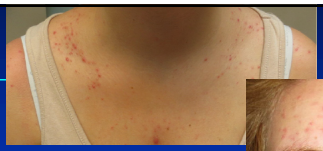
INITIAL Therapeutic Course

Prednisone 40 mg/d initiated due to patient's pain following OB-GYN consult

Erythromycin continued at 250 bid PO



20 -28 Weeks Gestation



Week 20: slight acne flare on trunk likely due to PO steroids

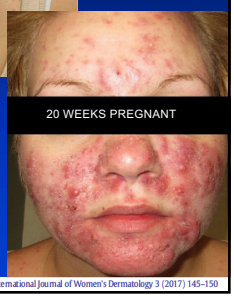
Prednisone lowered to 20 mg/d and PO erythromycin doubled to 500 mg bid PO

Week 28: no worsening BUT no improvement

Erythromycin PO D/C'd

Metronidazole PO started at 250 bid

Sodium sulfacetamide (10%) and sulfur (5%) topical solution started



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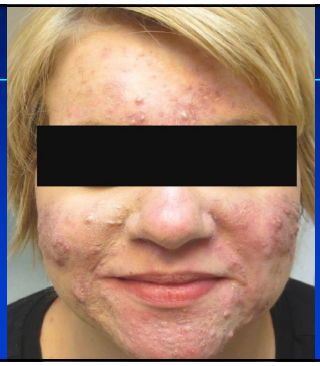
34 Weeks Gestation

Several weeks of: oral metronidazole, low dose prednisone and topical sulfacetamide and sulfur lotion

Prednisone tapered off



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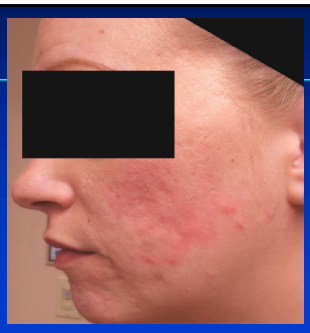
One Month of Isotretinoin Therapy Post Delivery and Breastfeeding

- Successful delivery and no complications
- Remained on therapy
- After finishing 3 months breastfeeding she was begun on isotretinoin therapy



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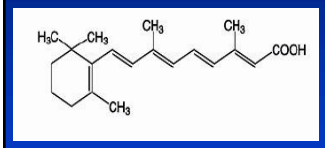
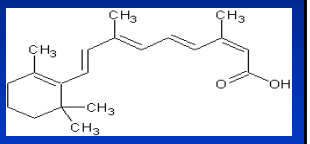
Changing the Paradigm on Isotretinoin Dosing

Retinoids



Tretinoin (Topical)



Isotretinoin SYSTEMIC Retinoid
13-cis-retinoic acid: developed by Michael Sporn MD

ISOTRETINOIN DOSING

- **Recommended duration and dose:**

  determined by clinical response

  NOT cumulative dose

[1]Layton AM. Disorders of the sebaceous glands. In: *Rook's Textbook of Dermatology (8th Edition)*. Burns DA, Breathnach SM, Cox NH *et al.* (Eds). Blackwell Publishing, London, UK (2010). [2] Goulden V, Clark M, McGeown C *et al.* Treatment of acne with intermittent isotretinoin. *Br. J. Dermatol.* 137, 106–108 (1997).
[3]Akman A, Durusoy C, Senturk M *et al.* Treatment of acne with intermittent and conventional isotretinoin: a randomized, controlled multicentre study. *Arch. Dermatol. Res.* 299, 467–473 (2007).

How Does Isotretinoin Work?

- ***Inhibition of sebum secretion***
  - Apoptosis of sebocytes (90% by 1 week on 1 mg/kg/day)
    - J. Invest. Derm 126:2178, 2006
- ***"Normalizing" anti-P. acnes response***
  - Down-regulates ***TLR2 receptor*** on mononuclear cells
    - J. Invest. Derm. 132:2198, 2012

High Dose Isotretinoin

- Traditional: 120 -150 mg/kg (i.e. 1mg/kg/day for 4 – 5 months) has a ~20% relapse rate
  - youth/severity/diet/hormones
- High dose[1]: 290 mg/kg (≥ 1.3 mg/kg/day) had 12% relapse over 3 years (retrospective study; n=80)
- High dose[2]: >220mg/kg - 27% relapse vs. 48% in <220mg/kg (prospective; avg duration 6.3 mos to achieve 1 mo. "clear")
  - Increased dermatitis

(1)Cyrulnik AA, et allnt J Dermatol 2012;51 (9): 1123-1130 (2)Blasiak RC1 etalJAMA Derm 149:1392, 2013

Isotretinoin Adverse Events

Common AEs
- dry skin
- dry lips
- high TGs
- acne flare

Uncommon AEs
- elevated CK
- elevated AST & ALT
- dry eyes
- decreased night vision
- depression
- acne fulminans

Setting Expectation: What Happens AFTER Stopping Isotretinoin

- F/U 1 – 10 years (> 1,100 pts) post clearance using Isotretinoin
  - Topicals alone: 16-21%
  - 3.3 – 39% topicals + oral antibiotics
  - 16 – 23% retreated w/ at least 1 course of Iso

Suppl JCAD Feb 2014 vol 7 #2

Patients (%) Receiving 2 or More Txs Based on Age

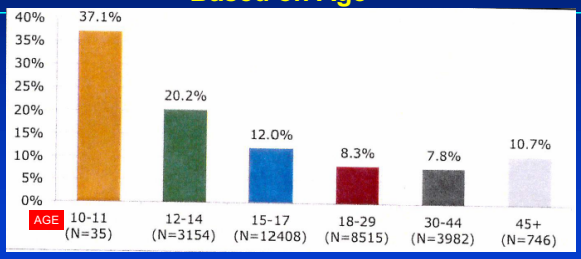


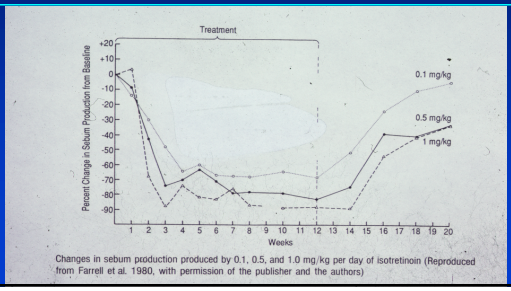
Fig 3 Suppl JCAD Feb 2014 vol 7 #2

A CASE FOR LOW DOSE ISOTRETINOIN: 0.1 mg/kg/day

Isotretinoin Efficacy

- Dose ranging studies in the 1970s showed 0.1 mg/kg/day is as effective as 1 mg/kg/day
- Relapse rate was dose dependent
  - 10-20% at 1 yr. following 1mg/kg/day
  - 40% at 1 yr. following 0.1 mg/kg/day
- Isotretinoin has a profound stimulus to granulation tissue

Isotretinoin Dose (0.1, 0.5 & 1.0 mg/kg/day Response: SEBUM PRODUCTION



Changes in sebum production produced by 0.1, 0.5, and 1.0 mg/kg per day of isotretinoin (Reproduced from Farrell et al. 1980, with permission of the publisher and the authors)

Isotretinoin Inflammatory Lesion Response Dose Ranging Study 0.1, 0.5 &1.0 mg/kg/day

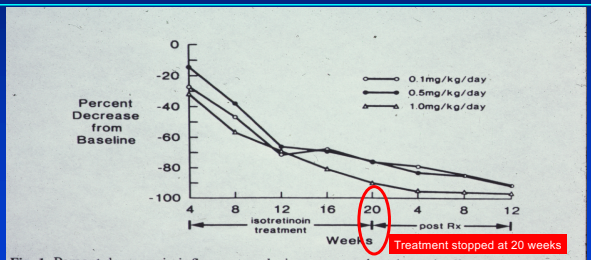


Fig. 1. Percent decrease in inflammatory lesions greater than 4 mm in diameter on the face during isotretinoin therapy.

Can We Give Isotretinoin Once Daily?

- No significant changes in PK profile after 5 days (steady state)
- After 25 days of Iso 40 BID serum levels were stable (n-20)
- Switch to Iso 80 QD after Day 30 caused a marked rise in peak (Cmax) Iso blood levels compared to Iso 40 BID
  - BID dosing may minimize side effects (***unstudied***)
  - BID dosing of Iso may minimize reduced GI absorption if there is an absorption ceiling with a single high dose (endogenous or exogenous)

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Treatment Duration….How Long Should We Treat?

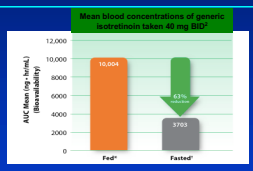
- Males: maintain on low dose (10-20 mg/day)….2-3 months after clearance; restart if necessary
- Females: Consider maintenance on low dose for 2-3 months after clearing then change to spironolactone to minimize isotretinoin exposure

Isotretinoin Failures: What Then?

Isotretinoin "Failures"

- 80% treated with 120-150 mg/kg (cumulative dose) never have acne again
- ***Causes of failure***
  - Under dosing (compliance/failure to take w/ meals)
  - Virilization
  - Young pt. with bad disease

High-fat meal enhances absorption[1]

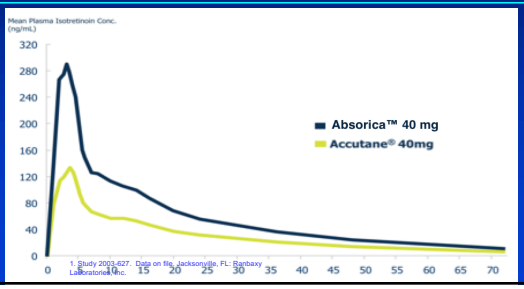


Dosed following a standardized high-fat meal
† Dosed following an overnight fast of ≥ 10 hours

In a fed state, the maximum drug concentration of generic isotretinoin was approximately 2.9 times more than in the fasting state.

Colburn WA, Gibson DM, Wiens RE, Hanigan JJ. Food increases the bioavailability of isotretinoin. *J Clin Pharmacol*. 1983 Nov-Dec;23(11-12):534-539 1.. 2. Sotret prescribing information. Jacksonville, FL: Ranbaxy Laboratories, Inc; February 2010.

Absorption of Absorica™ is ~2x greater (83%) than Accutane® in the absence of food[1]



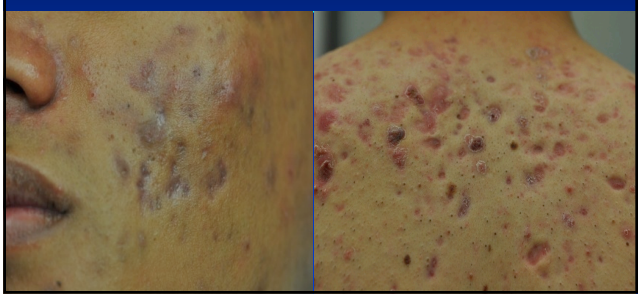
1. Study 2003-627. Data on file. Jacksonville, FL: Ranbaxy Laboratories, Inc.

Isotretinoin Flares: What to Do?

ISOTRETINOIN: Initial Severe Flare

- Approx. 6% of pts. will experience a moderate-to-severe flare in their acne during the first few weeks of treatment

SEVERE ACNE FLARE WHEN STARTED ON ISOTRETINOIN



Approaches to decreasing the risk of acne flares with isotretinoin

Regimen A

- ***FIRST***: Treat with p.o. prednisone 1 mg/kg/day for 3 - 4 weeks to calm the inflammation and taper off
- ***THEN***: add low dose isotretinoin 10 mg/day and gradually increase the isotretinoin as you taper off the prednisone

Regimen B

- ***FIRST:*** low-dose isotretinoin 10 mg/day *at the same time* as beginning prednisone at 1 mg/kg/day
- Treat with prednisone and low-dose isotretinoin for at least a month
- Then begin to taper the prednisone and increase the isotretinoin dose as in Regimen A

Isotretinoin Laboratory Monitoring ….What Should We Be Doing ?

Study Design

- Reviewed lab data from 515 patients with acne undergoing 574 courses of isotretinoin from March 2003 to July 2011.
- Frequency, timing, and severity of abnormalities were determined.

REF: Hansen TJ, et al J Am Acad Dermatol 2016;75:323-8.)

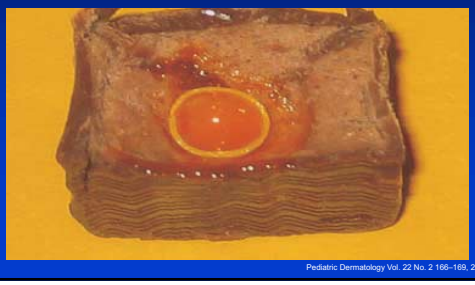
CBC, LFT, TG/Chol Levels: B/A Isotretinoin

- ***Leukopenia or thrombocytopenia*** (clinically insignificant) occurred in 1.4% and 0.9% of pts.
- ***Elevated LFTs:*** infrequent and not significantly increased compared with baseline (1.9% vs 1.6% at baseline).
- ***Significant elevations occurred with triglyceride (19.3%) and cholesterol (22.8%) levels.***
  - The most severe abnormalities were grade 2 (moderate).
  - Mean duration of treatment before abnormalities were detected was: ***56.3 days (increased TG),*** 61.9 days for (increased liver ALA), and ***50.1 days (increased cholesterol)***

STUDY: Lab Testing Recommendations

- ***Conclusion:*** In healthy patients with ***normal baseline lipid panel and liver function test results,*** repeated studies ***should be performed after 2 months*** of isotretinoin therapy.
  - If findings are normal, no further testing may be required.
- ***Routine complete CBC*** monitoring is ***not*** recommended.
  - REF: Hansen TJ, et al J Am Acad Dermatol 2016;75:323-8.)

Can I give Isotretinoin to young children?..... Frozen Isotretinoin inside a Milky Way Bar



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MAHALO AND ALOHA!