Acne
Causes and practical management
Acne
Causes and practical management

F. William Danby
Adjunct Assistant Professor of Surgery
Section of Dermatology
Geisel School of Medicine at Dartmouth
Hanover, New Hampshire,
USA
## Contents

Preface, ix

Practical acne therapy, xii
  Genetics, xii
  Diet, xii
  Hormones, xii
  Stress, xii
  Comedones (plugs in pores), xiii
  Blemishes—a brief catalogue, xiv
  Nodules, xv
  Scars and sinuses, xvi
  Support, xvii

Introduction, xviii
  Nomenclature, xix

The three acnes and grading, xx
  Acne vulgaris, xx
  Acne rosacea, xxii
  Acne inversa (hidradenitis suppurativa), xxiii

Grading the three acnes, xxvi
  Acne vulgaris, xxvi
  Acne rosacea, xxvi
  Acne inversa (hidradenitis suppurativa), xxvi

1 The three acnes and their impact, 1
  1.1 Acne vulgaris, 1
    1.1.1 Terminology, 1
    1.1.2 The starting point, 3
  1.2 Acne rosacea, 3
    1.2.1 The “pimply” part, 4
    1.2.2 The “redness” part, 4
    1.2.3 The third part, the firm fibrosis, 6
    1.2.4 Part four—ocular rosacea, 7
    1.2.5 Putting it all together, 7
    1.2.6 The inflammatory epiphenomena in acne rosacea, 8
    1.2.7 The “acne rosacea” versus “rosacea” controversy, 12
    1.2.8 Summary, 12
  1.3 Acne inversa (formerly hidradenitis suppurativa), 12
    1.3.1 Before the rupture, where and why?, 15
    1.3.2 After the rupture, what next?, 15
    1.3.3 So what invaders are important in acne inversa?, 15
    1.3.4 What makes this disease behave so much worse than acne vulgaris?, 18
    1.3.5 So what can one possibly do to settle down all this inflammation?, 21
    1.3.6 So how do you get rid of all this material?, 25
    1.3.7 What does the future offer?, 25
  1.4 The psychology of acne, 26
    1.4.1 Acne as a stress, 26
    1.4.2 Acne and self-image, 27
    1.4.3 Isotretinoin therapy and the psyche, 27
    1.4.4 The isotretinoin–depression question, 28
    1.4.5 Isotretinoin in perspective, 29

2 The folliculopilosebaceous unit—the normal FPSU, 31
  2.1 Anatomy, 31
  2.2 Genetics, 31
    2.2.1 Acne vulgaris, 31
    2.2.2 Acne rosacea, 34
    2.2.3 Acne inversa/hidradenitis suppurativa (AI/HS), 34
    2.2.4 The Scottish twins, 34
  2.3 Epigenetics, 35
    2.3.1 The farmer’s boys, 36
  2.4 Embryology, 36
  2.5 Histology, 38
    2.5.1 Onwards and downwards, 38
    2.5.2 What is going on inside the FPSU?, 40
  2.6 Physiology, 42
    2.6.1 Hair first, 42
    2.6.2 Oil second, 42
    2.6.3 Last but definitely not least: the follicle, 43
    2.6.4 Looking deeper, 44
  2.7 Biochemistry, 44
  2.8 Hormones, enzymes, receptors, and the intracrine system, 45
    2.8.1 The intracrine system, 48
  2.9 FoxO1 and mTORC1, 49
    2.9.1 The next step, 50
    2.9.2 The broad view, 51
3 Pathogenetic mechanisms summarized, 54
   3.1 Acne vulgaris, 54
   3.2 Acne rosacea, 56
   3.3 Acne inversa/hidradenitis suppurativa (AI/HS), 57
   3.4 Other variants, 60
      3.4.1 *Malassezia* folliculitis, 60
      3.4.2 Eosinophilic pustular folliculitis (Ofuji’s disease), 62
      3.4.3 Dissecting terminal folliculitis, 63
      3.4.4 Epidermal growth factor receptor (EGFR) inhibitor eruption, 64
      3.4.6 *Acné excoriée des jeunes filles*, 65
4 The acne hormones, 67
   4.1 The endogenous hormones, 67
      4.1.1 Androgens and their sources, 67
      4.1.2 Estrogens and their sources, 68
      4.1.3 Progesterone and the progestroids, 68
      4.1.4 Insulin, 69
      4.1.5 Growth hormone and insulin-like growth factor-1, 72
   4.2 The exogenous hormones, 72
      4.2.1 Anabolic steroids, 72
         4.2.1.1 Mothers’ milk, 72
         4.2.1.2 Muscle makers, 74
      4.2.2 Oral contraceptive hormones, 74
         4.2.2.1 Oral estrogens, 74
         4.2.2.2 Oral progestins, 75
         4.2.2.3 Extended cycles, 75
   4.2.3 Other exogenous birth control hormones, 77
      4.2.3.1 Implants, 77
      4.2.3.2 Intrauterine devices, 78
      4.2.3.3 Intravaginal devices, 78
      4.2.3.4 Topicals: the patches, 78
      4.2.3.5 Intramuscular (depot) injections, 78
   4.2.4 Dietary sources of hormones, 78
      4.2.4.1 The impact of diet on acne, 80
         4.2.4.1.1 The ice cream salesman’s son, 81
         4.2.4.1.2 Reproductive hormones, 81
         4.2.4.1.3 Insulin, 81
         4.2.4.1.4 Insulin-like growth factor 1 (IGF-1), 82
   4.2.4.5 Growth factors and androgens combined, 82
   4.2.4.6 Dairy intolerance, 82
   4.2.4.2 Carbohydrate load versus dairy load, 83
5 Exogenous acnegens and acneform eruptions, 87
   5.1 Chemicals and medications, 87
   5.2 Endocrine imitators and disruptors, 87
      5.2.1 Environmental contamination, 88
   5.3 Foods, 88
      5.3.1 Iodine and bromine, 89
      5.3.2 Chocolate, 89
      5.3.3 Casein and whey, 90
   5.4 Photodamage, glycation, and the acne and aging processes, 91
   5.5 Smoking and nicotine, 91
6 Follicular flora, fauna, and fuzz, 93
   6.1 *Propionibacterium acnes* (*P. acnes*), 93
      6.1.1 Normal role of *P. acnes*, 94
      6.1.2 Pathogenic role of *P. acnes*, 94
   6.2 *Malassezia* species, 95
      6.2.1 Normal role, 95
      6.2.2 Immunogenicity, 97
      6.2.3 Pruritogenicity, 98
      6.2.4 *Malassezia* in the acnes, 98
   6.3 Staph, Strep, and Gram-negative organisms, 99
   6.4 *Demodex*, 99
   6.5 Vellus hairs, 101
7 The inflammatory response, 103
   7.1 Innate immunity, 103
   7.2 Adaptive (acquired) immunity, 104
   7.3 Inflammation as the primary acnegen, 104
   7.4 Mediators, cellular and humoral, and neuroimmunology, 105
   7.5 Allergy (shared antigens), 106
   7.6 Inflammation, pigment, and PIH, 106
   7.7 Inflammation and scarring, 107
8 Management, 109
   8.1 Prevention, 109
   8.2 General principles of management, 111
   8.3 Diet, 111
      8.3.1 Dairy, 112
         8.3.1.1 The deli-planning heiress, 114
         8.3.1.2 The pharmaceutical executive, 115
      8.3.2 Carbohydrates, glycemic load, and hyperinsulinemia, 115
8.3.3 The paleolithic diet, 116
8.3.4 High-fructose corn syrup (HFCS), 116
8.3.5 Metformin, 116
8.3.6 Synthesis and summary, 117

8.4 Comedolytics and other topicals, 117
8.4.1 Standard topical comedolytics, 118
8.4.1.1 Retinoids, 118
8.4.1.2 Benzoyl peroxide, 119
8.4.1.3 Salicylic acid, 120
8.4.1.4 Alpha and beta-hydroxy acids, 120
8.4.2 Unclassified topicals, 120
8.4.2.1 Azelaic acid, 120
8.4.2.2 Sulfur, 121
8.4.2.3 Zinc compounds, 121
8.4.2.4 Resorcinol, 121
8.4.3 Systemic comedolytics, 121
8.4.3.1 Vitamin A, 121
8.4.3.2 Isotretinoin, 121
8.4.3.2.1 Teratogenicity, 122
8.4.3.2.2 Contraception, 122
8.4.3.2.3 Inflammatory bowel disease, 123
8.4.3.2.4 Depression, 123
8.4.3.2.5 Other side effects, 125
8.4.3.2.6 The convict who looked like Chief, 127
8.4.3.3 Acitretin, 127
8.4.3.4 Summary, 128

8.5 Anti-inflammatories and antimicrobials, 128
8.5.1 Antibiotics as anti-inflammatories, 128
8.5.1.1 In acne vulgaris, 128
8.5.1.2 In acne rosacea, 129
8.5.1.3 In acne inversa, 129
8.5.1.4 In dissecting terminal folliculitis (DTF) and acne keloidalis, 129
8.5.2 Antibiotics as antibiotics, 130
8.5.3 Ketoconazole, ivermectin, and crotamiton, 130
8.5.3.1 In acne vulgaris, 132
8.5.3.2 In acne rosacea, 133
8.5.3.3 In acne inversa/hidradenitis suppurativa and dissecting folliculitis and cellulitis, 135
8.5.4 Steroids, 135
8.5.4.1 The Marine, 136
8.5.5 Nonsteroidal anti-inflammatory drugs (NSAIDs) and biologics, 137
8.5.6 Phototherapy, 137
8.5.7 Post-inflammatory hyperpigmentation, 138
8.5.7.1 Prognosis, 141

8.6 Hormone manipulations and therapy, 141
8.6.1 Birth control pill selection, 141
8.6.1.1 Estrogens, 142
8.6.1.1.1 Warnings, 142
8.6.1.2 Progestins, 143
8.6.2 Androgen receptor blockade, 143
8.6.2.1 Spironolactone, 144
8.6.2.2 Cyproterone acetate, 146
8.6.2.3 Flutamide, 146
8.6.2.4 Drospirenone, 146
8.6.2.5 Topical androgen blockers, 147
8.6.3 Dihydrotestosterone minimization, 147
8.6.3.1 Finasteride, 147
8.6.3.2 Dutasteride, 147
8.6.3.3 Diet, 148
8.6.4 Phototherapy–hormone interactions, 149

8.7 Surgery, 150
8.7.1 Acne vulgaris, 150
8.7.1.1 Acne surgery for patients, 150
8.7.1.2 Acne surgery for physicians, 151
8.7.2 Acne rosacea, 152
8.7.3 Acne inversa/hidradenitis suppurativa, 153
8.7.3.1 Mini-unroofing by punch biopsy, 153
8.7.3.2 Unroofing, 154
8.7.3.2.1 The Trucker, 155
8.7.3.3 Wide surgical excision, 157
8.7.3.4 Healing options, 158
8.7.3.4.1 Primary closure, 158
8.7.3.4.2 Secondary intention, 159
8.7.3.4.3 Split-thickness mesh grafting, 160

8.8 Lights and lasers, 162
8.8.1 Light and other radiation in acne, 162
8.8.1.1 Radiation’s targets, 163
8.8.1.2 Light as a practical acne therapy, 164
8.8.2 Lasers, 165

9 Acne in pregnancy, 171
9.1 Epidemiology, 171
9.2 Pathogenesis, 172
9.3 Team up with Mother Nature, 173
9.4 Targeting therapy, 173
  9.4.1 Clinical manifestations, 173
  9.4.2 Pathology, 173
  9.4.3 Diagnostic evaluation, 173
  9.4.4 Overview and general approach to treatment, 174
  9.4.5 Milk and pregnancy, 174
  9.4.6 Active therapy, 175
    9.4.6.1 Avoidance of harm, 175
    9.4.6.2 Lesion-directed therapy, 177
    9.4.6.3 Nonprescription topicals, 177
    9.4.6.4 Antimicrobials, 177
    9.4.6.5 Combination topicals, 178
    9.4.6.6 Anti-inflammatories, 178
    9.4.6.7 Hormone blockers, 178
    9.4.6.8 Procedural therapies, 179
9.5 Discussion, 179
9.6 Summary and conclusion, 179

10 Putting it all together, 182
  10.1 Lifestyle choices and the acnes, 182
    10.1.1 The “processed cheese queen”, 184
    10.2 Therapeutic choices and the acnes, 184
  10.2.1 Acne vulgaris, 184
  10.2.2 Acne rosacea, 185
  10.2.3 Acne inversa/hidradenitis suppurativa, 185
10.3 Conclusion, 186

11 Appendices, 187
  11.1 Appendix A: the rosacea “classification and staging” controversy, 187
  11.2 Appendix B: the dairy versus carbohydrate controversy, 189

12 The handouts, 193
  12.1 Acne, 194
  12.2 The “zero-dairy” diet, 197
  12.3 The risks and benefits of isotretinoin, 199
  12.4 The Paleo diet, 204
  12.5 Acne inversa/Hidradenitis suppurativa (AI/HS), 209
  12.6 Yasmin/Ocella/Zarah or Yaz/Gianvi extended cycle for acne therapy, 213

Index, 215
Preface

This book came to be written for one very simple reason. Somebody suggested that Martin Sugden, my initial contact at Wiley, approach me to write it. While I had considered the possibility of a book—indeed, friends and colleagues had encouraged me to take the leap—the search for a publisher seemed daunting and life’s other commitments (plus a serious lifelong expertise in procrastination) ruled.

Martin’s invitation arrived at a time when, as the reader will see, there are very significant new thoughts and understandings arriving in the world of the acnes. Indeed, some have not reached the shores of North America, some have not yet been published, and some have just recently popped up as novel considerations. The field is moving fast enough that leaving something out is all but inevitable, and if you find I missed something you consider significant, please do let me know your thoughts. Now seems like a great time to start a file for a second edition.

All of this new material needs to be sifted and evaluated for logical consistency with the whole, and such reflection and consideration takes time. For me such time is usually stolen from the beginning of the day’s busy activities, in the shower. Indeed, it would not be too big a stretch to say that this present effort was written, or at least conceived and conceptualized and seriously mulled over, during about 40 years of morning showers.

Ultimately, this book is written for our patients. We commonly use the phrase “suffering from acne,” but usually without thinking how deeply the suffering goes. As a teenager with bad skin, Janis Ian knew about that. She composed and sang “At Seventeen” in the early 1970s. Her poignant lyrics are a lesson in the impact of acne on self-image.

I learned the truth at seventeen
That love was meant for beauty queens
And high school girls with clear skinned smiles
Who married young and then retired.
The valentines I never knew.

These lyrics have haunted me for decades while I’ve looked for explanations in the hope that the “ugly ducklings” of both sexes can eventually be spared the pains brought on by “the blight of youth.”

My initial interest in hormones, the fuel of the acnes, was “by exclusion” rather than by choice. As final-year dermatology residents in Toronto, we were each expected to write a review on a “basic science” topic. The only subject that was of any marginal interest to me and had not been dealt with by my senior residents was “Hormones and the Skin.” It has been a long road from 24-hour urine collections for ketogenic steroids, through the early days of dialyzable free testosterone, to the newly revealed mysteries of FoxO1 and mTORC1.

The original stimulus to look into diet as a cause of acne came from the first dermatologist in our family, my father. He had a case of a young dairy farmer whose well water was contaminated by agricultural bromides (see “The Farmer’s Boys,” Section 2.3.1). That original question got me wondering about diet as a cause of acne, partly because I was curious about the role of chocolate, and that led in due course to this book being...
written. I set up a semiquantitative patient questionnaire that included just about all common foods and drinks. I suspected the relationship between acne and milk after about two years of patient interviews done over 35 years ago. Osler’s admonition to “Listen to your patient, he is telling you the diagnosis” led not to the diagnosis but to a strong suspicion of the etiology of acne.

Already interested in “hormones in the skin,” I had been keeping an eye on the literature. I was unaware of the presence of hormones in milk until Janet Darling’s early 1970s papers came to my attention. “Chance favored the prepared mind,” and I found that a Pasadena dermatologist named Jerome Fisher had been studying acne, milk, and the steroid hormones he suspected in milk for years, since the early 1960s. A reference to his work appeared in Time magazine in 1966. I contacted him in 1979 and he sent me the carbon copies of his unpublished 1965 manuscript. Charles Bird at Queen’s Endocrinology did our first ‘free T’ assays. Thus, steroid hormones remained my prime suspects. By 2000 I felt that I was in a position to propose a formal study, so I asked for a meeting with Walter Willett, professor and head of the School of Nutrition at the Harvard School of Public Health.

That study was underway at Harvard in 2002 when Loren Cordain’s paper raised the question of the role of a low-glycemic-load (or Paleolithic) diet in preventing acne and other Western diseases. It had not occurred to the multinational team of which Cordain was a member that the absence of acne might have been due to the absence of dairy products. A phone call confirmed that the dairy intake of these tribes was indeed exceptionally low (in the New Guinea group) and absolute zero (in the Paraguay group). In late 2002 Clement Adebamowo, the Harvard group’s principal investigator, produced preliminary evidence of the epidemiological link between milk and acne in the Nurses Health Study data. In early 2005, the first of three papers demonstrating the significant association was published.

Meanwhile, another member of the Papua–Paraguay team returned to Australia and was involved in the design and conduct of several clinical studies that linked low-glycemic diets to clinical improvement of acne in a small number of young men. This reinforced the Australian thesis that the prime dietary mover of acne was the high glycemic load of the Western diet. Indeed, the most active collaborator, Robyn Smith, was awarded her PhD on the strength of that high-glycemic-load theory just a few short years after Clement Adebamowo earned his ScD based on the dairy and milk association with acne. Their contributions are reviewed in Appendix B.

Subsequently, Professor Bodo Melnik has presented us with what appear to be the pieces of the jigsaw puzzle that allow us to see almost the complete picture.

Understanding the complex relationships that form the background for these three diseases is essential in order to provide the “deliverable,” that is, a book on the acnes that will be, in Martin’s succinct description, “practical.” Within that word are several messages, including the need to write for a broad audience, from researcher to patient, and from busy dermatologists to patients’ parents. The researcher will need to forgive the helping hand of explanation that is occasionally extended to bring readers up to speed, and the beginner in the field will need to put up with (or look up) some unavoidable jargon. If and where I fail, always remember that Wikipedia is your friend, and deserves your support. While much of the book provides the necessary basic science to help with comprehension of the mechanisms discussed, this is not an academic text. Others are better at that than I. Nor will this be a catalog of every paper written on each and every aspect of these disorders, supplemented with my comments. It is instead my personal view, from the practical side, an overarching synthesis supported by selected references.

The first aim of this book is to provide practical guidance to managing the three acnes. There are several other books on acne that aim at being practical, so why is this book different? Simple. Because I believe that the longstanding concepts of the acnes’ cause and development, as still held by other authors are, in a word, outdated. That leads to the second aim of the book, to update the concepts upon which therapy must be based. The third and most important aim is to encourage prevention of the processes that lead to and perpetuate the acnes, ultimately making active, expensive, drug-based therapy unnecessary.

My intent is to provide the practical options, as I see them, for both patients and prescribers. At the same time I hope it will serve to nudge scholars and researchers in directions that remain both unexplored and promising.

It will also guide you to cost-effective therapy. I am not interested in marketing anything. I have no present financial interest in anything I am discussing, but if you
look up the medical literature you will find that I was involved in paid clinical trials in the distant past. That means I may annoy some of my colleagues. My challenge will be to disagree without being disagreeable. Because this work describes three variants of a single disorder, there are shared features and shared pathogenic processes. This leads to unavoidable duplication. The alternative would be to lead the reader on a merry chase through a book filled with links to other chapters and sections. I have kept these internal references to a minimum, providing a cohesive self-contained unit dealing with each of the acnes.

Continuing medical education (CME) standards in the United States require notification of audiences if any drug is used “off label,” meaning that it has not been specifically studied to US Food and Drug Administration (FDA) standards for the particular disorder being discussed. Most of the medications used in dermatology are regularly used off label. I will not bore the reader and use valuable space to repeat this caveat throughout the book. Almost this entire book is in my own words but where others’ words serve better than I can paraphrase them, I will quote them with attribution. As the sole author, any mistakes are mine and I do appreciate constructive criticism.

Thanks go first to Lynne Margesson. She “came on service” as my junior resident and is my spouse of 39 years, my practice partner, and mother of our two children. She did not hesitate at all in giving me the green light for this project, even though she had a pretty good idea what it would entail. I would love to thank my mentors, if I had any, but I do owe debts of gratitude instead to the several researchers, teachers, writers, and, most importantly, thinkers who have contributed to the field. Howard Donsky nudged his residents to look at the basic sciences in depth. My father, Charles Danby, was a dermatological innovator in his own right. Janet Darling did the initial determinations of the levels of steroid hormones in milk. Sir Kenneth Charles Calman detailed the existence of the first intracrine enzymes in the follicular keratinocytes. The late Jerome Fisher’s study of milk and acne and suspicion of hormones helped me down this road. Loren Cordain’s studies of aboriginal diets inadvertently set the baseline of “no milk, no acne.” Peter Pochi shared a confidence. Walter Willett had the courtesy to listen and then facilitate a fresh look at the Nurses Health Study II and other data.

I owe special thanks to Clement Adebamowo for doing all the heavy lifting for that work. Dawn Danby and Paul Waggoner provided the line drawings of the ‘FPSU.’

In the acne inversa/hidradenitis suppurativa (AI/HS) area, thanks are due to Michelle Barlow for lighting a fire under us, to Gregor Jemec for support and ongoing collaboration, to Christos Zouboulis for opening doors, to Stuart Maddin for encouraging me to “focus” (always a challenge) and for encouraging me to contact Professor Zouboulis, to Maximilian von Lefert and Prof. Wolfgang Marsch for collaborating on the “follicular support” project, and to Robert Bibb for being the first to try a dairy-free diet in AI/HS. Special thanks go to numerous patients willing to try novel therapies, some out of acquiescence to my requests, some out of curiosity, and many out of the desperation and frustration that often accompany AI/HS.

This book presents an overview of the way I believe the acnes begin and how they progress through their various stages. It also provides personal glimpses into areas not yet fully explored. I will offer new hypotheses, consider areas of controversy, and touch on other hormonally related disorders that need further investigation.

The acnes exist in a four-dimensional spectrum, changing with time. They share a common cause but are unique in their individual three-dimensional presentations. My hope is to persuade you to see the acnes as I see them, and to learn to prevent them. Where others have failed at prevention, I hope to provide you with a few new and original treatment approaches.

Bill Danby
Hopkinton, New Hampshire
Practical acne therapy

There is a common theme in the three acnes. Pores are blocked; they burst, get inflamed, scar down, and heal. Whether the patient (you, perhaps?) experiences acne vulgaris, acne rosacea, or acne inversa/hidradenitis suppurativa (AI/HS) depends upon variables that include lesion location, patient’s age, gender, family history, diet, sun exposure, and several others.

So let’s start at the beginning.

With a look in the mirror.

How bad is it?

Staging and grading acne are essential in research but of little practical value in individual cases.

If you’ve got it, you’ve got it. Measuring it doesn’t make it better.

Acne vulgaris that is “the end of my life forever” for one teen can be ignored by another.

Acne rosacea can be embarrassing beyond belief and a huge social handicap, or a minor nuisance.

Acne inversa can be an occasion “boil” every few months, or it can be life-destroying.

Be practical: If you’ve got it, and you want it gone, take the practical approach.

Genetics

If you inherited the genes for any acne, like 90% of us, that’s unfortunate. Nothing fixes genes.

Be practical: You might want to choose a mate someday with their genes in mind if you want to look out for your children’s risk of acne.

Diet

We know acne is caused by the male hormone dihydrotestosterone (DHT).

DHT works by linking to a male hormone (androgen) receptor.

It is like putting a key in the keyhole to open a door.

The androgen receptor (keyhole) needs to be open to accept the key.

Opening the keyhole requires insulin and/or insulin-like growth factor 1 (IGF-1).

Milk and milk products raise both insulin and IGF-1, opening the androgen receptor.

Sugar also raises insulin levels, helping even more to open the androgen receptor.

Foods that turn into sugar quickly (high-glycemic-index foods) also raise insulin levels.

Milk and milk products also actually contain androgens (the keys to the keyhole).

Milk and milk products also actually contain other hormones that turn into androgens.

So both dairy and sugary foods can open the androgen receptor.

But dairy also supplies the androgens to turn on acne.

Dairy is triple trouble.

Be practical:

- Change to a truly natural diet.
- Eliminate all dairy.
- Go “low glycemic load.”

Hormones

Hormones cause acne.

No hormones = no acne.

Eliminating hormones in either sex is not practical.

For males, hormone manipulation is used only rarely.

Dutasteride is used in men with acne inversa.

For females, hormones can be modified, replaced, and blocked. It is not natural, but it works.

Birth control pills with no- or low-androgen progestin are the best.

Look for drospirenone, norgestimate, or norelgestromin. Avoid all other progestins.

Postmenopausal hormone replacement? Progesterone (oral) and estradiol patch only.

Spironolactone blocks androgens and improves almost all acne in almost all women.

Be practical: The acnes are hormonal disorders. Manage your hormones.
Stress

Stress is a contributor to the cause of acne.
Stress also makes preexisting acne worse.
But living a stress-free life is not practical for most of us.
And we have no safe long-term stress-reducing medications.
Reducing stress is worth trying, as long as that effort is not stressful.
Yoga may be worth a try.
Be practical:
Eliminate the stress of looking in your mirror.
How? Follow the other practical rules presented here.

Comedones (plugs in pores)

In acne vulgaris:
*Blackheads* are plugged pores with open tops (Figure 0.1).
*Whiteheads* are plugged pores with closed tops (Figure 0.2).
Both are called *comedones* (open and closed). One (of either) is a single *comedo*.
Both grow until they empty themselves out or explode to the surface.
In acne rosacea, the pores explode superficially before the plug is actually visible (Figure 0.3).
In early acne inversa, the plugged pores are not prominent (Figure 0.4). The plugs tend to be deeper.

**Figure 0.1** Classic open non-inflamed comedones with early inflammation just starting.

**Figure 0.2** Mainly closed comedones with occasional “blackheads.”

**Figure 0.3** Central facial folliculopapules and folliculopustules, with no comedones and minor background erythema.

**Figure 0.4** These little nodules were the only clue to the disease. Family history was positive.
Practical acne therapy

These deep plugs often explode before the trouble becomes visible.

These plugs are caused by too much androgen (male hormone) activity.

The hormone turns on too many lining cells in the pore and, often with the help of nicotine, they form a traffic jam. The traffic jam leads to the explosion deep in the skin.

The best treatment to empty pores is a class of drugs called **retinoids**. They are cousins of retinol, better known as vitamin A (Figure 0.5).

Oral retinoids (given by mouth) are most effective, but they are usually reserved for worst cases.

Isotretinoin, used in low doses over a period of months, is the gold standard first choice for acne vulgaris (Figure 0.6).

Isotretinoin, used in low doses over months, is also the “last resort” for acne rosacea.

Acitretin, used in low doses over years, is the appropriate choice for acne inversa.

Topical retinoids are used on the skin surface in gels, lotions, and creams. They include tretinoin (the original—also called retinoic acid and vitamin A acid), adapalene, tazarotene, and isotretinoin (not in the United States).

Retinoids do three jobs in acne:

- They empty plugged pores (comedones, both open and closed).
- They prevent open pores from getting plugged.
- They modulate the inflammatory response.

So retinoids must be applied over the entire acne-prone area. Not just on “spots.”

Be practical:

No matter what kind of acne you have, you need at least one retinoid.

And absolutely no nicotine.

**Blemishes—a brief catalogue**

**Papules** are small elevated bumps; they are usually red and often tender (Figure 0.7).

If there is a collection of pus on top of a papule, it is a **papulopustule** (Figure 0.8).

A collection of pus standing by itself at the opening of a pore is a **pustule** (Figure 0.9).

If a pustule is at the top of a follicle, it is a **folliculopustule**.

Larger papules and larger papulopustules are **nodules** (Figure 0.10).

These are battlegrounds.

The enemy is the “stuff” caught in the pores.

Acne is your body trying to get rid of this “stuff.”

So what is the stuff down in your pores?

There are bacteria and yeasts and sometimes some little mites plus dead skin cells and hairs and irritating chemicals.

Be practical:

Use oral (isotretinoin) or topical retinoids to empty out the pores.

Eliminate yeast, bacteria, and other organisms.

Empty out the lesion if and when practical.

Cool the inflammation with anti-inflammatory antibiotics.

Use benzoyl peroxide to stop or limit the production of resistant bacteria.

Use other anti-inflammatories like dapsone or steroids as necessary.

---

**Figure 0.5** Retinol is the classic vitamin A. Tretinoin, also called vitamin A acid and retinoic acid, was first marketed as Retin-A®.

**Figure 0.6** Isotretinoin, which is now widely genericized, was originally marketed as Accutane® and Roaccutane®. Acitretin started life as a treatment for psoriasis.
Nodules

Although common in acne inversa (Figure 0.11) and acne vulgaris, these also occur in serious acne rosacea. These are raised or deep, red or purple bumps, and they are usually tender (Figure 0.12).

They occur anywhere on the body where folliculopilosebaceous units (FPSUs) exist.

They are sometimes crusted, draining, or bleeding (Figure 0.13).

They are filled with inflamed material trying to reach the surface, heal, or scar down (Figure 0.14).

In AI/HS, the ruptured nodules form a gelatinous material. This invasive proliferative gelatinous mass (IPGM) invades and travels deep horizontally under the skin, producing sinus tracts (Figure 0.15).

When the sinus tracts rupture and drain to the surface, they often become secondarily infected (Figure 0.16).

Be practical:

For acne vulgaris and acne rosacea nodules:
- Eliminate yeast, bacteria, and other organisms.
- Cool the inflammation with anti-inflammatory antibiotics.
- Start low-dose isotretinoin as soon as possible, whenever possible.
- At the same time, get diet and hormones under immediate full control.
- If isotretinoin is impossible, use aggressive anti-inflammatory therapy, including intralesional triamcinolone injections to minimize scarring.

For AI/HS lesions:
- Use topical resorcinol cream to dry up small nodules.
Use punch debridement to empty out fresh follicular nodules.
Use unroofing to empty out large nodules and early sinuses.
Use oral zinc and vitamin C, oral antibiotics, and injectable steroids regularly.
Continue all baseline dietary and hormonal care.
Escalate to ‘biologics’ to cool the lesions before surgical care as needed.

**Scars and sinuses**

Scars and sinuses are caused by failure to treat acne early and properly.
There is a genetic tendency toward scarring (Figure 0.17).

Some people scar badly, even in spite of minor lesions and early care.
Others with the same degree of acne do not scar at all.
Most acne scars are hypertrophic—raised above the original acne nodule (Figure 0.18).
True keloid scars, spreading beyond the original nodule, are rare.
Sinuses are likely produced by stem cells. This awaits proof. They must be unroofed as soon as possible.

Be practical:
- Treat all acne, especially AI/HS, aggressively and early to prevent scars.
- Start with strong medications first, and then reduce to maintenance.
- Use intralesional triamcinolone injections early to prevent scars.
- Ensure all early AI/HS lesions are punch excised or unroofed as soon as possible.
Over one hundred years ago, the von Jacobi–Pringle dermochromes were published [1]. These lovely old books contain colored images of wax models (called moulages) of numerous skin diseases, with a summary of what was known about each disorder in 1903 (Figure 0.19).

Regarding acne, the later English version of the text states that the cause “is not yet fully cleared up. Many morbid processes conspire to favour the existence of the disease” [1].

Pringle’s translation of Jacobi noted further that “a peculiar seborrhoeic condition is frequently present, which gives rise to the formation of comedones,” and “the specific significance attributed to various bacteria found in the pus of acne-pustules is contestable” [1].

Over one hundred years later, the debate continues. The three contenders for the cause of acne have been the plugging of pores, the overproduction of oil, and the results of bacterial colonization of the sebaceous follicle (oil gland). Over the past 40 years, reputations have been built on these three concepts. Strauss [2–6], Pochi [7–12], Kligman [13–17], and Shalita [18–22] built careers on the slippery foundations of seborrhea, plugged pores, and comedolytics, with Leyden [23–28] and others concentrating upon the bacterial microorganisms and their relationships to antibiotics. More recently, Thiboutot [29–34], Zouboulis, and a growing host of other investigators [35–41] have greatly broadened our understanding of the basic science (those “morbid processes”) behind the acnes.

Despite all this research, the picture of acne vulgaris did not change much until recently. In a recent monograph, Webster stated honestly and flatly, “The cause of the faulty desquamation that leads to comedo formation is not known” [42]. The situation has been clarified significantly since then. Melnik’s molecular-level model of the mechanisms activating acne has changed all that [43–45]. We now have a reasoned and reasonable explanation of the way that the pores are plugged and the acnes develop. This is what physicians call the pathogenesis of the disease.

While irrefutable clinical trial–based proof of the cause has eluded us, I believe we now know the best path to follow. Meanwhile, the economic impact of acne has been, and continues to be, immense. The acnes remain the number one reason for visits to dermatologists in the United States.

The acnes generate millions of prescriptions worth hundreds of millions of dollars annually. They form a disease complex whose treatment has spawned an industry in its own right. In turn, it drives other economic
activities ranging from cosmetic cover-up to surgical repairs and resurfacing. It is now beginning to show up as a driver of several photomediated techniques, from red and blue topical lights to laser-driven photodynamic therapy (PDT).

“The blight of youth” and its fellow travelers, rosacea and acne inversa/hidradenitis suppurativa, are still with us, but we now have many tools to treat them [41].

The next step, in the words of Professor Albert Kligman, is “to actually achieve the ultimate goal in medical practice, namely prevention” [46]. That is also the ultimate goal of this book.

Nomenclature

The three generally recognized types of acne are acne vulgaris, acne rosacea, and acne inversa (usually called hidradenitis suppurativa in the United States). All are caused by a disorder centered on the structure usually called the pilosebaceous apparatus, so named because of its two products, hair and sebum.

So that we all understand what I will be talking about, the reader needs to know that I will be using a slightly different but more accurate name for these little appendages. It is essential to understand that there are really three parts to this classic little organ, not two. Furthermore, they are responsible for producing three products, not two. The three parts (or subunits) are distinctly different, as are their products. The subunit usually ignored in discussions of the cause of acne is the follicular part. Its product, the keratinized lining cells, likewise usually ignored, is often unrecognized but is nevertheless the major factor in the pathogenesis of acne. Fortunately, the appendage lends itself to a very natural subdivision into three distinctly different parts (Figure 0.20):

1 The follicular canal is that part of the structure that is represented at its top end by the pore. It is basically a tube whose job is to produce lining cells that produce a fibrous protein called keratin in cells called keratinocytes. These cells are normally shed into the lumen (the central open area of the canal). The size of the lumen varies depending upon a number of local effects, but the most obvious influence is from the size of the hair or hairs that pass through the unit. From almost invisible pores on a baby’s face, bearing almost invisible wisps of downy vellus hair, can come thou-
prevents us getting stuck in the birth canal [48]. At the other end of life, hardly any oil is produced on the skin of the truly aged and dry skin becomes a problem. One of the last areas to lose its oil is the scalp, the area that pushed its way into the world first.

The sebum is measurable with some difficulty, but it takes little in the way of observation to note that patients with acne rosacea have oily skin. This fact is important to the cause of the inflammation in rosacea, to be proposed shortly.

Putting these three terms together produces a bit of a mouthful, the folliculopilosebaceous unit. To make things easier, I will use its short form, FPSU, throughout this book. This recognizes the fact that the follicular part that is usually called a hair follicle or sebaceous follicle is really neither. There is a simple reason why it is neither—because it is both. It delivers both the hair and the oil to the surface. It is also highly distinctive in its mission and in its contribution to the various acnes, so it deserves a place of its own. As you will see later, the junctional area (where these three parts of the FPSU meet) has its own special features (Figure 0.20). Each part contributes to the various diseases of the appendage in its own way. For now, just keep in mind that the three subunits comprising the FPSU behave differently in each of the various kinds of acne.

The three acnes and grading

Acne vulgaris
This is common acne, and it takes many forms. The disorder starts when the follicular portion of the FPSU is plugged, producing two kinds of plugged pores (comedones), open and closed. Open comedones are the classic blackheads (Figures 0.21 and 0.22). Closed comedones are called whiteheads (Figures 0.23 and 0.24).
**Figure 0.21** Folliculopilosebaceous unit with detail and orientation of the sebofollicular junction area. The black oval shows the top and bottom limits of the isthmus section of the pilofollicular tube. The necks of the sebaceous glands that “plug into” the isthmus through 360° form the sebofollicular junction. The bulge area is likewise a 360° wrap around the upper portion of the pilar unit. It is composed of a series of stem cells—the ones closest to the sebofollicular junction are Lgr6 type and may be the source of the invasive proliferative gelatinous mass (IPGM), which is to be further discussed in this book. From http://upload.wikimedia.org/wikipedia/commons/7/7c/Insertion_of_sebaceous_glands_into_hair_shaft_x10.jpg.

**Figure 0.22** Plewig’s Follikel-Filament—the earliest form of follicular plugging, with compact pink lamellae of lining keratinocytes, a fine hair that is barely visible, and purple colonies of anaerobic Propionibacterium acnes. Note that the stratum corneum equivalent and the intraductal keratin layer near the hair at the top end are thin and loose, indicating that terminal differentiation and desquamation are occurring normally. From Acne and rosacea, 2e, Kligman, Albert M; Plewig, Gerd.

**Figure 0.23** The early comedo starting to accumulate deep in the infrainfundibular part of the follicular unit, showing thickening of the stratum corneum underlying multilayered compact keratin as terminal differentiation fails. From Acne and rosacea, 2e, Kligman, Albert M; Plewig, Gerd.
Introduction

Acne rosacea

For reasons that are discussed in this book, comedones are not seen in acne rosacea. The diagnosis is made based upon the appearance of folliculopapules (Figure 0.29) and folliculopustules (Figure 0.30) on the convex surfaces of the central face and chin and forehead. The background skin is a rosy pink color that gives the disorder its name (Figure 0.31). It usually onsets after the teen years and may last into the senior years.

There may be accompanying telangiectasia (Figure 0.32). This has led to the definition of a subtype of rosacea called erythematotelangiectatic rosacea [49]. More on that later (see Appendix A).

There may also be a peculiar thickening of the involved tissues. The nose is most commonly involved, but cheeks and chin and other facial areas may show swelling, thickening, and eventually a woody firmness (Figure 0.33). This is called phyma (nodule or swelling) formation, and the classic involvement of the nose induces rhinophyma. Finally there may be, for reasons undetermined, involvement of the soft tissues of the eye, which carries the designation ocular rosacea (Figure 0.34).

The “whiteheads” that contain real pus are called pustules. Dermatologists use the term whitehead to describe pores plugged with keratin (not pus) that show no obvious opening to the surface.

Each comedo can have several possible fates.

An open comedo may simply stop growing, empty out, and disappear. It may get very large and sit quietly for months or even years. It may get inflamed, turn into a folliculopustule (Figure 0.25), empty out its contents onto the surface, and heal up. It may rupture “deep” (Figure 0.26), causing an inflamed acne papule. It may join with other nearby comedones (both open and closed) and nearby papules and pustules to become an acne nodule. If a number of these nodules join together and the inflamed tissues break down between them to form a continuous inflammatory mass, this is called conglobate acne (acne conglobata) (Figure 0.27). If this type of acne is accompanied by a sudden onset of aching joints and fever, it is called acne fulminans.

Closed comedones may turn into open comedones and follow the same paths described here, but they may also rupture directly into papules and pustules.

As the inflammation dies down, scarring occurs. It may be so mild that it is unnoticeable, or it may just show as discoloration (post-inflammatory hyperpigmentation, or PIH) that will fade with time.

Destruction of tissue by the inflammation causes total or partial loss of the FPSU plus pits and depressions of various sizes. If the body’s attempt to repair the damage has produced tunnels under the skin, these “sinuses” may be permanent (Figure 0.28). And if the body has been overenthusiastic in healing, hypertrophic scars are formed, appearing as smooth raised lumps over the active areas. (See Figure 0.18.)
Acne inversa (hidradenitis suppurativa)

This variation shows up in areas where the FPSU plugs up and then the follicular wall ruptures deep in the sebofollicular junction area. Most commonly this onsets in the axillae (Figure 0.28), inguinal creases, perineum, genitals (Figure 0.35), and perianal areas, but this

---

**PRACTICAL TIP BOX 0.2**

The scars that follow acne are called *hypertrophic* because they grow vertically over the injury. Dermatologists use the term *keloid* to describe scars that spread beyond the area of original injury, like burn scars.

---

*Figure 0.25* Open comedones are not static plugs in the follicle. New keratinocytes are added to their outside layer, and the central keratinocytes are slowly lost through the follicular opening. From *Acne and rosacea, 2e*, Kligman, Albert M; Plewig, Gerd.

*Figure 0.26* The rupture in the wall of this follicular unit has allowed intraductal material to escape, causing the surrounding peri-follicular inflammation and allowing inflammatory cells to enter the duct.

*Figure 0.27* Inflammatory papular, pustular, nodular, and scarring acne coexisting with extensive non-inflammatory comedonal acne.

*Figure 0.28* The exaggerated webbed scarring that can occur in acne inversa/hidradenitis suppurativa, as in this right armpit/axilla, can be destructive and invasive instead of a healing influence.

---
Acne rosacea is basically a folliculocentric inflammatory reaction directed at material in the follicular duct. The inflammation varies in depth and degree depending upon the variable content of the pore, the varied immune responses of the patient, and the varied therapies undertaken. This woman failed to respond to topical metronidazole and oral tetracycline group antibiotics but cleared with combined therapy directed at *Demodex* and *Malassezia*.

These very superficial folliculopustules are the hallmark of *Demodex* involvement in acne rosacea.

This man’s rhinophyma involved only the bulb of the nose. It responded to nothing but low-dose oral isotretinoin over several months. The undelying fibrosis has left him with a prominent nasal bulb, but it is much improved from the original bright-red swollen condition.

This is ocular rosacea. Note the residual conjunctival telangiectasia and cheimosis (edema) despite active treatment.