

PROLOGUE

THE ORPHAN PATIENT

An orphan patient is one with a unique, inchoate, baffling, and often disabling disease not yet clearly discernible in the medical literature. Although technically this patient has an orphan disease – one defined as affecting fewer than 200,000 people in the United States – in reality he or she is an outlier, standing alone. With a cohort group closer to 20 than to 200,000, the orphan patient has no political constituency, no funding for research, and only serendipitous access to the rare physician with the time, energy, enthusiasm, knowledge, or research skill to “adopt” such a patient and solve his or her problem. Such a patient is a true foundling, often with a disease that knows no name and a physician who must turn away in sorrow and in ignorance . . .

Clinical medicine thrives on the study of the unique patient, as well as the study of DNA. Don’t we in medicine need these orphans as much as they need us?

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Walter B. Shelley and E. Dorinda Shelley

Excerpt

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PRAYER OF THE ORPHAN PATIENT TO THE DOCTOR

Listen to me

- Don't be cynical, indifferent, or in a hurry.
- Ask me what makes my problem better or worse.
- Ask me what I think the cause is.
- Ask me to look for clues and teach me what they are.

Think about me

- Think of my problem when you read those books, journals, and atlases.
- Think of my problem when you attend meetings.
- Think of asking your colleagues about me.

Test me:

- Order specific tests to help you decide on my diagnosis and treatment.
- Could I have AIDS, cancer, or lupus?
- Do I need a biopsy? A challenge with a medication?
- Do I need hospital help?
- Do I need to see a consultant?

Don't give up on me:

- There is always one more treatment you can try. Just imagine I have a different disease and treat me for that.
- See me during an attack to get new ideas and new tests.
- Ask me lots of questions during every visit.

I won't give up on you, for I am an orphan.

INTRODUCTION

HOW TO BE A DERMATOLOGIC DETECTIVE

You have your whole day filled with removals and restorations, to say nothing of documentation and administration. Why become a Sherlock Holmes investigating the crimes committed in your patient's skin? Here's why:

Skin sleuthing is fun. Solving a patient's problem makes for a better day, perhaps not financially, but intellectually. It may take weeks, but the delight of satisfying your curiosity for the benefit of your patient is great. It is not enough to repair a wrecked car. You must know why there was a wreck.

Solving problems, explaining the inexplicable, is a higher order of achievement than making diagnoses. And, bear in mind, your patient is much less interested in the "what" of dermatology than the "why," but really wants to know both.

So, you want to be a Dermatologic Sherlock Holmes. It is not enough to don a deerstalker cap and smoke a curved pipe. You must acquire skills in these four areas:

I. THE HISTORY

Because many dermatologic diagnoses are simply labels for reaction patterns, it is up to you to look beyond the diagnosis and look for the cause. This is done best with a sharply focused history directed at probable or possible causes. All this calls for knowledge that comes from experience, from reading the literature, and above all, asking the patient what he or she feels is the cause.

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We recall a patient at the University of Minnesota who presented with a swollen painful tongue. All of the attendants and residents felt a culture and biopsy would give them the answer. When it did not, they called on their chief, Henry Michelson. He simply asked the farmer, “What do you think caused this?” The reply: “I reckon it was a toothpick caught in my tongue,” and so it was.

Knowledge and experiences can lead to sharply focused quick histories. We remember the CEO of a large corporation who had intractable rosacea. When asked how many cups of coffee he drank a day, the answer of twenty-five cups gave us a look behind the diagnosis and a cure.

History taking must not be passive. It should be probing. It should be detailed. It is not enough to ask, do you have a balanced diet? Witness our eighteen-year-old weightlifter patient who had developed severe cystic acne on his face and neck. A simple, yet focused, in-depth history disclosed the cause. He was drinking two gallons of milk a day. He was cured without retinoids or antibiotics by the simple elimination of milk.

History taking needs to be comprehensive, ranging from personal medical history to family history, occupation, and hobbies. Diabetes may explain the blister on the great toe. A family history may explain the blisters on the hand in porphyria. Chromium sensitivity may account for a hand eruption in those working with cement, whereas a golfer may be prone to poison ivy.

The history must center on medications. Drug sensitivity explains many a strange rash. Remember that a complete drug history is difficult to secure. Memory is feeble and often fails to recall the ordinary, routine events. Patients often have to be seen at the time of a flare to be successfully cross-examined. When you diagnose acute explosive skin eruptions, the best history is taken at the time of the flare up. We had one patient who had been hospitalized five times for attacks of erythema multiforme. She could give doctors no clue until we told her to come to our office within hours of her next attack. It was 9 A.M. Monday morning. The attack had come at 5 A.M. By going back over every inhalant, contactant, and ingestant throughout that night she finally said, “Oh, yes, I took an Ex-Lax at bedtime.” It was that very medication that had eluded innumerable questionings by several dozen doctors and was the cause of each of her attacks, which was proven later by a blind challenge.

A history is best when it is layered, incremental, and repetitive. As the patient begins to know which of his or her observations you value

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most, history taking becomes more profitable. And do not forget the clues provided by the patient's family and friends or other involved medical personnel. A vivid example involved an infant we had hospitalized because of unexplained blisters. All of our sophisticated laboratory studies were negative. The answer came from the floor nurse, who had noticed that the baby screamed every time her mother came to visit. Flinging open the door of the private room at the next episode of screams, she saw the mother applying a liquid to the baby's skin. It proved to be a strong acid.

Remain curious and your practice will always be interesting. We recall the professor at the University of California whose residents complained about the routine and boring nature of the patients on their ward. She said, "Take me to your most uninteresting patient." Once there, she elicited the following:

"Have you ever been in the hospital before?"

"Yes."

"Why?"

"Broken arm."

"How?"

"The boat shook me out of my bunk."

"What boat?"

"The Titanic." The residents learned their lesson when they saw the history they never took on the front page of the evening papers!

Taking a history is one of the most personal, friendly things you can do as a doctor. You bond with a fellow human being. You are a clinician privileged to glimpse another world. By having a deep interest in your patients' problems and treating them with warmth, you can provide them with a sense of hope, even when their problems remain elusive.

2. THE CONJECTURE

By knowing the patient's history and by viewing their lesions, you must now speculate as to the cause of the problem.

Could it be due to drugs?

Your history suddenly becomes more focused. What medicine does the patient take? Here it is necessary to use both direct and indirect questioning. They may deny all medicines, only to tell you on indirect questioning, "Yes, I take ibuprofen for headaches." They may need time

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to rake away the leaves of forgetfulness, so that repetitive queries are often needed. You must ask about over-the-counter vitamins, laxatives, homeopathic concoctions, tonics, douches, eyedrops, and ointments. Also, be sure to check the contents of their over-the-counter remedies in the Physicians' Desk Reference for nonprescription drugs and dietary supplements. Chemicals come in many guises. All must be searched out, e.g., breath fresheners, lozenges, chewing gum, air fresheners, perfumes, disinfectants, moth repellants, and glues. We are exposed daily to hundreds of chemicals.

Litt's Drug Eruption Reference Manual (11th edition, 2005) is an invaluable aid in all of this detective work.

Could it be due to contactants?

Poison ivy is the most common troublemaker and do not let the patient dismiss it by saying, "I am not allergic to poison ivy, and I am never in it." Sensitivity may develop after years of handling it with impunity, and pets may carry the resin on their fur.

Again, the location of the lesions can help identify the causes of the problem, such as foot eczema in patients sensitive to leather.

The texts on contact dermatitis and occupational dermatoses will give you many clues. A visit to the workplace or the patient's home can yield unsuspected exposures not sensed by the patient. We recall a patient with a widespread contact dermatitis so severe as to require hospitalization twice. The case was solved only when we made a "house call" and were fascinated by her all aluminum kitchen. Her comment, "But I hate having to polish it," closed the case by revealing the criminal contactant never mentioned before.

Could it be due to foods?

Here the history must be provided by the informed patient. They must keep a detailed diary of everything entering their mouth. They must know the flare will come within two minutes to two days. Suspect foods in cases of urticaria, flushing, chronic hand eczema, and erythema annulare centrifugum.

Could it be due to an internal cause?

Some internal malignancies are heralded by skin disease. These include dermatomyositis, Bazex's syndrome, pemphigus, and necrolytic migratory erythema.

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Other changes, such as Beau's lines in the fingernails, give clues of significant systemic illness over the past five months.

The most subtle internal cause for skin disease is focal infection. Watch for psoriasis initiated and maintained by chronic tonsillitis and streptococcal pharyngitis. Suspect focal infection as a cause of alopecia areata. Always look for the elusive periapical abscess, even if the patient has had good dental care. Think of focal infection in recalcitrant hand eruptions. It may clear only after cholecystectomy. Consider chronic cystitis as a cause for lichen planus. The search includes prostatitis and sinusitis.

3. THE INFORMED PATIENT

You have made your assessment and you now inform the patient as to possible causes. The well-informed patient is your most valuable ally in your search for the cause. Take unexplained pruritus as an example. Your patient must be made aware that your search is on for over-bathing, the most common cause of "winter itch" in the elderly. Next, that you suspect drugs including vitamins and homeopathic remedies, as well as chemicals in cough drops, chewing gum, douches, air fresheners, disinfectants, formaldehyde, and vitamin E creams. Next, comes suspicion of a low grade dermatitis from clothing, bath salts, hair sprays, or flowers. All of these are valuable leads for alerting the patient to his personal exposures. The best-informed patient gives the best history.

The patient then needs to have the appropriate medical studies. These may include blood studies for polycythemia and CT scans for Hodgkin's disease.

Any patient with pruritus or an unexplained dermatitis, also needs to have a KOH (potassium hydroxide) scraping for fungi and mineral oil scraping for the itch mite.

The patient must learn that what seems harmless, even though FDA approved, can turn on them and cause their malady. They must know that:

- eyedrops can cause an exfoliative dermatitis
- blood pressure medications can cause hair loss, along with many other medicines, including high doses of vitamin A
- cholesterol lowering drugs can induce dry skin
- a bouquet of Chrysanthemums, as well as their derivative insecticides, may cause intractable dermatitis

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You have an incomparable advantage over your mentor, Sherlock Holmes. You can test your deductive reasoning by recreating the crime. You can reproduce the disease and thereby confirm or refute your conjecture. Dermatology has long provided this very satisfying venue for proving the cause.*

The challenge rests on your assessment of possible causes. In the case of dermatitis, the patch test is the sovereign challenge. Using standardized kits or improvised samples of the suspect allergen (proven innocuous on control individuals), one can reproduce a miniaturized version of the crime in two to four days under a closed patch. Subsequent exposure of the area to ultraviolet light (UVL) will permit confirmation of a photocontact dermatitis. Photodermatitis, per se, can be elicited by spot exposure to UVL sources.

The second challenge is with suspect drugs. Usually, confirmation comes with improvement and clearing of the eruption when the offending drug is discontinued. However, at times, this is a slow process due to persistence of the drug in the skin. Metallic drug antigens may remain for years as with silver and gold.

The simplest test is a closed patch containing the drug, but this is useful mainly in identifying the offender in the fixed drug eruption. For urticarial reactions, the scratch or prick test is available. Intradermal testing is also possible, but more hazardous. A direct challenge by the administration of suspect drugs orally or otherwise is the ultimate method for reproducing the disease, but must be used with great caution and the full consent of the patient.

Other indirect, yet conclusive confirmation of hypothetical causal primary or focal infections can be obtained through the use of antibacterial, antifungal, or antiviral therapy. A positive response to surgical excision of such foci of infection, e.g., tonsillectomy, cholecystectomy, or prostatectomy, is also striking proof of the validity of such hypotheses.

Many plausible or possible etiologic agents are found in the diet. After all, we are what we eat. Close attention to the history of suspect foods via

* Shelley WB. Experimental disease in the skin of man. *Acta Dermatol Venereol* 108: 1–38, 1983.

a food diary permits confirmation of an allergen by either elimination or challenge.

Recall that in all cases, for two to three weeks following a flare, the body may be totally refractory to an immune challenge, which leads easily to false negatives. Note also that a successful challenge may require two factors acting simultaneously. Thus, the patient with exercise urticaria and anaphylaxis requires a challenge with the food allergen at the time of the exercise. Similarly, allergy to fish may appear only in the cold weather of winter.

Imaginative challenges to airborne allergens and inhalants, including pollens and fragrances, may require breathing into a paper bag containing the suspected offender.

Verification of your suspects is most convincing with a positive challenge. But remember, simply eliminating all criminal suspects also ends the crime wave, to the delight of any long-suffering victim.

Repeated challenges may be necessary. We had one patient, a dentist, who had to experience a positive challenge with coffee three times before he would concede that his hand eruption was due to this beverage.

L'envoi

- Be a curious and inquisitive dermatologic sleuth.
- Be interested, because then your patient will become interesting.
- Be well informed, scanning texts, journals, and the Internet, and inform your patient as well.
- Be thinking of your patient's problem outside of office hours.
- Be imaginative, sympathetic, and optimistic.
- Be able to assimilate and coordinate random observations.
- Be like Sherlock Holmes and never give up.

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I

THE CASE OF BLACK SWEAT

Improbable as it is, all other explanations are more improbable still.

– Sherlock Holmes

“Black sweat” was the complaint of a twenty-nine-year-old woman. For ten long years she had suffered from black droplets appearing all over her face whenever she became excited, tense, or overheated. She had seen numerous doctors who had no explanation and no cure. Indeed, many had doubted her story, because her skin appeared perfectly normal at the time of her office visit. The burst of black droplets would appear when she was dancing, and her partner would wipe them away, remarking, “you’ve got soot on your face.”

Of far more concern than such embarrassment to this young woman was her mounting anxiety. Could the “black sweat” be a sign of black cancer? Was it a sign of the black plague? Yet, she seemed in perfect health. But neither she, nor anyone she knew, had knowledge of such an ominous secretion. Her doctors could provide no reassurance, because her problem was not in their textbooks of medicine. She was truly an “orphan patient.”

When we first saw her, we were equally puzzled. We had only her history. Her skin was perfectly normal. There were no black spots. Could she be hallucinating? Could it be a form of the bloody sweat described as a stigmatization as in the case of Saint Therese Neumann? Could it be of hysterical origin? Or could it be a case of deception?