

## **Ackerman on Kligman: A Shameful Story in American Clinical Research**

**By Norman Goldfarb**

*Disclaimer: This article contains statements of fact and opinion that the author and Journal have not verified. Dr. Kligman declined to be interviewed or to comment. The University of Pennsylvania responded with the file statements at the bottom of this article. The University of Pennsylvania Center of Bioethics declined to comment.*

### **Albert M. Kligman**

Albert M. Kligman, M.D., Ph.D., is among the most celebrated dermatologists in U.S. history, but he has had a checkered career, to say the least:

- Dr. Kligman developed Retin-A, an "anti-wrinkle" cream widely used in the treatment of acne and sun-damaged skin. Retin-A is considered by many to be one of the most important scientific advances in the history of U.S. cosmetic dermatology. He has made numerous other contributions to the field of dermatology and has authored well over 1,000 medical articles.
- Dr. Kligman created and led a clinical research program at Holmesburg Prison that, for 23 years, set new standards for unabashedly unethical clinical research. During the course of this research, he may have routinely violated all ten articles of the Nuremberg Code. He cannot compete with the record of Josef Mengele (the Nazi "Angel of Death"), but he makes up in quantity for any shortcomings in quality of horror. Neither of those two physicians ever admitted publicly any moral shortcomings in their clinical research programs. Dr. Kligman also experimented on retarded children and senior citizens. Some of his articles, by his own admission, are based on fabricated data.

What are we to make of a man of such great accomplishment and such great inhumanity? In weighing his good deeds against his bad, the medical profession has come down solidly on the side of the good. For example: The Department of Dermatology at the University of Pennsylvania has a chair in his name; the American Society of Cosmetic Dermatology & Aesthetic Surgery recently named its first two honorees for the newly-created Albert M. Kligman, MD, Visionary Award in Cosmetic Dermatology; and an editorial in the April 2006 issue of the Journal of Investigative Dermatology celebrates him on the occasion of his 90<sup>th</sup> birthday.<sup>1</sup>

Dr. Kligman continues to play an active role in clinical research as Emeritus Professor of Dermatology at the University of Pennsylvania. He maintains memberships in the Society for Investigative Dermatology, the American Academy of Dermatology, the American Dermatologic Association, and the American Medical Association.

The publication in 1998 of Allen Hornblum's devastating book titled, "Acres of Skin: Human Experiments at Holmesburg Prison", apparently made no dent in the high esteem in which the medical profession holds Dr. Kligman. Moreover, in 2000, a lawsuit against him and Penn by 300 prisoner victims was dismissed. A 2003 protest march by 30 subjects of Dr. Kligman's research failed to deter the University of Pennsylvania's College of Physicians

from honoring him that same year with its lifetime achievement award. It merits mention that Dr. Kligman has made substantial monetary gifts to these institutions.

### **A. Bernard Ackerman**

A. Bernard Ackerman, M.D., is generally regarded as the leading dermatopathologist of our day. Following graduation from Phillips Academy, Andover, Princeton University, and the College of Physicians and Surgeons of Columbia University, he did residencies in dermatology at Columbia, the University of Pennsylvania, and Harvard before doing a fellowship at Harvard in dermatopathology. For four years, he was Director of Dermatopathology at the University of Miami and for 20 years at New York University. For six years, he headed the Institute for Dermatopathology at Jefferson Medical College, and for 5 years he was Director of the Ackerman Academy of Dermatopathology in New York City, a center that he founded and that for the past 2 years he remains, part time, as Director emeritus. Dr. Ackerman began the International Society of Dermatopathology and two journals: The American Journal of Dermatopathology and Dermatopathology: Practical and Conceptual. He has served as President of local, national, and international societies of dermatology and dermatopathology and has been the recipient of an honorary degree in medicine from three European universities, Giessen in Germany, Patras in Greece, and Pavia in Italy. For nine months in 1966-1967, under the supervision of Dr. Kligman, Dr. Ackerman, while a second year resident in dermatology at Penn, engaged in clinical research at Holmesburg Prison in Philadelphia. In 1998, Dr. Ackerman, in a publication, apologized and expressed regret for having participated in research studies at Holmesburg and for errors in the results of those studies.

For the past 10 years, Dr. Ackerman has led a lonely and courageous battle to communicate the horrific nature of Dr. Kligman's work at Holmesburg prison and to prevent similar "research" in the future. In this interview, his first of this length, he tells the inside story. He pulls no punches and makes no excuses for his role. It is a chilling tale, and a shameful one, that will continue until the perpetrators accept responsibility after decades of denial. Dr. Ackerman calls special attention to the University of Pennsylvania, which, to this day, has never acknowledged fully and unambiguously its culpability, refuses to teach its medical students the lessons that should be learned from it, and continues to heap honors and awards on the man responsible for all of it, Albert M. Kligman, thereby making him a hero rather than a pariah.

### **The Interview**

*Dr. Ackerman, how did you come to work with Dr. Kligman at Holmesburg?*

I decided to go to Penn for my second year of residency in dermatology in large measure because of Kligman. He had a lot of style at a time when most university dermatologists were without any flavor at all. Before I arrived on July 13, 1966, we had met on several occasions and talked about his research. He told me he had acres of skin at Holmesburg Prison, and what a tremendous service we were doing the prisoners there by doing research on them.

About a week after I arrived, the FDA banned Kligman from doing research because he had fabricated data in studies of DMSO at Holmesburg. Moreover, the FDA had forbid him from doing that research and he had gone ahead with it anyway. He disappeared from Penn until mid-September, so I never made it to Holmesburg Prison until then. I did research at Holmesburg for about nine months and then, for reasons various, left Penn to go to Harvard.

### *The FDA ban lasted only until September?*

Yes, and it's quite a story. Kligman had the good fortune of having a Chairman at Penn, Donald Pillsbury, who had clout in Washington. Kligman had other colleagues in dermatology who were helpful to him, but the biggest bonanza of all was that the Surgeon General of the United States at that time was Luther Terry. In an unbelievable stroke of good fortune, Penn offered Terry the deanship. He accepted it, but he didn't want to arrive at Penn in the midst of the Kligman scandal. So Terry, with Pillsbury and others, quashed the whole thing. Francis Kelsey, the FDA Commissioner, who was responsible for banning Kligman, was completely outflanked. To be reinstated by the FDA, Kligman was required to write an apology in JAMA. He acknowledged in a Letter to the Editor that the data was fabricated, but he claimed it wasn't his fault; it was the prisoners' fault.

### *What research did you do at Holmesburg?*

My project was about dandruff. Kligman told me it was a disease. In years to come, I came to understand that dandruff is normal; it is dander and not a disease. Our article about the subject received first prize from the Society of Cosmetic Chemists, but it was totally wrong because it was based on the misperception that dandruff was pathologic, rather than physiologic. Furthermore, when I read that article and re-examined the photomicrographs 30 years later, and knowing dermatopathology as I had come to, I realized, with chagrin, that what we biopsied often wasn't dandruff at all; it was seborrheic dermatitis. We were not dealing with a physiologic process; we were dealing with a real disease unrelated to dandruff.

### *Did he fabricate other data?*

I only know personally about my project. All of the numbers he submitted and that appeared in the article about dandruff in The Journal of the Society of Cosmetic Chemists reflected a marked increase in the turnover of epidermal cells in "dandruff", some cases of which were really seborrheic dermatitis which, in fact, may be associated with an increase in turnover of those cells. But some of the patients truly had dandruff, not seborrheic dermatitis, and those specimens should not have shown any increase at all in turnover. Almost certainly the numbers in that article were fabricated. We know that Kligman admitted in the JAMA to fraudulent data about DMSO. It was an admission, not an apology; he blamed the prisoners for the errors. All of this was in keeping with what Kligman used to tell us residents repeatedly: "To paraphrase Claude Bernard, the only reason I do the experiments is to please the critics. I know the answers ahead of time."

Certainly Kligman was not scrupulous about numbers. For one example, we once went together on a fundraising expedition to a pharmaceutical company. After I had presented the work ongoing on dandruff, someone asked, "Al, how many samples have you taken of Pityrosporum for culture from the scalps of these men?" We'd done, let's say five, but he answered, "We've done hundreds". When he made up numbers, they were off the charts. He was fond of saying that "50% of everything I say is untrue and it is up to you to find out which 50%". His estimate was not far off; much of what he wrote proved to be dead wrong, such as the findings about DMSO and dandruff, and his claim in 1966 that testosterone applied topically to the scalp reversed male baldness.

### *Who actually conducted the research at Holmesburg?*

In large part, the prisoners collected the data. The person who worked for me was a sociopath. He was engaged in all kinds of underhanded activities. He ran a homosexual ring there; food from the commissary was used to obtain sexual favors. This guy was a no-goodnik of no small proportions, and there was no small number of them in prison.

*When did the ethics of doing research on prisoners become an issue for you?*

For the first several months, I didn't give any thought whatsoever to the propriety of what I was doing, because it seemed thoroughly legitimate to me. It had the imprimatur of a full professor and of everybody else at the University of Pennsylvania, the first medical school in the country.

In the late Fall of 1966, I invited my younger brother, who then was Chairman of Orthodontics at the Dental School at Penn, to visit Holmesburg. I wanted him to see what was going on there; I was proud of it. One look around and he said, "Have you ever heard of the Nuremberg Code?" That started me thinking. Up to that point, I'd never heard of it. Nobody at Penn, certainly not Kligman, ever mentioned it. I had gone to medical school at Columbia; the word "Nuremberg" was never mentioned during my four years there either.

I didn't grasp fully the implications of what was happening for some time. Kligman was a very charismatic, daring, flavorful character, intelligent, witty, and ostensibly generous to students who worked for him. I didn't disabuse myself immediately of the idea it was really all that wrong, rationalizing that what I was doing with the prisoners was just gathering scales of skin.

Kligman portrayed a very idealized view of what his so-called research was all about. I call it "so-called" because it was the antithesis of what research is supposed to be. It could not have been more sloppy, yet there had been many a medical student and resident at Holmesburg before me and there were many who came after me and all of us were led by Kligman to believe that we were doing something very special: (1) The prisoners were being paid; it was little, but they were being paid; (2) we were giving them a distraction from the miserable routine of prison life; and (3) many of the prisoners not only served as "volunteers", but many of them actually ran the experiments, so we were preparing them for jobs in laboratories or in other medical institutions after they left prison.

*What was your relationship like with Kligman?*

Kligman and I were very close. We went to the steambaths at the Y every Friday afternoon (he had no compunction about lifting someone else's bathing suit). We did folk dancing together. We went skiing together. Our relationship was intense. It was heady being treated as a peer, on a first name basis from the outset, by a full professor, when one was only a second-year resident. This was a major allure of Kligman to many scores of trainees, including medical students.

I was not un-enamored of Kligman for some time. Soon after I had left Penn, I remember having dinner with him at a Chinese restaurant in Boston. I was in charge of choosing guest speakers for a weekly conference at the Massachusetts General Hospital and had invited Kligman. Midway through dinner he asked me, "What are you going to do when you finish your residency?" I said, "I'm going to do a fellowship in dermatopathology. I'm going to be a dermatopathologist." And he yelled, "You want to be a giant dwarf!" That kind of behavior offensive was no problem for him and he usually got away with it. Because he did not think much of the dermatopathologists at Penn, he used to excoriate them consistently at conferences, calling them in public, "retinal animals", the meaning of that being someone whose retina is not attached to the brain.

*Did you do real clinical research after you left Penn?*

I never did it again. My experience at Penn was so disillusioning, the purported research being so contrary to accepted ethical medical practice, that I never wanted to do studies on humans again. Kligman became a model for everything I did not want to be. He became the antithesis of what my hopes were for myself in a life academic.

*When did Penn figure out that Holmesburg had been a bad thing?*

It never has. Everybody at Penn knew about Holmesburg and seemed to buy into the Kligman version of what it was all about. Because Donald Pillsbury, the department chair, was an alcoholic and weak, and Kligman was much brighter, much more energetic, and much more determined, he had *carte blanche* there until Philadelphia closed the research program at Holmesburg Prison in 1974.

No colleague who participated in the experiments at Holmesburg ever has said anything derogatory about it to me. No one at Penn has ever taken responsibility for what went on at Holmesburg or the two institutions, a home for retarded children, and a home for the elderly, all of which served as reservoirs of skin for Kligman's commercial enterprises. I have had correspondence about these serious matters with two Presidents of the University of Pennsylvania, Judith Rodin and Amy Guttmann, and with the present Dean of the School of Medicine, Arthur Rubenstein, and my message to them could not have been more forceful about the wrongs committed under the aegis of that university on populations of human beings who were vulnerable or defenseless. There was nothing resembling, even remotely, informed consent.

I have encouraged the authorities at Penn to instruct their medical students about deviations from behavior ethical using Kligman's operations as a vehicle to that end. In addition, I volunteered to give "The Abuse of Man" by Wolfgang Weyers to every second-year medical student at the University of Pennsylvania, and Dean Rubenstein wouldn't permit it.<sup>3</sup> What harm could there have been to making students aware of conduct unjustifiable in the recent past of their own medical school? Penn continues to insist, however, that what went on at Holmesburg for nearly 25 years was par for the course; everybody was doing it, which is all too reminiscent of the refrain of the defendants at Nuremberg. Kligman, by contrast, has been fêted many, many times by the University of Pennsylvania. He's 90 years old and he's still active in the dermatology department and in his company, S.K.I.N.

*When did the medical profession figure out that Holmesburg had been a bad thing?*

The medical profession did not figure it out then, and there is no evidence that it has figured it out now. No one, to the best of my knowledge, was raising questions about the ethics of the "research" at Holmesburg, the institution for retarded children, and the home for the elderly. During the ensuing 40 years, I am the only person, of the hundreds of physicians and non-physicians who worked at Holmesburg Prison, to speak out about what went on there being wrong undeniably.

Sad to say, the NIH and Institute of Medicine are now discussing changing regulations in order to revivify research on prisoners.<sup>4</sup> And in American dermatology, Kligman is a hero. In fact, he is a hero in dermatology everywhere, especially at the University of Pennsylvania, which is very much in his debt. His business at Holmesburg proved to be a windfall for it. Curiously, we care about what the Nazi physicians did. We care about what the Japanese physicians did. But we don't seem to care at all about what we American physicians have done since Nuremberg.

*Which Nuremberg articles did Kligman violate?*

He violated all of them! My impression is that Penn's "research program," directed by Kligman, consistently violated all ten of the Nuremberg articles.

*Have you published any articles about Holmesburg?*

I've written a lot. On our website, [derm101.com](http://derm101.com), you can read "The Enduring Shame of the University of Pennsylvania, and Especially the School of Medicine." I wrote an article, with regret and apology, about my experience at Holmesburg because I felt that that was the proper thing to do. Not only has Kligman never apologized, he has never expressed any regrets. He is unrepentant and defiant. Parenthetically, on two separate occasions during the past 15 years, Allen Hornblum and I, together, have addressed the City Council of Philadelphia at hearings it conducted about the role of the University of Pennsylvania at Holmesburg. We described that role graphically and asked that Penn be called on to acknowledge its culpability in conduct disgraceful for 23 years at Holmesburg and to give due consideration to compensating those prisoners who were deserving of it.

*Kligman did the key research on Retin-A, right?*

He did the principal research on Retin-A and is given all the credit for it, but it may not have been his idea. Phil Frost, when a resident at Penn in dermatology, two years before me, did research with Kligman at Holmesburg. He later took over Key Pharmaceuticals and started IVAX. We have known one another for 40 years; I saw him just the other day. Phil has told me, on more than one occasion, that it was he, as a resident, who suggested that Kligman try Vitamin A, a cousin of Retin-A, for acne. That was back in the 1960s. It wouldn't surprise me if that were true, because Frost is a very imaginative, capable guy.

*Were the prisoners injured?*

When I was there, I heard stories that prisoners ended up in the hospital. Kligman, himself, acknowledged in an article published in the *Journal of Investigative Dermatology* that subjects had to be taken to the prison hospital because of serious complications of experiments that had been performed on them. There also were other experiments injurious, for example, on children with ringworm, a fungal disease, in which formaldehyde, in high concentration, 70%, was placed under a plastic bathing cap. You know that is going to burn like hell. A 5% concentration of formalin (formaldehyde gas dissolved in water) is what biopsy specimens are preserved in. Kligman used Agent Orange on prisoners. He used psychedelic drugs, LSD among others, on them. He used radioactive isotopes on them. All this was done by a dermatologist. Although much of what the prisoners said later about damage sustained by them is hyperbole, there certainly was injury to them, as well as to the very young and the very old.

The experiments with radioactive isotopes supposedly had the approval of The Atomic Energy Commission. The agent employed at Holmesburg was tritium-labeled thymidine, one of the four nucleic acids in DNA. I had the sense that the material should not be used on human beings. I asked Kligman, "Al, is this legit? Are we really allowed to do that?" And he said, "We have permission from the Atomic Energy Commission." Many years later, Hornblum's book revealed that it was pure fakery. According to Hornblum, someone, presumably Kligman, forged the name of the official at Penn responsible for overseeing that research. Based on that signature, the Atomic Energy Commission gave permission to do those experiments.

*How many different residents worked at Holmesburg?*

Over the course of almost 25 years, surely at least 50. There were medical students, too. None of them want to speak frankly about the subject. When it is raised, they cower or run for cover. It is a peculiar response from physicians who once thought of themselves as "researchers."

*Do you have any idea how Kligman got started down the wrong road?*

I don't know for sure, because I was not there at the beginning of the Holmesburg project. He was a Ph.D. in mycology before he became an M.D. In the early 1950s, he realized that doing experiments on prisoners was a vehicle for making lots of money. Even though he was not a very good businessman in the sense that he oversaw the details of the operation carefully – he left that to others – he understood very well how to seduce the pharmaceutical companies, and they were pleased to be seduced; Kligman was giving them the numbers they wanted. I went with him to J & J, to Revlon, to Schering. It was all about the money. Kligman charged tremendous fees to those cosmetic and pharmaceutical companies. He and Penn made many millions of dollars.

Another factor in determining Kligman's path was his utter lack of capability to manage patients one-on-one. He didn't care about patients and they could sense it. He was in the private practice of dermatology for a grand total of maybe four months, and gave it up. So he embarked in a very deliberate, rational way to generate money from the skin of persons unprotected by society. That led not only to fortune but to fame.

*Did the pharmaceutical companies send people out to inspect the operation?*

That was not done. Representatives of industry would come to Kligman and meet in his office, a small one in Duhring Laboratories, away from Holmesburg Prison. There was no oversight by anybody. Kligman had free reign and he exercised it. No one at the University of Pennsylvania oversaw anything. During the nine months I was at Holmesburg, I never saw a single faculty person from Penn. There was Kligman episodically, some Ph.D.s, some dermatologists from abroad, employees of Kligman who previously had worked for pharmaceutical companies, and the prisoner supervisors. The supervisors were overseen by Sol McBride, Kligman's right hand at the prison, who, being black as well as affable, had the confidence of the prisoners. Beneath all of them were the prisoners, 97% of whom were black. In short, Kligman made the deals and his staff ran the operation without interference from anyone.

Kligman came to Holmesburg only on Saturday mornings and not every Saturday morning, because he traveled a lot. He was a very popular speaker; he was all over the world. In a 52-week period, Kligman was probably at Holmesburg Prison 30 times. There he met with Sol McBride and the ex-pharmaceutical guys to find out about the status of the projects for the pharmaceutical and cosmetic companies, the Army and the CIA, [no research with academic funding?] but he wasn't terribly concerned about the data. For example, he would say to me about my project concerning dandruff, "Just keep picking flowers. Just put them in the basket. Just keep picking flowers. Toss them in the basket."

Most of the pharmaceutical companies took what he said at face value. A couple of his handlers eventually jettisoned him because a deceit became known, but probably 95% of all the companies that he dealt with did not have any hesitancy about working with him, none. They had no suspicions; they loved him unconditionally. It was a big fraternity. The 5% that figured it out did so because something went terribly wrong, like their being given two different sets of numbers. One or two companies may have complained to the FDA, but it was very rare. You must remember, they already had submitted data to the FDA provided by Kligman.

*Why do you think nobody else blew the whistle?*

Most of the physicians who worked with Kligman at Holmesburg, like Kligman, himself, to this day, do not think that there was anything wrong with what transpired there. Some, a few, certainly have come to realize by now that what went on there was profoundly wrong and that none of us physicians ever should have been at Holmesburg. But they don't have

conviction about it, and even if they did, they don't have the courage to act on it. They, like the University of Pennsylvania, remain silent.

### **Statement by the University of Pennsylvania**

In the 1950s and 1960s, the use of willing, compensated prisoners for biomedical research was a commonly-accepted practice by this nation's scientists – most of whom were associated with major universities or the federal government. It is now understood and agreed throughout the global scientific community that prisoners – regardless of their consent to participate and/or their receipt of monies for same – cannot be considered appropriate candidates for any biomedical studies.

Today, the scientific community – including the University of Pennsylvania – operates within a system of strict rules and regulations concerning the use of human subjects in research. As part of the current framework governing such university-based research, formally established bodies known as Institutional Review Boards – which consist of scientists, ethicists, and members of the local community – review all proposed research involving human subjects for compliance with an array of ethical and other considerations.

In the past several years, Penn has invited any former inmate who feels he may have sustained long-term harm as a result of Penn-sponsored studies at Holmesburg Prison prior to 1973 to call us, at 1-800-789-PENN, for a free medical evaluation and follow-up care, as deemed appropriate. That offer still stands.

### **Statement by Albert Kligman Provided by the University of Pennsylvania**

As I have stated repeatedly in the past, my use of paid prisoners as research subjects in the 1950s and 1960s was in keeping with this nation's standard protocol for conducting scientific investigations at that time. To the best of my knowledge, the result of those experiments advanced our knowledge of the pathogenesis of skin disease, and no long-term harm was done to any person who voluntarily participated in the research program.

### **References**

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2. "Acres of Skin: Human Experiments at Holmesburg Prison", Allen M. Hornblum, 1998
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4. "US ponders unlocking the gates to prisoner research", *Nature Medicine*, January 2006, p. 3

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