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SOME MEDICAL ASPECTS OF RADIONUCLIDE INTAKES*

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ABSTRACT

In the field of medicine, particularly industrial medicine, the radiation aspect of the practice probably takes about 1/10 of 1% of our time. All the health physicist's tools of principles of internal dosimetry, lung models, mathematics, chemistry, etc. have little meaning until applied to an individual who has had an intake. This article discusses some of the medical aspects of internal dosimetry.

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SOME MEDICAL ASPECTS OF INTERNAL DOSIMETRY

G. A. Poda, M.D.

In the field of medicine, particularly industrial medicine, the radiation aspect of the practice probably takes about 1/10 of 1% of our time. All the health physicist's tools of principles of internal dosimetry, lung models, mathematics, chemistry, etc. have little meaning until applied to an individual who has had an intake. Let's take a look at some of the medical aspects of internal dosimetry.

All the knowledge of health physicists seems quite reasonable until some physician comes along and upsets the applecart. To physicians, the retention patterns are not applicable. In my 35 years in industrial medicine, I have learned that people are more important than any fancy calculations. We physicians are more interested in prolonging a useful life span; we don't "try to assess" the risk, or how long this person might live, or whether the retention period will be 25 or 50 years. We are interested in the here and now. We are going to treat in order to reduce future risk. Many times it will play havoc with HP calculations.

Our primary concerns at the Savannah River Plant are the transuranics, with some tritium. In some 35 years with this type of activity, I have not clinically observed any of the so-called effects of low dose radiation. I have observed the effects of noises causing a decrease in hearing; I have seen the fibrosis

caused by asbestos; I have seen people knocked out from a good whiff of hydrogen sulfide. Name it, and from the industrial aspect, I have probably seen it. As far as I'm concerned, those who do the figuring are calculating more than we see about radiation.

I joined Du Pont primarily because of their philosophy that the employee's welfare comes first. We have developed a short training tape about uptakes and chelation that is shown to all our new employees. It is reviewed with them annually so that they can understand the medical aspects of decorporation therapy. Once an accident or an incident - terminology is unimportant occurs, it is too late to introduce the subject. After having seen the tape, when something does occur, a physician can talk to them; they know they have been exposed and know what it's all about. The tape is titled "Plutonium Chelation" and is available for loan.

There are also two excellent books, NCRP Report 65 and the Safety Series 47, that are very informative.

In order to institute therapy early enough to be effective, the physician is literally "flying blind." This goes against the grain of almost every physician. We are trained to go by history, symptoms, and findings. Therefore, intakes are an entirely new ball game. There are certain things, however, that the health physicist, patient, and supervisor or fellow workers can do to help make a decision on whether or not a person should be treated.

For this discussion, I will concentrate solely on the trans-uranics. Immediately after an incident, our health physicists will get nasal swipes or a blow to count for activity. I am glad to see that others recognize that the nasal swipe merely tells us that "Kilroy was here." It doesn't tell us how many times, how much he left or anything else - "Kilroy" being the transuranic. A cold or hay fever with a runny nose will very quickly dilute what is found in the nose. Someone who has nasal polyps, allergies or a broken nose with a crooked septum can concentrate material on the nose and give an over-exaggerated opinion. For some time the British said that if there were a thousand counts on the nose, you treat; anything under that, you don't. For a while in this country, we went to 500. If you rely on count alone, it will drive you insane. We have had a person with as low as an 80 count and another person alongside him with 2500 counts; the 80 count had a significant uptake, the other had nothing. So, don't be fooled by nasals; they only tell you that something went by.

Tom Lincoln of Oak Ridge was talking about getting coughs and sputum to try and get a calculation for that. He even devised the ethylene-glycol mixture to give people to make them cough. This may work in some of the people who have blown their noses or have already showered. For those of you who are concerned about the mouth breather, this may be one mechanism for getting an indication of whether something went by. The old story still holds, however,

when all else fails, get a good history. What was being done? What happened? What was the duration of exposure? Was it one single breath or was the person in there for a while? Was the skin contaminated? Was the hair contaminated? What do the smears of the work site show? What does air sampling show? What protective devices were being used?

Then, and this is where the health physics personnel come in, it would be helpful to know what the chemical form is, what the solubility is, what the particle size and isotopic composition is. In order to adequately block absorption, some therapy must be given early, preferably within the first hour, so time is valuable.

You know about body counts; they are great. But what about that whole body count? The body does need to be decontaminated, but in spite of that, many times you will find residual skin contamination which gives a wishy-washy result. Body counters are calibrated by phantoms. The count is not always 100% accurate versus the actual body. You have heard something about the thickness of the chest wall and how it varies with intercostal spaces. You will get a differential between a female and a male chest because of the density of the bone. We have not yet conquered that particular problem on how to adequately make up for the chest wall thickness in calibrating what is underneath. Fortunately, most of our intakes are a combination of americium or similar element, which makes it a little easier to do some counts and to be able to

calculate percentages, etc. The big thing, however, is that it takes time. Consequently, we try to do this after the initial chelation.

Once this material has been inhaled, we have certain time frames for clearance of particles. The material in the nose takes about 60 minutes to go from the nose to the pharynx. From the nasal pharynx, it takes about 10 more minutes to be swallowed. Most likely, however, an awful lot of material has bypassed both of these routes and has already been swallowed. About 12-1/2% of the inhaled matter goes to the lungs. Whether it really is 12% or 30% makes little difference; we try to get ballpark figures to help us in early treatment at the time.

Most of the material from the trachea to the bronchials is cleared by ciliary action up to the pharynx and swallowed. From the trachea, it takes about a tenth of an hour; from the bronchi, an hour. Bronchials take about 4 hours and the terminal bronchials up to 4 hours. As you know, all the uptake is being pushed up and swallowed. Heavy smokers may take more time.

The termination of the respiratory tract, the alveoli or the terminal bronchials, take anywhere from 100 to 500 days to clear. This is usually by translocation - you have heard about macrophages and the direct translocation to the lymphatics and blood and all of that. If it goes into the lymphatics, it will take anywhere from 500 to 10,000 days; some of the insolubles are there ad infinitum. That is the real 50-year model. But, once it hits the intestinal

tract, it clears the stomach in approximately 6 hours; the small intestine in about 14 hours; upper large intestine a good 18 hours; and the lower bowel in 22-24 hours.

Because of this long residual time, we do use a saline laxative. Gene Sanger, when he first became involved in treating uptakes, told me to give Epsom Salts - and it worked! We used Epsom Salts until our chemists told us that the magnesium ions in it were playing havoc with the chemistry because it causes turbidity and bothers the endpoint. Since then, we have been using Fleets Phosphosoda. Using a quite nonscientific approach, the first stool or stools after a saline cathartic are placed in a counter. I then assume that this figure is about 50% of what went through the naso-pharynx to give me a ball park figure that I can work with. In the early stages, the whole process is unscientific. It is only later that scientists get involved and tell us the real McCoy. I don't have time to wait for that. At that point, evaluation of the bioassay is of limited value because it takes too long.

If you are going to bioassay, take the time to do it right. Take both feces and urine. At best, our fecals and urines will overestimate what is really in there by about 3 to 5 times, which isn't bad.

What can be done early on? The first thing we do with our people when we have a suspected uptake is to alkalize the stomach. I don't know how much good it actually does, but in an acid stomach

most of the transuranics are more readily solubilized. If it doesn't do anything else, it does put a coating on the stomach so that when we later chelate, the alkalinity in the stomach somehow acts as a buffer. Someone once asked me why I did it. I asked him to tell me why not and I would quit. He replied, "I can't." So?

For most transuranic compounds, we first alkalize and then chelate. After the health physicists are through with their counting, we give the Fleets laxative.

With most transuranic compounds, the generally accepted method of treatment is that of chelation. We did use EDTA at first, but it is more effective on lead than on the plutonium compounds. Hopefully, Jack Shubert can come up with some cochelation which he is working on, and show us something different. I am pleased to see that we are still working on new techniques because DTPA is not the total answer. BAL has been tried, but it is primarily useful for other heavy metals, not the transuranics. Desferoxamine - DFOA - has been tried. In fact, just recently, the New England Journal of Medicine came up with an excellent use for it. People who must have multiple transfusions 30 or more - wind up with liver damage. By using DFOA on these people, you get rid of the excess iron and they can live a fairly long life and not wind up with cirrhotic livers. So it does have a use after all, but it took the study of transuranics to bring it out. Penicilamine has been tried, alone and in combination with aspirin - it didn't work. It works well on copper, but not on plutonium.

DTPA - diethylene triamine pentacetic acid - is one of the most effective current chelates. As you know, it has been around for over 25 years, but is still an investigational new drug. In order to use it, one has to become a co-investigator with Dr. Clarence Lushbaugh at ORAU. DTPA is administered in four ways - not just three. In addition to the gram dissolved in saline and given slowly intravenously, it can be given directly into the vein - what we call mainlining it. It is a 25% solution, so it's best to dilute it up to about 20cc at least and give it very slowly. I always pick a very small bore needle so that no matter how energetic I feel, the needle puts a physical block in my way and I cannot give it fast. No matter how smart you are, there is sometimes a tendency to rush.

We once had five people to chelate; I didn't want to wait, to take the time to give it either intravenously or by aerosol, so we gave it in the gluteus - intramuscularly. I learned one good lesson then; if it's going to be given intramuscularly, first inject a local anesthetic - the stuff really stings and burns. I had five angry people looking down my throat the next day. I'll never repeat that mistake.

The most effective route, however, is the aerosol. We use an inexpensive Devilibus #40 and a standard ear-nose-throat pump that most every doctor's office or first aid has. You can use the fancier atomic sprays and the like, but it is not a necessity.

Vic Smith of Battelle and the British, according to the last issue of Health Physics (Vol. 44, No. 1, pp. 45-52, Jan. 1983), have said that the aerosol route is about twice as effective as the intravenous route. I didn't know this when I first started. I just knew it was a lot easier to give and I also recalled from my old high school chemistry that by the law of mass action, if you want two chemicals to react best, you put them in the same crucible; you don't place a semipermeable membrane between them. The lung, being a nice large reservoir, apparently does hang on to it and leeches out the DTPA a little bit slower than by giving it intravenously. At least that's the thought behind it all.

We have two forms of DTPA, both the calcium salt and the zinc salt. For years we used the calcium salt. Then it became unpopular because researchers found that a large dose in mice and beagles caused mutagenic or abortive actions. We were told that we couldn't use it on pregnant females or for long term. I, personally, have a few doubts about that, but nevertheless, I'm not going against society and bureaucracy. Bear in mind, however, the calcium salt is much more effective in the first 2 or 3 doses. After that, it is questionable whether the calcium or the zinc is most effective. Jack Shubert maintains that zinc binds the DTPA much tighter than the calcium. The dosage we use is probably many more times what is actually needed, so I suppose it doesn't make that much difference. I don't mind using zinc DTPA except for one

thing. I refuse to give the zinc by aerosol anymore. It has a metallic taste, leaves an awful taste in the mouth, and the patients resent this. We did have one person show symptoms very much like an early case of flu after having a single dose. These symptoms lasted for 3-4 hours. I am not sure of the cause. At any rate, if we are going to use the intravenous route, we use zinc; if we use the aerosol, we use calcium.

If there is any question of a significant uptake, we chelate as soon as possible, block the deposition, then take our time in doing things like a body count and all of the other things that health physicists like to do and should do; then we know where we are. I feel much more like a real physician after our health physics people have told me what I need to know. I know then whether I have anything to worry about. Up to that point, everything is a calculated guess. Followup excretion rates will determine how often and how long we need to treat. We will treat as long as there is a significant elimination. If we hit a plateau, why inject something that is foreign to the body any longer?

Those of you who are concerned about doing your statistics and calculations in spite of "physician interference," please refer to Health Physics, Vol. 34, published May 1978, pages 419-31. My colleague, Roscoe Hall, was the principal reason for this article. We gave each other a hard time until he devised a system to keep both of us happy. He developed some formulations on how to

calculate dosages, intakes, residuals, etc. That publication contains a ready built formula so you don't have to worry about Langham's curve, since it won't tell you anything about chelation. Now you have the best of both worlds. You have the Wright-Langham curve plus the Hall curve; you can calculate what you please in spite of the physician.

Another thing to remember about chelation - chelation is not discriminatory. It will not remove just the transuranics. For instance, with diabetics who are on a protamine zinc insulin type of medication, you must be very careful because if you chelate often enough or vigorously enough, you will chelate out the zinc and that person will go into an insulin reaction because you have cut the effectiveness of the long-acting protamine zinc. We had one person whom we chelated for over two years - he lost his senses of taste and smell. What had we done? We had chelated out the zinc. My health physicists had told me that I could expect DTPA to be effective on excretion for about 100 days. We waited exactly 100 days, and on the 101st day he started getting his taste back. It was amazing. We gave absolutely no treatment except a neurologic and otolaryngologic consultation because we wanted to see what was going to happen. It took about a month, without any zinc supplements, to naturally rebuild his body concentration and regain the senses of taste and smell completely. We kept him advised of what we were doing and why, and he was extremely cooperative with our protocol.

This brings up another point - most of these people are extremely frightened. When I am involved, I'm frightened too. Since health physicists are the people who will be seeing them first, you must learn to put on a beautiful poker face. They will be looking at your face, not listening to what you are saying; and if you are scowling - they're scared. Put on a happy face and reassure the patient, no matter how badly he is contaminated. Be optimistic.

What about other chelates? PuChel was very notorious for some time, but quietly disappeared, whether from shortage of funds or lack of interest, I don't know. It is being studied again as a part of co-chelation by Jack Shubert and others. Co-chelation was advertised for a time. At that particular time, it didn't work out, but it is still under study. Licham C showed promise, but proved to be too effective. It chelated everything out of the experimental animals - many died. It apparently is a bit too toxic for clinical use.

The other element we must deal with is tritium. Most of you know the biological half-life, the different forms of oxide, and the basic tritium. The gas itself gives no problem except through inhalation, but the tritiated water will pretty well balance in everything in the body. In our experience in treatment of tritium, our main problem has been absorption of tritiated water through the skin. When our health physics personnel uncover someone with too much tritium, we are called in. Unfortunately, being in a

security area, we can't bring in the beer barrel, which is touted as an excellent treatment for tritium. We have tried different types of diuretics and found only one that is really effective - Hygroton. Hygroton is a diuretic that has about a 72 hour biological life in the body. It is one of the few that is absorbed through the liver; consequently it is re-absorbed and has a 24 hour effect where most diuretics have a limited effect. We feel Hygroton does increase water secretion significantly enough to give a deletion of tritium.

I was involved in an effort to prevent uptakes, along with our industrial hygienist, J. J. Croley. I recalled that when I lived in the North, we used silicone on an old brick and stone house to repel water so that in the winter time they wouldn't freeze and crack and wondered if that would work with tritiated water. We took some polyvinyl suits and sprayed on silicone. Much to our delight, tritium wouldn't go through it. The only problem was that the silicones would not adhere very well to polyvinyl. We then tried Saran plastic wrap, which proved to be too difficult to handle. Finally someone at Jackson Labs figured out how to anneal Saran to other plastics by laser. That product is now on the market.

In summary, the more important aspects of internal dosimetry and decorporation really have very little to do with the chelating agents, the ability to use models or formulae, or to calculate dosage. It takes a full and complete cooperation of management,

health physics and the physician. Without that, there is no successful treatment. None of us stand alone. We all need each other. The physician needs all the early data the health physicists can give him, he needs all their expertise and experience. Once we get all the data they can give, plus the history, then we physicians must make an assessment of risk versus benefit. Am I going to hurt the person if I treat him, or am I going to do less harm by not treating him? That is not an easy decision, but a decision must be made. The only clear-cut cases are the catastrophes - fortunately, we have had none. Thus, responsibility rests with the cooperative efforts of the health physicists and the physician team. Don't wait until the accident happens to develop a good rapport. You must share your expertise in advance. You must make cooperative emergency plans so that when an accident happens there won't be any surprises for either party. Indecision on the part of either the health physicist or the physician creates confusion in the patient's mind. We don't need that. As professionals, remember this: Both the physician and health physicist are morally committed to the patient's welfare. If you bear that in mind and work together, you will have the same type of cooperative venture and, hopefully, as good a record as we have managed to maintain at our plant.