5. May 22, 1948
"The Calculation of Radiation Dosages from External and Internal Sources." L.D. Marinelli

The following is the verbatim transcript, taken by the secretary, of his live lecture:

"Mr. Chairman, Ladies and Gentlemen:

The subject of my talk requires reviewing the definition of the unit of dose whish has been in use in radiotherapeutic work for the last 20 years. The roentgen, many of you have probably already heard, is that amount of x or gamma radiation such that the associated corpuscular emission will produce in 1.29 milligrams of air, ions carrying one electrostatic unit of charge of either sign. You notice that we have measured x or gamma radiation by its absorption in air..."

"...When we speak of a dose in roentgens, as given by the gamma ray and x ray source, then the amount of energy given to the tissue may be in doubt by 10% or 12% in the therapeutic range. So much for the unit of dosage that we like to employ.

"The calculation of the radiation dosages in experimental therapy is a complex one. We have to describe the source accurately and we have to describe the absorption of the radiation emitted by that source accurately in a very complex system. I am going to tell this audience that, in attempting to describe the source of one milligram of radium in terms of does in roentgens, [it took] me in ten years of experimental work before we came to that value of any point for roentgens in any material at one centimeter when the point source of radium is surrounded by $\frac{1}{2}$ millimeter of platinum. That was only one isotope...for we have quite a number of them. In order to make matters sufficiently intelligible, I think that I will divide the subject into [two kinds of emitters]: gamma ray emitters and beta ray emitters. Although in practice, of course, a single isotope may emit both. We shan't try to conjugate them, as we are____ the emission of a source in roentgens spread out from a source one millicurie in strength at one centimeter distance That can be done as outlined in the first slide.

"If you have a source of one millicurie in the center of a _[shell]_____of cells and if you calculate the energy absorbed from that cell in that shell in terms of a cc of air, we come to this expression, which is nothing else but the number of gamma rays emitted from_____. {One sentence is unintelligible as he is speaking while showing a slide)...multiplied by that fraction of the flux, which in this case is gamma ray flux, multiplied by that fraction which is converted into ionizing energy and these are represented by two _____, one marked "a," which takes care of a constant effect, the other [marked___], which takes care of the directed conversion. If we express the energy absorbed in this cell in terms of the number of ions and in terms of the current, we have to divide by a factor which is ____the number of ions produced times the energy that is required to produce a ____of ions. Finally, we ___with the consummation of this constant, that I call "isotonic," which represents, as I said, the number of roentgens per milligram hour times the sum of the energy of the gamma ray times the conversion factor for electrons. For iron 131, this expression comes as 2.6.....

"...To calculate the emission in grams per millicurie source, we must have knowledge of the disintegration scheme. When that is known, then [Slide} it is easy to calculate that emission in roentgens. This is the emission in roentgens per millicurie at one centimeter as a function of the energy of a gamma ray in MEV's under the assumption that there is one gamma ray per disintegration. In other words, [it] is the factor that you have seen before_____and only one term in the sum. You can see that if you have an isotope which emits only one gamma ray per disintegration of about one_____.

"What we have done [up to this point], is to consider the point source and [the] calculated emission at one centimeter distance [from the source.] Where do we go from here? [From here] it is a matter of calculations and approximations... You may have extended sources, [ones]

~~it is a matter of calculations and approximations... You may have extended sources, [ones]~~ outside of the body...[or] inside the body if the isotope is distributed with any degree of selectivity....

[Slide] One way to do it is to consider a case, a difficult case. Let'[s suppose we have a biological object ...and inside the biological object we have a certain isotope for which we know the ____. And let us suppose, also, that on that biological object we have a uniform distribution, a uniform concentration of the isotope and we call it "c" microcuries and millicuries per gram. Then, we can calculate the dose at a certain point "o" by performing this calculation here. This is the rate in hours, roentgens per hour, besides gamma as specified in roentgens per hour. Multiply the concentrations, and multiply a geometrical factor which is _____and yield. That is, in other words, nothing else but the sum of the contributions.

Now, this looks very simple here. It is very simple in the case of the sphere, much simpler than in the case of the cylinder, less simple in the case of an_____, and certainly not calculable in the cases of many shapes that conform to biological objects. The best that we can do right now is approximate it. Make approximations and hope that we can perform experimental observations on distribution of dosages on biological objects of any size. That would require ingenuity and it would require time and patience. But, happily, we cannot say that it is impossible.

In the next Slide we are going to show just what that absorption coefficient is like --that new part which you saw in the exponential of that _____, I have to have a word of caution of this coefficient of absorption of the radiation . In the sense that in the ranges of energies of the gamma rays emitted by them isotope which is practically from 0.1 to 1 to 2 MV, the absorption per centimeter is more-or-less constant. It does not vary very much. And it is not the total coefficient of absorption that you see in the tables, because of the presence of scattered radiation. It is much more likely the sum of the conversion coefficient [that you see.]

We now come to the subject of beta ray emitting isotopes. This subject is slightly different, not in principle, but in the geometrical considerations. As you see, in calculating our dosage, we do account for the fact that the radiation is not absorbed at the point [at] which [it] is emitted. Gamma rays do travel quite a bit. With beta rays, the situation is slightly improved for biological objects of sizes comparable to man. The utilization and range at which the beta rays and energies utilize ____ is quite small compared to the dimensions of the object. Therefore, we can simplify our calculations and arrive at some simple formula that correlates the concentration of the isotope to the dose in the tissue. Without going into too much detail, I might say that what we really do here is calculate the energy absorbed per roentgen_____or 5.22 time 10^{13} electron volts. What we do afterwards, then, is assume that there is a certain number "n" of atoms per gram of tissue and we multiply that by the number of electron volts emitted, on the average, per disintegration in the form of beta rays. And we assume that that is absorbed therein. By doing that, and taking into account [that] the total number of atoms disintegrated is tied up with the millicurie by means of the decay constant, as Dr. Curtis pointed out yesterday, and by taking into consideration that the definition of a microcurie, which is in this case the amount of the _____of which disintegrations___2.7^4 atoms per second, we come to this formula, which we make. The dose due to beta radiation in a ____with the concentration in microcuries per gram of an isotope or ____ and having an average energy per disintegration, [___] the average base. This is the total dose emitted by the isotope to its ultimate disintegration.

If we want to gain some information as to rate at which the dose is given, then we must do what is represented in the next Slide. [Now} we multiply the total dose by the fraction disintegrated from this, and that's the rate for this. I have here an example for radioiodine, the factor disintegrated per day in 3-.66 per cent, the average _____, and the beta comes to 144 grams per microcurie destroyed. Although 144 equivalent roentgens are delivered by 12.5 time the concentration during the first day, biological systems are not so static as to allow that comfortable calculation. In addition to radioactive decay, we are confronted with biological elimination, and care must be taken of that, and if you omit all this, why, we come to the formula which is very

similar to the one that I gave before----------but the half life is different. That's the biological half-life, not the radioactive half life. I will say that [it's] the effective half life, which is the half life that corresponds to the actual disappearance of radioactive atoms in biological material.

May I have the next Slide? This is a graph which will help in determining the average energy per disintegration. It shows the relationship between the average energy in beta and the fixed energy of the beta ray spectrum. E_o is usually given in all physical tables. Unfortunately E_b is not. So we have tried to relieve that situation by giving the relationship of the average energy to the fixed energy as a function of the fixed energy. [Although] I will not go into it, I [would] like to just mention that it is a function of both the energy and the atomic number of the isotope with disintegrates. The ratio of the average energy to maximum energies ranges anywhere from .25 to .46 or .47. This curve here is for positron emitters and these are from beta ray emitters of different atomic numbers.

May I have the next Slide, please? Now this is an example of a calculation done in connection with a case of thyroid carcinoma to whom was given two doses of radioiodine: 160 millicuries on this day and 125 millicuries on the other. By means of a biopsy, we determined the approximate volume of tissue to be treated and we came out with about 2,000 cc. Except for excretion, we assumed that the given dose all went to the tumors. Our concentration in this case is just the extrapolation of this slope the day after the dose was given. The concentrations were given by the sum of the doses divided by the weight of the tumor. _____is not any other than a constant of the formula for ___-beta. The energy in MEV is 0.205, the average energy in MEV per disintegration of Iodine-131. Point 5.7 is the effective half life of the element in the tumor of the patient which we had determined experimentally. You can see that the total dose was of the order of _____roentgens, and it was accumulated as shown by this slide. In other words, the whole dosage was administered in about 30 days.

may I have the next Slide, please? This slide refers to orderly elimination of the isotope when you can express it by exponential. In another case, we were not able to do so because it would interfere with the elimination of the isotope from the gland. It was an experiment also done on a cancer of the thyroid and we wanted to study what happened to the radio-iodine in both its elimination and its pick-up when the thyrotropic hormone was administered. So, we started at zero time with a small dose of radioiodine, around 10 microcuries, and we noticed the concentration, the total reading over the gland, which corresponded to 200 microcuries. Then we watched, day by day, while between the 5th and the 9th day, the throtropic hormone was administered. This was on a Friday. On Monday we found just a little change in the elimination of the isotope. Following the first doses, 144 and 488 microcuries, several days after the administration of the thytropic hormone, we found a tremendous increase in the uptake--of 30% to 80% that increase to 60%, with the reading of the thyroid confirmed by the excretion picture. But the question was this: what was the relation of this to the plan? If this curve is plotted in Cartesian coordinate, not logarithmic, and the area underneath that curve is determined, then we have a measure of the dose given and that particular curve, that rectangle, bound by one day and one night of curie per gram if equal to 12.5 roentgens, and therefore the dose given to that gland is equal to the ratio of those two areas, the area of the curve and the area of the particular rectangle. My point is that, in the concentration of the blood, after administration of P-32 and by following a calculation of this sort, we can have some idea of the dose given to the hemopietic system.

May I have the next Slide, please? This column refers to the patient's weight, this is the dose given to the patient in millicuries per kilogram, and this is the dose that we have obtained as an average, if no elimination has taken place. This is the dose that would have taken place within the body, on average, taking into account the elimination. And this column,_____, is the ratio of the actual blood dose as calculated by the preceding formula, which I will repeat. You can see, in the case of P=32, that the blood itself takes only from 25% to 30% of the dose of the body, on average. That means, of course, that some other part of the body must take doses higher than average. And, as a matter of fact, in animals, and in some material that has come to

autopsy, we have reason to believe that this dose is really the highest obtainable in the body and is found in the bone and in the marrow. I mention this because, at this dosage, severe hematological responses occur. We have followed the same type of study in patients to whom large doses of radioactive iodine have been administered. And by means of this calculation, we could more-or-less foresee what hematological response would be..

May I have the next \Slide, please: This is a series of cases to whom radioiodine was given at different dosages and whose activity in the blood was followed at periods varying from 5 to 21 days. On the basis of the concentration, we have tried to follow and calculate the total dosage to the blood. You can see that it is remarkable uniform. These doses, let's say a rough figure of 100 roentgens per 100 millicuries of radioiodine administered, is strangely constant. Why? Because this patient here eliminated only forty per cent of the radioiodine in four days, whereas, this one eliminated eighty per cent. Thus, it seems as though elimination is not an important factor in dosages in the blood when radioiodine is administered. It looks as though the patient who has glands or tumors that absorb iodine from the bloodstream is exposed later on to the same isotope that is released by the gland or the tumors in the form of protein [bound?] iodine. The picture of Iodine-131 is not as clear as this.... Nevertheless, when we are considering localized radiation which certainly may happen in the stomach, in the mouth, a d in the kidneys, due to the concentration in which radioiodine is found in the fluids bathing the structure, 31000 millicuries of iodine is administered. The dosage may be as high as ten times the dose shown here. But we do have an index of what to expect when doses of this magnitude are given.

Thank you.

{Applause)

Question/Answer "Yes, we have published one complete paper in the Am J of Roentgenology in the Feb. issue. and Nucleonics is carrying 2 papers.

5. Standards of radioactivity. L.F. Curtiss, Chief Radioactivity Section, National Bur. of Standards, Washington, D.C.

Friday Afternoon (Chairman W.M. Manning, Director, Chemistry Div. ANL)
1. Evaluation of methods of measuring radioactivity. Walter H. Zinn, Director ANL

2. Problems in the measurement of C-14. W. F. Libby, U of Chicago

3. Demonstrations:
Methods of radioactivity measurement. W. P. Jesse, Instrument Research Div. ANL
Monitoring methods. J.E. Rose, Director, Health Physics Div. ANL
C-14 absorption by the mouse. Austin M. Brues, Dir. Biology Div, ANL
Handling of isotopes in the laboratory and clinic. W.P. Norris and Walter Kisieleski, Biology Div;
James R. Gilbreath, Chemistry Div., W. B. Neal, Biology Div and Billings Hospital.

Saturday, May 22 Chairman: R.E. Zirkle, Director, Institute of Radiobiology and Biophysics, U of Chicago.
Morning
1. Statistical evaluation of radioactivity measurements. T.P. Kohman, U of Chicago
2. Radiation hazard regulations. J.E. Rose, Health Physics Division
3. Calculation of radiation dosage from external and internal sources. L.D. Marinelli, Memorial Hospital, N.Y.
4. Techniques of autoradiography. Titus. A. Evans, State Univ. of Iowa.

Afternoon

1. Round table discussion of the use of isotopes in chemistry, biochemistry and physiology. E. Rabinowitch, U. of Il (Chairman), R. H. Burris, U of Wisconsin, R. G. Gould, U of Illinois, H.S. Anker, U of Chicago.

2. Round table discussion of the use of isotopes in the clinic. L.T. Coggeshall, U of Chicago (Chairman), H. L. Friedell, Western Reserve University, Dwight E. Clark, Univl. of Chicago, J.W. Carpender, U of Chicago.

Notes of LDM Presentation (Chicago 5-22-1948) "Calculation of radiation dose from external and internal sources."
(5 pages)
Unit - roentgen: that quantity of x or γ radiation. Such that the associated corpuscular emission releases per 0,000 1.29 grams of air, ions carrying 1 e.s.u. of charge of either sign. Note: roentgen ® unit of measurement of radiation on basis of energy absorption (83 erg) unit weight gram of air-
Convenient thus far because energy absorptive in most tissues in therapeutic ranges does not differ greatly from 83 ergs.
With supervoltage x-ray, β, $\prec$ (α?), and neutron radiation - it is not possible to focus the attention the agent. **We must shift it to the dose absorbed.**
In order to leave things in radiotherapy ranges as they were, we can define as unit of dose the amount of energy absorbed per gram of air when exposed to 1 r of γ radiation to this unit r.e.p. or eg. roent.

Calculation of radiation doses (meant as energy absorbed) resulting from radioactive isotopes is complex: 1) sources complex, 2) recipient biological systems are complex - metabolism. years to determine r/mg-hr at 1 cm $\frac{1}{2}$ Pt from point source of Ra. The subject, therefore, is in preliminary stage of preparation.

Shall consider γ- and β-ray sources separately. γ- rays + as in the care of Ra it is useful to calculate I γ
1st slide (some emitting several γ 's) - [calculations]
2nd slide - [calculations]
3rd. slide; dose at point O from distributed source.... [calculations]
4th slide - show absorption coeff. obtaining in water for small distances.

β-rays
Since roent. def. for e. magn. radiation, must use r.e.p. Simple principle in uniform distributions.
e.r. = energy/83 ergs = 5.22×10^{13} 3.v.

5th slide [calculation]
6th slide - dose rates. elimination due to turnover of radioelement. Explain equilibrium
7th slide

Practical Applications.
8. I-131 Kuecht (exponential elimination) effective half life 5.7 days (isotope 8 day) calculation from formula
9. When concentration does not vary exponentially with time, then calculation must be done on basis of e.r./day
Area under curve (now logarithmic) divided by area bounded by 1 μc - day = 12.5 r.
10. P-32 given to patients - illustration of order of magnitude - Blood dose low, hence some tissue must get more than D' (average) most likely bone which show D.A.R. (no elimination) hence Dose very nearly D.
11. I - 131 blood and body dose (assumption) describe doses to blood higher than P-32 yet not severe hematological changes; must be due to marrow (recovery different) receiving dose close to that of bone or body dose when P-32 is used.
12. graph of concentrations of I-131 in blood
13 Apparent doses by intravenous injection. What may happen to stomach, kidney and bladder.

[From these notes, LDM gave a talk. This talk was transcribed and typed into rough draft by Brues' secretary, Florence Mohri, which is attached to the notes. JMG]

Obviously, this was a very important meeting and Marinell's method was of interest to all and made changes to people's thinking. He actually brought to U of Chicago and to Argonne the knowledge that resulted from nearly 2 decades of research that had taken place in N.Y. and transplanted it to the Midwest.

6. N.D. [Same legal pad as 5/22/48]
"Lecture I - Physics of Radiations
What we mean by radiation: alpha, beta, gamma, neutron
Loss of energy of [ionizing?] [particles?] through matter.
General laws - stopping power - range - Cherenkov = ions [neutrons?] etc - radioactive losses
Transfer of gamma and neutron energy to matter -
gamma = [ph_____?], Compton [pair?] production - photo disintegration
neutron - collisions: elastic, inelastic, capture
details: gamma radiation : phantoms; scattered radiation build up.
Neutrons - elastic collision, cross sections = light atoms

References: Siri [Sici?], Fermi, M.I.T.; Heilter

7. Oct. 19, 1948
Program of "Symposium on Low Level Irradiation" Argonne National Lab, Chicago.
A.M. Chairman: Leslie F. Nims, Brookhaven NL

1. E. Lorenz ANL and National Cancer Institute (Comments L. Marinelli, H. Lisco)
2. N.P. Knowlton, Los Alamos Scientific Laboratory (Comments L O. Jacobson)

P.M.> Chairman H. Blair, AEC Project, U of Rochester

3. A. Hollaender, Oak Ridge NL (Comments T.T. Tahmisian)
4. R. Boche, Inst of Radiobiology and Biophysics, U of Chicago (Comments, G.A. Sacher)

Evening Chairman: R Zirkle, Inst of Radiobiology and Biophysics, U of Chgo

5. E Barron ANL
6. A Brues. ANL

LDM Comments on Dr. Lorenz's talk, "Effects of Continuous Low Level Irradiation of Laboratory Animals with respect to life span, hematoporesis and carcinomagenesis."

Marinelli: *Commends Dr. Lorenz or his thorough approach in clarifying understanding of the effects of total body radiation on mammals. LDM comments on the public "hysteria" roused by "well meaning but insufficiently informed commentators." "The hysteria is by no means limited to the public; it pervades certain section s of the medical profession with unexplained intensity." He gives some examples: legal action taken by public at large against a leading scientific institution by a patients claiming to have contracted leukemia from being wheeled through the x-ray dept and a single visit to the cyclotron room. He says,* "It is gratifying to be assured that ...the level of 0.1r per day was well chosen before the advent of the nuclear reactor. The evidence presented here shows that this daily rate does not shorten the lifespan within the experimental error of these investigations. ...It would be tragic to dictate to the nation criteria of safety based on 5 or 10 surviving mice.

8. Feb. 24, 1949
"Control of Health Hazards in the Use of Radioisotopes as Tracers" - University of Minnesota

Intro: Radiation effects found soon after discovery of x-ray and Radium. These were localized to hands. Burns and conditions modified to prevent them. These were acute exposures. These were acute exposures. The results of radiation levels which did not produce acute exposures were apparent after many years (anemia, leukemia) Radiologists' leukemia.
Radiation protection was always a corrective measure.
Practical results bad. Palpable injury per 3-man year (estimate).
Levels of radioactivity are bound to increase and propagation of use in labs unfamiliar with them will increase injury rate unless the administration of Universities and research Institutes take steps to prevent it.
Control for protection of scientists, technicians, and public is parallel to demands of most scientific work which demands prevention of contamination in labs and equipment (example: C-14 and P-32.)

Classification of Hazards
a) Deposition of radioelement in the human body: physically this can happen by

1)Ingestion - mode: accidental drinking, contamination of food and H20 by hands, surfaces, wrappings, etc. Result fate and distribution: digestive tract and metabolic distribution
2) Inhalation: gas, vapors, spray or dust.
Result: deposition in respiratory track; lung alveoli, ciliary action, some ingestion
3) Absorption: through intact [sic] or injured body surface

Comments: most insidious and most difficult to control.

b) Exposure to radiations (β & □): whole body and limited parts

Principles underlying protective measures

a. prevention of ingestion, inhalation, and interstitial absorption in the body.
this requires confinement of radioactive isotopes and prevention of spread- analogy with infectious diseases: differences- no spontaneous reproductions (advantage)
but no means of radical disinfection (disadvantage)
b. prevention of harmful exposures to radiation: shielding and remote control manipulation
the measures to be put into practice will depend on levels and type of radioelement used.

Practical realization of control - Maximum permissible levels

Well-known natural limits of background radiation and natural radioactivity:
External
1 Cosmic ray [there is a 4" high table with]
Natural Levels, M.P. L.[maximum permissible levels], and ratio .....

...

Notice that m.p.l. for ingestion exposure are closer to natural levels than external exposure. This is so for Ra because of its property of concentrating in human bone-Actual cancer has been observed at 1μ□, none at lower level; with beta ray emitters, levels have not been established but they are apt to be substantially higher than those for Ra except for the long-lived one which unfortunately are bone-seeking, as eliminated slowly and have a long half-life. I refer to S-90, Ca-45, Y-91.

Present knowledge does not permit accurate establishment of m.p.l that can be fixed in the body except for order of magnitudes. Quantitative evaluation of hazards in terms of contamination can be surmised approximately from animal experiments in the case of ingestion through water, food, and a certain degree through inhalation, but it is very difficult to establish in terms of contamination of surfaces and instruments.

Provisional levels have been suggested for short-lived isotopes: 10^{-5} μc/liter for air and 10^{-1} μc/liter for water. For long-lived bone-seeking isotopes, it is better to rely on figures at least three or four order of magnitude lower.

Example of calculation of water contamination

N = amount of Ra, permissible in body = 10^{-4} grams t = 50 years assimilation
R = daily intake per day in water
$\lambda_{□}$ = chronic daily rate of elimination 5×10^{-5}
[several mathematical formulae]....

Toxicity levels are function of half-life $\lambda_{□}$; *Energy and character of radiation* N; *degree of* selective localization in the body N; ratio of elimination $\lambda_{□[?]}$

Let us analyze, coarsely, what can be done to maintain these standards of safety when working with tracer amounts. We shall define tracer amounts as amounts less than one millicurie - Whether this is dangerous or not depends on the factors mentioned before and in addition to the chemical and physical state and mode of handling - it is obvious that in some cases shielding can be omitted or attained with relatively small thickness of materials and I should not be surprised if ordinary bricks would not do for certain □ emitting isotopes. This will take care of whole body radiation. The realization of overexposure will come when some rough calculations are made on the exposure to the hands: at 10 cm distance, the mr/ hr per mc varies from 2 in the case of I-128 to 191 in the case of Na-24 and this is due to □ radiation alone these levels are to be compared to the M.P.L. of 6 mr/ hr- It is obvious that in most cases handling with tools is necessary to keep hands to about 25 or 30 cm away.