

Symptomectomy

A chat with Robert Cathcart, M.D.

B. J. Luberoff

Incline Village, Nevada, is a community of 5000 souls, more or less, except during skiing season. Then it swells beyond 15 000. It's on the North shore of Lake Tahoe. a beautiful hour's drive over Mt. Rose from Reno.

Make believe that you're there, sitting in the living room of the 5000 square foot lakeshore home designed by Robert Fulton Cathcart, III, M.D. There's a fire crackling in his wall to wall, floor to ceiling stone fireplace. The first thing you might want to ask him is how in the world he came to practice medicine in Incline Village? Did it have anything to do with his being an orthopedic surgeon and how some people ski?

Well I had the chance to spend such an evening with Bob Cathcart and to ask him that question, and some others. Here's how it went.

A. Orthopedics isn't what really brought me here. I had practiced five years in San Mateo—that's on the San Francisco peninsula. During that period I invented and patented what's now a widely-used hip prosthesis ... we can talk about it later ... but then I became interested in nutrition, specifically vitamin C. After reading Pauling and everything else I could on the subject, I started "experimenting" with vitamin C first on myself and the family and then on a few selected patients. I made some basic discoveries, and it's them I really want to tell you about.

Now in San Mateo I had little opportunity to treat patients with vitamin C. Peer pressure at that time, about seven years ago, was pretty much against the physician using vitamin C. Besides, as an orthopedic surgeon, in a region where specialization was respected, I seldom saw patients who had colds, or other viral diseases. So I commuted to Incline Village every week for a year. It's only a few hours' from San Francisco. Here I went into association with a general practitioner who planned to go to another town after about a year. During that year I demonstrated that *properly used*, vitamin C could decrease most of the morbidity and all of the mortality from viral diseases. I contacted Pauling about this and he said that he knew of no other physician who was doing exactly what I was doing.

Q. What was that?

A. Well first let me give you some background. Fred Klenner of Reidsville (*I*), North Carolina, one of the greats in vitamin C therapy, has been working with it for what seems like twenty or thirty years. He found that he could detoxify most virus diseases with intravenous doses of "C". Now he even uses it for carbon monoxide poisoning, barbiturate poisoning, even snake bites. Now what I discovered, which was different, is this: the average person, at least 80% of normal individuals, when they are well can take, orally, between 10 and 15 grams of vitamin C, in divided doses, during the day before—

Q. Hold on, did you say 10 to 15 grams?

A. That's correct, 10 to 15 *thousand* milligrams a day. Most people can take that much before it produces diarrhea. Some people can tolerate less, a few can take more ... *when they're well*. The astonishing thing is that this same person ... the patient who when well gets diarrhea on say 12 grams ... when ill with a moderate cold can take 30 to 60 grams without diarrhea; with a bad cold or a flu, 100 grams, sometimes even 150 grams, and with viral diseases such as mononucleosis or viral pneumonias, I've used in excess of 200 grams a day without it producing diarrhea...

Q. That's nearly a half pound ...

A. That's correct. In some cases the body evidently

with vitamin C

needs that much, albeit for only a short time. With mononucleosis or viral pneumonias, during the first couple days of the disease we sometimes see a need for that half pound—more or less. Patients with bacterial diseases will absorb similar amounts depending on level of toxicity. Of course, they should get the appropriate antibiotic, too. Essentially, the sicker you are the more you can take; and taking enough—and *that's important*—seems to detoxify you. You get well quickly. And as you do you find that you can tolerate less and less ascorbic acid until you go back to normal when you're well.

Now there's been a lot of talk about double blind studies and about the benefits of vitamin C in preventing colds and things like that. Your article by Coulehan (2) is a case in point...

Q. Let me slow you down just a minute. What you're saying is that an average, healthy person can take about 10 grams a day. If he's well and takes much more he'll begin to feel malaise in the gastrointestinal system, and if he persists he'll get diarrhea.

A. Right.

Q. But if he has a viral illness then he can take a lot more, and doing so will make him feel very much better, very fast. What's this saying about what is happening in the GI system and elsewhere?

A. Well, we think that ingested vitamin C in the GI system is in equilibrium, you might say, with that in the bloodstream. It's absorbed through the stomach and the intestines into the blood stream to maintain some kind of "saturation" there. Now if, for whatever purpose, the blood is "throwing off the vitamin C at a high rate, then more and more will be absorbed so that the vitamin C in the intestine does not reach the rectum. If it does in sufficient amount to create a hypertonic situation, then body fluids migrate to dilute it and that produces mild diarrhea.

Our genetic defect

Q. So you kind of "titrate" the illness. But if the body really needed all that ascorbic acid, wouldn't it just make it?

A. Ah, that's the point—*it can't*. Irwin Stone (3) and others say that man has some sort of genetic defect, that in the evolutionary process the higher primates lost the ability to synthesize ascorbic acid. Only a few other animals share this "defect": the guinea pig and an African fruit-eating bat and some minor species. By and large the lower animals synthesize ascorbic acid in the kidneys; higher up the evolutionary tree, they make it in the liver. It really is a liver metabolite in higher animals. Now how did this happen? Well, the higher primates evolved in areas that had fruits and vegetables in profusion. Just think of the monkey sitting around eating bananas and

leafy things that have a lot of ascorbic acid. He was fit enough to survive in this environment. The stresses on him were not great. He was not exposed to as many infectious diseases as we are. So the ability to synthesize vitamin C offered little survival value and was lost. Now along came man with his great capability and curiosity, and he ventured out from these Gardens of Eden and went into areas where food ascorbic acid was scarce. His diet changed. The biggest change came when he went out on the sea. There, without any fruits and vegetables, he got scurvy, that's the acute deprivation of vitamin C. It was only when the British discovered that lime juice could prevent scurvy (8) that men were able to go for long distances out on the sea. Scurvy will be induced in two to three months if you're on a completely vitamin C free diet. Then you'll start manifesting symptoms of the disease and without treatment you'll die in another month or so. But preceding the scurvy syndrome are a variety of low blood ascorbic acid states. Stone and Pauling popularized them and pointed out that they lead to various diseases from which mankind suffers.

Q. What does ascorbic acid do normally?

A. The non-controversial functions of ascorbic acid (4-6) include several enzymatic processes, the body's ability to make collagen, dentine, adrenalin, corticoste-

roids, maintain proper functioning of the immune system, the blood coagulation system, metabolism of several amino acids. Lewin (7) believes that ascorbate aids in formation of cyclic AMP and inhibits its hydrolysis which, if true, means that vitamin C indirectly affects almost every hormone function ...

Q. That's quite a spectrum of different kinds of activity.

A. That's right, and everyone agrees on the need of ascorbic acid here. The quarrel is over how much is needed for these functions. When someone is well, the amount needed may be small. But what happens when he's ill? What attracted me is that if someone dies suddenly; say has been killed instantly in an automobile accident, then his tissues contain a lot of ascorbic acid. (The adrenal glands have the highest concentration.) However, when

a person dies after an illness, the body contains almost no ascorbic acid.

Now isn't it striking how many people who have been admitted to the hospital with one disease get phlebitis, or a heart attack, or a stroke, all disorders of the vitamin C sensitive blood clotting system? Or they get pneumonia, a disorder of the immune system. How many illnesses seem to occur after a period of physical stress, after some previous disease, viral, bacterial? There's even been work that relates emotional stress to physical disease. Well, it just figures that if we see some chemical run down under stress we ought to try to replace it.

Q. Fair enough—but how much do you need? How much, for instance, do other animals make? Well ones.

A. The goat is often taken as a reference point because he weighs about the same as a person.

Q. And because he, too, eats a capricious diet?

A. Well... no ... anyway a 70-kilogram goat will make about 13 grams of vitamin C a day.

Q. In light of that, the numbers you mention, 10 to 15 grams for a healthy adult human, is not totally inconceivable. How about other models?

A. Several other animals have been assayed. These are ballpark figures for most of them. Cats and dogs make ascorbic acid, but perhaps they can't always make as much as might be ideal so they suffer from such toxic diseases as distemper. A veterinarian in San Jose has been curing distemper with ascorbic acid injections (9).

Isn't it interesting, when you reflect on it, that the guinea pig, who can't make vitamin C, is a generally accepted model for testing human diseases? I've often said, tongue-in-cheek of course, that if you've got a disease you can't give to anything but man, monkey, and guinea pig, you've got a sure bet that you can cure it with vitamin C.

Clinical insight

Q. OK, let's go back to curing things. You referred me to Lewin's new book (7). It's very thorough and goes to great length in its discussions of modes and mechanisms of action and metabolic pathways and so forth. As a biochemist that's about all Lewin can do. Now we may not understand how the body is doing whatever it's doing, but people will get sick and have to be treated. You approached things pragmatically. You treat patients. Tell us about that.

A. My practice is to let the body take as much vitamin C as it needs ... take an amount proportional to the amount of toxin that's around. Remember, everyone else has been talking about a *fixed* dose, usually at what I consider to be only a homeopathic level. Their studies go from 2 to maybe 4 grams a day and they see little clinical effect and none statistically. That doesn't surprise me. Such doses simply do not take on a disease after it's established. So that if you have a 100-gram cold ... it's my custom to put a number before the name of a disease to represent the amount of vitamin C which that patient can consume the first couple of days of the disease without diarrhea ... so that if you have a 100-gram cold and the patient is taking roughly 100 grams a day, you will quickly eliminate perhaps 90% of the symptoms of the disease. But if you treat that same cold with 2 grams or even 20 grams a day you won't see much happen. In some cases, especially if treated early, it almost seems as if megadoses were killing viruses.

With bad colds or influenza we don't seem to shorten

the duration of the infection, but we render patients sufficiently asymptomatic so that they weather the infection without complications. Most of the time my patients don't have to miss any work time. If you're using enough ascorbic acid it will promptly take a fever down to normal, and you won't have the normal aches and pains of flu-like diseases.

Q. So we're talking about treatment versus prevention. That seems a little hard to demonstrate in a normal double blind experiment: the dose has to be tailored to the individual's disease and to its stage. Before we look further at that problem—and it's a real one—let me ask you to share more of your clinical experiences.

Pneumonia

A. Let me give you a typical case, a lady here, about, oh, 28, developed viral pneumonia. As far as I could tell she did not respond to antibiotics and she never did "culture" any place. When she presented herself she was very ill, high temperature, the right upper lobe infiltrated with the pneumonia process; difficulty breathing. So we hooked her up to intravenous ascorbic acid, about 1 gram per 18 cc's, and ran it in just as fast as we could. I gave her about 55 grams by vein and the remainder orally, about 215 grams went into her between 11 o'clock in the morning and 9 o'clock that night, at which time the pneumonia went into crisis. She drenched three sets of bed clothing that night. The next morning she was feeling much better. We did the same thing the next day. She returned to work less than a week after I first saw her. We have daily x-rays that demonstrate the rapid dissolution of the pneumonia process.

At that time I treated two other people in town who had the same thing, and got similar results. Three other patients in town went to other physicians and were hospitalized about two weeks and weren't much better when they came out.

Q. I'm sure a lot of scientists will say "Well that's just anecdotal...." To me it seems that when we don't know how a therapy works or can't demonstrate efficacy in a rigid protocol, then we have to rely on individual clinical experience.

You'll recall that I first contacted you because I suspected that vitamin C might have some value in treating my son's mononucleosis, a very debilitating disease particularly common among students. It knocked my son out for the entire summer and we were told that it has no treatment, other than lots of rest. Can you do anything with mono?

Mono

A. The first patient that I ran into with it was a junior high school librarian who was about 22 and weighed about 100 pounds wringing wet. She came in with a severe case of mononucleosis. I told her about the bowel tolerance idea and explained to her how to do this self-titration. I saw her three or four days later; she was almost completely well.

Q. This lady really had mono?

A. Oh yes. Mononucleosis is a disease we can spot without a tremendous amount of lab work. Usually you do a heterophile test and look at the white cells. A positive is quite definitive; a negative can be misleading.

The typical patient who gets mononucleosis is exactly

the one who does the best on vitamin C: older teenagers or young adults are just fantastic vitamin C takers. They can understand the bowel tolerance idea, have iron stomachs, and couldn't care less about slight gas and diarrhea when they have this horrible disease ... In fact the sicker a patient is the better he does because the relief of symptoms is so dramatic that they don't need any arguments to convince them to continue treatment. So what usually happens is that in three to five days the symptoms are 90% relieved. Then some get the message loud and clear: if they stop the vitamin C too soon they get sick all over again.

The infection may go on just about as long as it would have in the first place, but the person is functional and doesn't develop complications. He can go back to school or work or whatever. But he must continue to take vitamin C doses as high as the bowel will tolerate. It can be many months, sometimes a year, before he's down to a normal 10-15 grams per day. He just titrates between relief of most symptoms and diarrhea. The titer will decrease from day to day unless he stops taking the vitamin C. Then there's a resurgence of the disease, and you go up to higher doses again and bring it back down.

The important thing with mono or other responsive dis-

eases is that we can get people back to work in days. You know we're in ski country here. I would be unhappy if one of my ski patrols wasn't back on duty within a week or ten days after having contracted mononucleosis.

Q. This is a disease that has a unique, positive diagnosis, so it's not possible that we're seeing some kind of artifact. You're sure that you're seeing mono?

Hepatitis

A. Oh, sure. The other disease that is very specific is infectious hepatitis. Let me tell you about it. It's a cinch for vitamin C. The difference between the course of the disease with and without vitamin C is quite obvious if only because hepatitis is a disease that we can put numbers on. There are various enzyme systems that we can follow to

show the course of the disease. Infectious hepatitis can be mild where the patient is just a little yellow and maybe a bit tender in the abdomen, but not very sick. But the patients I'm talking about—20 of them, at least—were profoundly ill with hepatitis, and here again we were able to detoxify them in three to five days. The patient is feeling essentially well in three to four days. It generally takes about six days for the jaundice to clear. In two to three days the urine returns to normal color. (You see, with hepatitis the bile is blocked in the liver so that the urine turns brown and the stool turns clay white.)

Hepatitis is a serious problem following blood transfusions. As a matter of fact the whole system of gathering blood in this country is undergoing revision because people who sell their blood have a high incidence of hepatitis. That's why they're trying to go completely to a voluntary system. I'm not sure that's necessary because it's apparently so simple to control hepatitis: just give patients vitamin C after blood transfusions. One Japanese physician (10) has shown that his patients don't get hepatitis if he puts them on maintenance doses of ascorbic acid following blood transfusions. Anybody who is stressed enough to need a blood transfusion should be getting large doses of vitamin C anyway.

Psychoactivity

Q. You use the term stress. To the layman that means psychological stress. Do you mean to imply that vitamin C has any benefit in that kind of situation?

A. I've been using the term stress in its broadest medical sense, but the average person under mental stress can often take a few grams more than he could ordinarily tolerate. Patients who do, say that they feel better and subjectively think that they can meet the stress better.

Vitamin C is definitely psychoactive (11). Schizophrenic patients require 10 times as much vitamin C as others to develop the same ascorbic acid level in their urine.

A Dr. Libby (12) in Los Angeles discovered that ascorbic acid or sodium ascorbate, I think he uses about 60 grams a day, can detoxify heroin addicts almost immediately. (He administers a protein extract with the "C" because he found heroin addicts to be low in proteins.) I had a little experience in this but didn't have enough patients here to follow up on it. Libby practices near a Methadone Center. He found that on his program, patients get no effect from the fix. If they take their 60 grams of sodium ascorbate they can do the heroin and it has no effect whatsoever; later they find they have no withdrawal symptoms, and soon give it up. Heroin addicts mostly want to give up their addiction, but previously all they had was a choice between feeling rotten and feeling horrible.

You know, Stone feels that there is a receptor site in the brain that would be filled by ascorbic acid if there were enough (12). But instead that site is filled with such things as heroin or morphine or barbituates. One end of the molecule fits in where ascorbic acid ought to fit but the other end sticks out and that's what does the crazy thing. Well, if you give ascorbic acid, it displaces the unwanted molecule and also blocks the need for it, so no withdrawal symptoms.

Side effects

Physicians have difficulty in thinking of something that does so many different things. We're used to medicines

that are fairly specific. Now ascorbic acid has these myriad, noncontroversial functions that go on in many many different systems of the body. Essentially what I found is that by giving huge amounts of ascorbic acid, it would tune up, if you will, all of these functions to high efficiency, far more than what's been experienced with the lower doses. Some of the enemies of ascorbic acid point out that there is no ascorbic acid in the body when a person is sick, yet he gets well anyway. They say that proves that you don't need ascorbic acid. It's like recommending that a football coach hold his first team on the bench because he's just barely winning with his second team.

Q. OK. So with all that we must come around to why this megadose therapy isn't widely used. The first thing that comes to mind is that it must have some absolutely terrible side effects. What would you say is the worst side effect other than diarrhea that ascorbic acid produces?

A. Well some people don't like the taste.

Q. And that you call a terrible side effect?

A. Certain patients feel they have trouble with acids in general. They are usually nonspecific about it and have avoided oranges, lemons, grapefruit, and things like that all their lives. These people frequently have a lot of difficulties late in life, I think because they're unusually low in vitamin C. Some patients do indeed have difficulties in first taking ascorbic acid.

Q. How about sodium ascorbate?

A. I've been reluctant to use large amounts of sodium ascorbate—that's a friendly differences between Stone and me. Stone feels that the problems people get into when they take large amounts of sodium could be avoided by taking sodium ascorbate. For instance the hypertensive, who shouldn't eat large amounts of sodium, wouldn't have been hypertensive in the first place if he or she had taken large amounts of ascorbic acid all his life. Well that may be true, but when I see a patient with an acute viral disease I don't want to flood his system with sodium. Imagine how much sodium is needed to neutralize 200 grams of ascorbic acid. So I use the free acid. One in a couple thousand may break out in a rash about the face or soft parts. This is transient and, usually, if they persist in their vitamin C regime, it goes away.

Many people who are intolerant to vitamin C by mouth become tolerant after a few days on intravenous vitamin C. I've never found a person who was intolerant to vitamin C injections.

People who have ulcers sometimes don't tolerate ascorbic acid. Interestingly half the people with ulcers swear that they get well with vitamin C and the other half say they get worse. I'm not entirely sure why that is.

Q. How about kidney stones?

A. I've never seen an oxalate kidney stone among my regular vitamin C takers. There is a theory that says that ascorbic acid breaks down to oxalate so that if a person had difficulty handling oxalate he could precipitate oxalate stones. But the situation is paradoxical: I'll grant that if a person did have difficulty handling oxalates, and he took maybe 500 mg of ascorbic acid a day, he might increase his oxalate load, but the paradox is that if a person takes the powder in large doses, as large as I've been talking about, it somehow makes the oxalate more soluble in the urine. (Ed: Cation chelation?) Anyway, the pragmatic fact is that in my experience oxalate stones caused by vitamin C are not something to worry about.

I have had four patients complain that they had some

Cathcart on malpractice

Now that I have a house and a family and so many responsibilities I wouldn't dream of trying to apply this technology in view of the present malpractice crisis.

If the Federal Government would lay off and consumer advocates understand health care delivery, then market pressures would rapidly bring into being things people need. All the do-gooders, the people who would like to protect us from malpractice, are doing the exact opposite of what they set out to do and they're doing it in a big way. Technological advance renders malpractice and incompetence almost insignificant. Today the least competent doctor can prevent polio better than the best physician could treat it 30 years ago. Studies on ascorbic acid that I was starting with post-operative patients just as I quit surgery were yielding results which, if pursued, probably would have alone decreased the annual morbidity from surgery far more than all of the morbidity involved in malpractice suits in a year in the United States. But we're afraid of new things and as long as we are we're not going to get them. This fear retardation accumulates like compound interest. Research accumulates like compound interest; it builds on itself. If something new is delayed we're stuck with that delay forever. The amount of human suffering for the remainder of history of mankind caused by unreasonable fear retardation, by this loss of compounding of interest in clinical research, means that we are causing astronomical amounts of human suffering.

burning sensation on urinating when they took large doses of ascorbic acid, but I've certainly never seen anything like the report that came out shortly after Pauling's book that in Europe, where they use ascorbic acid in the treatment of tuberculosis, that screaming could be heard from the sanatorium men's room. My experience with this is vast and I can say without qualification that that story is an absolute lie. It does not happen. The other thing that has been said is based on a study by Victor Herbert (13) that indicated that vitamin C blocked vitamin B-12 metabolism. This was front page news; but I understand that other studies indicate that there were some difficulties with his tests *in vitro* and that, indeed, this does not happen in humans. In any event, I have never seen any evidence of B-12 blockage or pernicious anemia. As a matter

of fact our patients seem to have pretty thick blood. Of course we're here at high altitude so we could expect that.

In summary then, I find no difficulty whatsoever, except those minor things I've mentioned.

Q. No side effects. Doctor, to how many patients would you estimate you've given megadoses of vitamin C?

A. I think it's been about 7000 patients over the last 10 years. During epidemics in my village, the local pharmacies have sold as much as 250 lbs of ascorbic acid crystals a month. (Editor's note: 250 lb/mo = 3700 g/day). That doesn't count pills. That's for a permanent population of 4 to 6 thousand. We have transients of course. Manufacturers think that Incline Village consumes more vitamin C per capita than any other place in the world.

Q. And no problems?

A. There is one aspect of which I think we should be wary: that's if the patient goes on high doses, 10-15 grams. He's usually the person who has hayfever or asthma or the like. After two to three years on these doses this patient will become dependent upon ascorbic acid; he'll get the feeling that he will get sick right away if he were to stop using ascorbic acid. Also, they frequently seem to get what are best described as sub-clinical infections that they have to take massive doses of vitamin C to block. This apparent dependence can usually be averted by giving the person high minerals and vitamins. What may be happening is that the vitamin C is chelating minerals and probably creating an additional need for other vitamins. Enemies of vitamin C might say that this is a reason not to take vitamin C. I think the solution is to take your minerals and vitamins.

You know there's another danger. If a patient who's accustomed to high vitamin C intake is hospitalized or otherwise comes under the care of certain physicians, the physician may cut off the C ... and do it just when the patient needs it most.

Maintenance

Q. Now we're talking about maintenance. Until now it's been therapy; now we're into prophylaxis. One of the things I don't understand is why in vitamin C prophylaxis studies the controls never seem to be healthier than the treated group. That's clear in Coulehan's survey. He's always in the position of explaining why the superiority of the treated group appears to be insignificant—never the other way around. How much C do you take regularly?

A. I think that a person who has no really good reason to take vitamin C, no immediate illness, probably should do as Pauling says and take somewhere around 4 grams a day. People with allergies may find that they are more comfortable with higher amounts. I'm the last person in the world to maintain that you will never get a cold if you're taking maintenance doses of vitamin C. I get occasional colds. *But I can block the symptoms with vitamin C.* I never cease to be amazed at the number of patients that report to me that they used to get colds all the time and never get them since they take vitamin C. I don't know why the double blind study doesn't reflect this kind of subjective opinion.

I take 10 to 15 grams a day, first because I used to have hayfever. Vitamin C takes care of hayfever nicely in about two-thirds of all cases; and second, because there is evidence (14) that it reduces cholesterol and thus helps prevent arteriosclerosis, and third, I believe that vitamin C contributes to prevention of some cancers.

Q. What's your basis for the part about cancer?

A. What comes to mind immediately is work by Cameron in Scotland who has written with Pauling (15). They took 100 terminal cancer patients—terminal in that the chemotherapist, the radiotherapist, and the surgeons had no other treatments for them—put them on 10 g of vitamin C a day, and matched them with about 1000 untreated cancer patients. The worst results he got were in cases of cancer of the ovary. They lived only twice as long as the controls. Patients with cancer of the bowel lived seven times longer ...

Q. And this is with what I can now call *only* 10 grams a day?

A. That's right. The overall average increase in survival exceeds fourfold, but this figure is going up all the time because all of the controls are dead, whereas a few, not many, but a few of the vitamin C patients are alive and without any sign of disease. I think that anyone with cancer should be taking high doses of vitamin C.

Now this experiment provides a therapeutic indication. It doesn't say much explicit about prevention. As far as a prophylaxis is concerned all I can say is that as a nutritionist I always seem to get at the cancer patients once everybody else has given up. Recently tests indicate that ascorbic acid does, indeed, reduce the amount of cancer in the bowels and I think that urologists have been using it in some cases of bladder cancer (16).

Q. So we have some 7000 patients with a variety of diseases whom you've treated over 10 years with vitamin C megadoses. Results have been uniformly good. No one has experienced a side effect that couldn't be reasonably handled. How come everybody isn't following you?

Science or sacred cow

A. That's not an easy question to answer. The answer has several parts. Part of the answer stems from the fact that experimentation that comprises the conventional wisdom, though honestly done, has been done on doses that are too small. Coulehan's review is a good illustration. In no way do I doubt the objectivity of his study or the sincerity of his conclusions. The problem is that he was using doses which are simply too small to mitigate symptoms. Let's go back to my custom of putting a number before a disease. The so-called common cold is caused by over a hundred different viruses so there are 20-gram colds, 50-, 100-, even 150-gram colds. It all depends on the toxicity of the particular case. Now if a person has a 20- to 30-gram cold, he has sniffles, he doesn't go to the doctor with that. Let's say he's read Pauling's book and decides to take 2 grams every hour. That rapidly eliminates the mild cold. Now see what happens. I'm sure that thousands of physicians have secretly read Pauling's book and decided that the next patient who comes in with a cold is going to get 2 grams every hour just like Pauling says. So the patient arrives at the office with a 100-gram cold. His throat is so sore that he thinks he has "strep;" he's aching all over and thinks he has the flu. His physician takes a culture and finds out by examination that he really has a bad cold. So he prescribes 2 grams of C an hour and nothing happens. To make something dramatic happen the physician would have had to use 100 or more grams. You just don't send a boy in to do a man's job.

Q. What you're saying is that the patient who has Pauling's 20-gram cold just isn't going to show up at the

The Cathcart prosthesis

Q. Bob, tell me how your hip device came into being.

A. It's a modification of the Austin Moore device, a metal ball that fits inside the upper leg bone. It's used, for example, on the elderly person who falls and breaks the head of the thigh bone so that it has to be removed. The Austin Moore device was used for many years even though about a third of patients experienced a pain with erosion of the cartilage of the socket. Sometimes the ball would erode right through the socket. The Austin Moore ball is perfectly smooth and spherical, 41-47 mm in diameter. At first everyone thought that the metal was incompatible with cartilage, but that didn't prove to be the case, so the solution seemed to be to make the ball rounder and smoother. Now real bones didn't seem perfectly round to me, so at Stanford I measured 45 hips and found out exactly what the shape of the femoral head was and it wasn't round. I made some aspheric prostheses but didn't take the full 1 mm correction—just a little bit egg shaped—with the result that we have had no unexplained problems. There have been cases that have been infected ... things like that... but the old problem of the prostheses just mysteriously sinking seems to stop. As a result the number of these units being used is increasing; it's now about 500 a month.

Q. Now any one who knows anything about mechanics knows that if you want a universal ball and socket you make it spherical; yet Nature made it egg shaped. Why?

A. Cartilage, which is porous, derives its nutrition from the synovial fluid. It's the "oil" within the joint. These irregular shapes pump this fluid through the porous cartilage, giving it its nutrition. A perfect sphere, no matter how you turn it, doesn't cause a pumping action. So in essence these out-of-round shapes create pumps. By the way, for your technologists I should point out that animal joints in a sliding friction situation have a coefficient of friction that's less than that of ice on ice, which is partially accomplished by this porous lubrication situation (17).

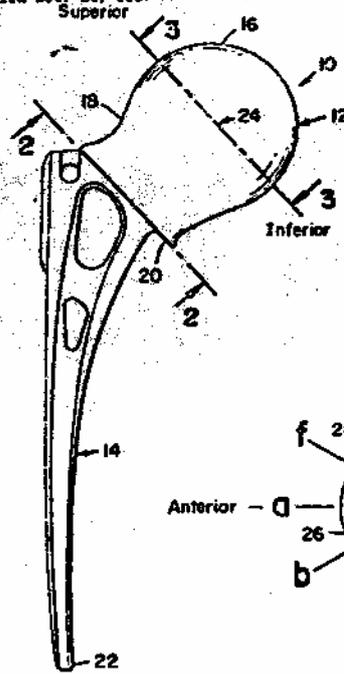
May 12, 1970

R. F. CATHCART III
JOINT PROSTHESIS

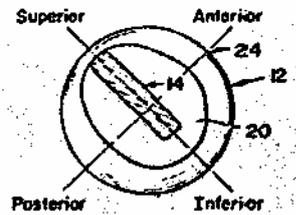
3,510,883

Filed Oct. 30, 1967

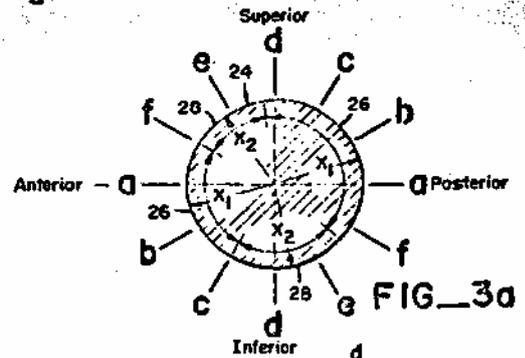
2 Sheets-Sheet 1



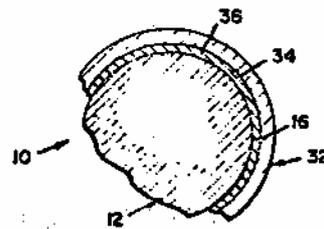
FIG_1



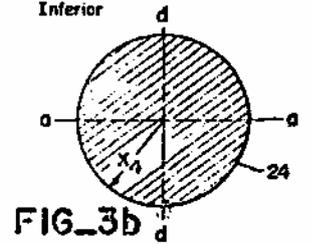
FIG_2



FIG_3a



FIG_4



FIG_3b

INVENTOR
ROBERT F. CATHCART III
BY
Townsend Townsend
ATTORNEYS

physician's office because people have learned that if you go to the doctor with a cold all he can tell you is take two aspirin and go to bed? Now you're saying that we should shoot at a cold with a 100-gram cannon. Well, if that's the case it seems to me that a plain, old fashioned, sensible double blind experiment ought to convince everyone. Right?

A. Well yes, but there are difficulties with that. I cannot conceive of how one could double blind these amounts of vitamin C. We are titrating between relief of malaise and onset of diarrhea. How can you find a double blind protocol to do that? You know we're all worshipping at the altar of double blind studies now. But obviously a reasonable person can tell for sure that something is working. In the first place I think we have to take account of this very interesting increased bowel tolerance which, of course, doesn't need a double blind study to prove. It demonstrates to anyone who has ever experienced it that something is going on that they just don't understand. But the result is certainly spectacular. Let's say you're testing a medication and get results that are, say, 40:60. Then you're going to have to double blind it. But if you hook up an IV and run a material in rapidly and within minutes you see that the symptoms of diseases are mitigated then

you really don't need a double blind. It would be very easy to take a hundred patients admitted with hepatitis to a large university center and give them ascorbic acid and compare them with the last hundred hepatitis patients that were admitted to that hospital. I think that the results would be convincing. The problem with double blind tests is that in a way you sometimes deceive yourself.

Q. Yes, I can almost see a group of patients each somehow identified as having a 100-gram cold. We split them. Give one group "C" and try to find something sufficiently sour to pass for vitamin C, which the patient can tolerate at 100 grams per day.

Have you published what you have done in the standard medical journals?

Why in CHEMTECH?

A. No, but I've tried. My manuscripts were rejected.

Q. What did the referees say? In chemical periodicals the editor refers the paper to referees he chooses, experts

in the field, and then forwards their comments, anonymously usually, to the author. Is that the practice in the medical periodicals?

A. In my case the manuscripts were just flat out refused.

Q. Just like that without any explanation?

A. Yes.

Q. Wow. Might it have something to do with an establishment protecting itself or something like that?

A. Well...

Q. Do you want to comment on this?

A. Well, really I don't. You know I really believe that the doctors involved in these decisions don't believe that this is true.

Q. In other words you think they're saying that this qualified physician who has an international reputation for his hip prosthesis has made all this up. Colds, flu, hepatitis, mono ..., diseases a second-year medical student could recognize with high probability ... they don't *believe* this?

A. Yup. They just don't believe it. They think I'm deceiving myself somehow. They see placebo effects as being very significant. I agree that placebo effects are significant, but I don't believe that they are *this* significant. Take the effects on children, on infants. In seven years I've not had to hospitalize a child who came in with a virus-induced fever.

Q. Wouldn't placebo effects be non-quantitative? If the physician gives the patient a couple of pills it won't make any difference whether he gives him big ones or little ones or two instead of four. How can we explain by placebo effect such a thing as a 50-gram cold and a 100-gram cold? It's the bowel telling you which you've got, not your head.

A. No question. This increased bowel tolerance is a spectacular phenomena that I wish all physicians could experience because once they experience it they know that something is going on.

Q. Is it conceivable that one can psychogenically control a case of diarrhea that normally appears at 10 grams and now all of a sudden when you're ill appears at 200 grams?

A. Oh there's no way that this can be psychogenic.

Q. And so we have, we have a problem here ...

A. I think of communication.

Q. How do you feel about it?

A. Well, it worries me. It worries me in a lot of ways.

Q. The normal procedure in chemistry is if peers question a colleague's results, published or otherwise, they endeavor to repeat this work in their own laboratories. If they succeed they publish and if they don't succeed they publish. Doesn't that happen in medicine?

A. Well, understand first that this wasn't even published so people know of it only by word of mouth. One of the three physicians here in town is now using vitamin C for at least hepatitis cases. A fellow physician in Reno he's convinced to use it was amazed at the results. I treated an orthopedic surgeon in Carson City who had a serious case of hepatitis, and another in San Bruno who phoned because he knew of my work. Both these physicians are convinced beyond doubt that my megadose therapy altered the course of their hepatitis. But my work isn't widely known. I'm hoping that our chat will help, but it isn't easy to introduce new methods in medicine. It used to be that if a new physician came to town and he had

some new treatment then the senior physicians in the community would look at him, yes; but, because they had seen so much development in the past, it was a professional thing to stay out of this physician's way unless he showed that he was doing something really wrong. Competition would prove whether or not his ideas were right.

Malpractice!

Q. Patient would tell patient whether they believed this physician cured them or didn't?

A. Right. Now we're all living in a state of anxiety called the Malpractice Crisis. The first physician in town who does something new is not employing "practice of the community," and the last physician in town who adopts some procedure is also not employing "practice of the community." So there's a feeling that if we stop all progress, we will all get so practiced at "practice of the community" that we can't get sued anymore.

Q. "Practice of the community?" That's a legal term?

A. Yes, it's the criterion by which a physician is judged in court. Any change creates a debate within the medical community, which under ordinary circumstances is healthy, but now a change means that the "practice of the community" is in a state of flux so that attorneys for either side can get physicians for their side to testify that the defendant physician was or wasn't using "practice of the community." Take your pick.

Q. Do you have any idea how big a "community" the law uses in defining "practice of the community"?

A. I'm certainly not an expert on that, but as I understand it, it used to be more of a local community. Now it's getting to be more ... almost an international community.

Q. International?

A. Yes, this creates a problem for us in rural medicine because when we're away from the large medical centers we don't have the facilities that they have in the big city. Sometimes we're forced to render care ... don't have time to send them to the city ... yet there can be criticism of the equipment that we have, for instance, and there can be a suit.

Now just because a suit is filed doesn't always mean that it's going to prevail, but defending a suit is a *miserable* experience for the physician. It puts him in a state of anxiety. The more idealistic he is—the more he used to care about patients—the worse it hurts him.

Q. And you've seen intensification in this. Seen it, for example, in what you pay for insurance. How has the premium changed over the years?

A. It went into a mad frenzy right after no-fault automobile insurance went into effect. Attorneys didn't seem to have anything to do so they launched a campaign against physicians. When I started practice I paid about

\$800 a year for insurance. That was in 1969. I quit surgery because of the whole malpractice thing three, four years ago, when the jump was from \$4000 to \$8000. In some cases insurance now costs \$20 000 to \$30 000 for an orthopedic surgeon.

There's an interesting paradox here: the more surgery a person does, the more insignificant a large malpractice premium becomes in his overhead. So a surgeon who tries to avoid doing surgery is the one who's kicked out of the surgical field first. I know a fellow in San Francisco who does, oh maybe 100, 150 laminectomies a year... that's back surgery, disk removal. Anyway, some people do a lot of laminectomies but the frequent need for them is a debatable point in orthopedics. So what happens? Those of us who feel that fewer should be done are in a sense being taken out of competition by the malpractice crisis.

Q. Are you saying that a physician who is doing this kind of surgery is going to pay, say, \$30 000 a year for insurance no matter how many such operations he performs? For our friend who does 150 operations a year—3 a week—that's \$200 per case just for insurance. It's obvious what happens if he talks himself out of doing half of those.

What kind of patient do you most often find involved in malpractice suits?

A. First he's a patient with the more serious kind of problem, so that means that the more specialized a physician is, which means often the more competent he is, the more likely he is to get sued. The neurosurgeon, the cardiovascular surgeon ... they get sued the most because they take on the most responsibility. The orthopedic surgeon gets sued a lot not only because he handles difficult problems, but also because many of his patients have had accidents, so their cases are automatically reviewed by attorneys. It's interesting that the doctor who avoids serious problems is perhaps less of a scientist, less up on his work, concentrates on simple things, has a good personality, relates well with his patients. He's less likely to get sued.

Q. Is he the one who sets the "practice of the community," not deviating not doing anything new?

A. That's right. Whereas the highly skilled person who may be a little introverted ... that's the only reason he can stand to be that skilled ... has to go to class a lot, spend his life studying, not watching football games, drinking beer Saturday night...

Q. Reading a lot of journals?

A. Yeah, so that this fellow may not have the personality but he's the specialist and he's more likely to get sued.

Q. Fair enough. But maybe tonight we can break that lock step. Let me buy you a beer before we call it a night.

A. OK, and I can tell you about the hip prosthesis I developed. I don't have hours *that* early tomorrow ...

EPILOGUE

It's amazing, sometimes, to what extent an Editor will go to assure the quality of his publication! Like in this case—I went out and caught the flu. Wednesday evening I realized my scratchy throat had gotten worse and I ached, so after dinner, I added two more grams of ascorbic acid to the four I'd already taken that day. By 10 my fever was a bit over 101° so I took another 3 grams, which seemed like a lot, and went to bed. I probably should have continued popping pills all night 'cause next day I woke up achy with my temperature already a degree above normal. I im-

mediately started a vitamin C regime of 4 g per hour; by 11 my temperature was down and I felt fine. That afternoon, with my pocket full of gram-size pills I attended a Board meeting, an open house (SIPI), a dinner of the Research Directors Association, walked briskly about 2 miles to and from the train and tumbled into bed, tired but symptomless. I'd kept up a steady 2 g/h all afternoon so my daily take was 44 g.

That night I didn't sleep very well: I must have groped to the John a half dozen times. (Dr. Cathcart did warn me

of that. Said he, "I even got blamed for an apparent increase in Incline Village's population. " "Oh, does C do that, too?" "No, but they use a T.V. toilet-flush index to estimate population and in the flu season in Incline Village it goes up."

On my 2:00 a.m. return trip I started medication so that by wake-up at 7:30 I had 15 g in me already ... and a low fever. I upped the dose to 5 g/h and then at noon to 6 g/h. That's equivalent to 144 g/24 h day. That calculation convinced me that I must be really sick, though I felt fine—well, not absolutely. I had finally gotten close

enough to bowel tolerance to have developed a fine case of *magensprache* (literally, stomach speaking); and was so flatulent I felt like the Hindenberg reincarnated. Anyway, having convinced myself that I was really ill, I phoned Dr. Cathcart.

"Yes, at that dosage you're close to something that would put you in the hospital if you weren't on ascorbic acid at bowel tolerance."

"Yes, take it every hour; No, a 6 g dose isn't too much. My experience is more with powder than pills but I've used a single dose of 2 tablespoons of powder in water for mono." (That's about 25 grams)

"You could use a controlled release formulation at night."

"Oh, I'd *certainly* see your physician. You could have something bacterial on top of the virus. He may want to do a culture. *Do* see him."

"Yes, you *are* contagious but at least you're not sneezing all over everyone."

So, off I went to my internist and tried to explain to him why I was there without any symptoms.

"Oh, you have something; throat's red. No need to culture it now. Just take it easy for 5 days. If you want to take all that vitamin C, go ahead. It'll just come out in your kidney; probably can't do any harm. Just don't get a lab test for gout. I've seen a lot of false uric acid positives since Pauling started everyone on ascorbic acid."

"But couldn't I have something terrible that the C is masking? It takes all the symptoms away."

"I can do that with aspirin. Call me if anything comes up. You're vulnerable even if you feel good."

Saturday, day three, I took it easy. Also I took about 75 g of C. I didn't keep track. By then I was popping 1000 mg pills like bar peanuts.

Sunday I spent in the office. At 30 g in four hours I found out what happens if you exceed bowel tolerance. No big deal. The rest of the day I felt fine and took no more pills 'til it was time for dinner and the theater. Then I popped a 5 g "prophylaxis".

Monday, day five, I decided to see if I was well: I took "only" 4 g and waited to stop aching and sneezing. By noon I was functional but mildly miserable so I tried my physician's aspirin routine. It didn't help much. But a 5 g dose of C at 3:00 p.m. and another at 4:00 had me feeling fine—just a bit gassy.

By Thursday, day eight, I had morning catarrh, more severe than usual, a throat tickle that came and went, and four empty, 100 g, vitamin C bottles.

Friday found me fine on 4 g maintenance.

References

- (1) Klenner, F. R., *J. Appl. Nutr.*, 23, 3-4 (1971).
- (2) Coulehan, J., *CHEMTECH*, Dec. 1977, p 728.
- (3) Stone, I., *The Healing Factor. "Vitamin C' Against Disease*. Grosset and Dunlap, Inc., N.Y., 1972.
- (4) National Research Council Recommended Dietary Allowances, National Academy of Sciences, Washington, D.C., 1974, pp 63-64.
- (6) Harper, H. A., Rodwell, V. W., Mayes, P. A., *Review of Physiological Chemistry*. Lange, Los Altos, Calif., 1977, pp 156-157.
- (7) Lewin, S., *Vitamin C. Its Molecular Biology and Medical Potential*. Academic Press, London, N.Y., San Francisco, 1976.
- (8) Lind, J., *A Treatise on Scurvy*, 1753.
- (9) Belfield, W. O., Stone, I., *J. Int. Acad. Prev. Med.*, 2, 10 (1975).
- (10) Morishige, F., Fukuoka, Japan, as quoted by Murata, A., *Proceedings First International Congress of Microbiological Societies*. 3, 432-442 (1975). Science Council of Japan.
- (11) Vanderkamp, H., *A Biochemical International Journal of Neurochemistry and Psychiatry*, 2, 204-206 (1966).
- (12) Libby, A. F., Stone, I., *Orthomolecular Psychiatry*. 6,300 (1977).
- (13) Herbert, V., Jacob, E., *J. Am. Med. Assoc.*, 230, 241-242 (1974).
- (14) Spittle, C. R., *Lancet*, 2, 1280 (1971).
- (15) Cameron, E., Pauling, L., *Proc. Nat. Acad. ScL USA*. 73, 3685 (1976).
- (16) Schlegel, J. U., Pipkin, G. E., Nishimura, R., Schultz, G. N., *J. Urol.*, 103, 155 (1970).
- (17) Cathcart, R. F., *Orthop. Rev.*, 2, 15 (1973).

Write On

continued from page 259

RE: SYMPTOMETOMY with vitamin C: March 1978 CHEMTECH: This surely is a classic article which should be widely circulated as it is at once an essay and a satire on the scientific establishment and the self-aggrandizement business which has come to be a major characteristic of modern science. As science itself, this article is a double-edged sword, for it both slashes enemies and cuts friends. On the one hand, it feeds the "anti-scientific" fires, which have been burning brightly lately, and is bound to be widely quoted by many health faddists as evidence that the scientific establishment is not really relevant. "The tragedy of modern science is that it is only certain about things which are absolutely trivial" (direct quote of lay letter to editor).

The quotes of the (late) Sherry Lewin, as an authority on vitamin C mechanisms of action, are inappropriate. Dr. Lewin (who was a close friend) was an imaginative, enthusiastic physical chemist in my opinion who had to write books to get many of his ideas published. I found his ideas new and exciting—well worth pondering—but did not necessarily feel I had to believe all of them. I do not think that he thought all his ideas were proven either.

This article is an indictment of the "Scientific Establishment" who would not publish Cathcart's ideas where they could be discussed and confirmed or denied. Again, are the editors of scientific and medical journals only sure about things that are absolutely trivial? ... While one is wary of the small town MD making 'a priori' conclusions without conventional experimental evidence, where would he go for funds to try to test his ideas experimentally? ... Would the Peer-Review-Grant system give him support, or would they reject him, saying that he is "not-qualified" to do biochemical and metabolic research? ... Has our scientific establishment assumed such a defensive position that we are no longer willing to listen to imaginative new ideas from people like Lewin and Cathcart? ... Are we really so confident of our scientific precepts and logic that we can reject such ideas out of hand?

Perhaps the recent CHEMTECH article by Paul Mok (Dec. 1977, p 20) puts things in perspective. He would likely classify people like Lewin and Cathcart as "Intuitive Personalities" most interested in ideas and concepts. This might be contrasted to the "Thinker" type of scientist who is most interested in "Facts" and "Logic"—the bricklayer type building up the edifice of science by accumulating data and publishing 40-page papers on data alone. Perhaps the balance between the "intuitives" and the "thinkers" has been lost. Perhaps the Peer Review System and the system of choosing editors of "reputable" journals favors the "thinkers" over the "intuitives"? Have the "thinkers" really come into control of the scientific administration process? Wouldn't it be too bad if people like Paul St. Gyorgi, Linus Pauling, Sherry Lewin, and Robert Cathcart continue to be kept out of the smoke-filled rooms where decisions are made on scientific priorities for funding and publication on critical issues of the day? ...

Thomas R. Henderson
Albuquerque, N.Mex.

P.S. I wonder if I shouldn't submit all my future manuscripts to CHEMTECH first. Those which you reject because they are non-controversial, unimaginative and trivial would then be readily published in almost any other journal I would select...

I have read the article, 'Symptomectomy' in the February CHEMTECH. Devotion of space to such anecdotal material is, to me, a serious error in editorial judgment. Indeed, the desirability of publishing even good clinical material in CHEMTECH is lost on me.

The personal epilogue to the article is tasteless in content and, in publication, another lapse in editorial judgment.

Is CHEMTECH changing its policies as to what is suitable material?

Jack P. English
Grantham, N.H.

In reading the interview with Dr. Cathcart (CHEMTECH, Feb. 1978, p 76) I began to wonder if it was really the vitamin C that was producing the reported beneficial effects. Perhaps, these effects could have been produced by some impurity or *byproduct* of vitamin C decomposition which may be present only in extremely small amounts, but which would show up with the massive (!) doses used.

E. D. Miller
Nanticoke, Pa.

it yourself you surely know what I mean.

Depending on where you buy it, those 250-gram bottles can run as high as \$16. For a working person this beats a day or two in the hospital, but pity the poor college student (and quite a few will read your article) who has to count the nickels and dimes. Johnny, don't throw the aspirin bottle out yet!

How about another article on how to synthesize vitamin C in the kitchen from some cheap starting material, say brown sugar!

J. Bates
Hixson, Tenn.

Regarding your article "Symptomectomy" about Dr. Cathcart's use of vitamin C: *How can you print such dangerous garbage?*

Robert E. Pincus, President
Permier Malt Products
Milwaukee, Wis.

In your otherwise superb article on vitamin C therapy (CHEMTECH, Feb. 1978, p 76) why didn't you say a few words about the cost of such treatment? Having tried

Write On

continued from page 519

Reader Robert Pincus, who called the Cathcart Vitamin C Symptomectomy article "dangerous garbage (June CHEMTECH), should be encouraged to publish the results of *his* research, which proves that it is!

"Poor" students and others can buy vitamin C from drug supply houses for \$9.50/kg. Bronson Pharmaceuticals, La Canada, Calif. 91011 is an example of such a supplier.

Gregor H. Riesser
Houston, Tex.

I enjoyed reading Luberoff's article on "Symptomectomy" in the February CHEMTECH, but enjoyed even more reading the letters attacking the article and its conclusions (re: J. P. English and R. E. Pincus, CHEMTECH, June 1978).

The attackers write about "dangerous garbage" and/or merely "anecdotal material" without further comment. The term "anecdotal material" is used to dismiss findings of other physicians who have experimented with the use of vitamin C and other drugs in the treatment of numerous disorders. What I do *not* see in attacks such as these are references to materials which explain some of the admittedly interesting observations reported by scientifically-trained medical practitioners. All the more confusing when one considers:

(i) that great advances in the field of medicine have resulted from such "anecdotal" observations by individual scientists who have dared to consider unorthodox but reasonable explanations for specific diseases and/or disorders. In fact, I challenge your readership to provide references describing major advances in medicine which have been made as a result of "rigorous clinical testing"—including, of course, all of the latest "accepted" techniques (double blinds, control groups, placebos, and the rest).

(ii) that the detailed observations of physicians such as Cathcart adjure rational, scientific explanation. Why, for example, does the body exhibit an increased tolerance for vitamin C when the symptoms of a cold are present? Until questions such as these have been answered by the "responsible" medical opinion-makers, Cathcart's hypotheses are certainly as acceptable as anyone else's until they are rationally and scientifically disproven.

R. C. Forrester III
Knoxville, Tenn.

P.S.

Ever since we wrote about the mega mega dose, "bowel tolerance titration" with Vitamin C (CHEMTECH, February 1978), we've been hearing anecdotal cases pro and con. Now L. K. Altman, writing in the *New York Times* of September 27, tells of a trial mega dose of Vitamin C that was put through at the Mayo Clinic. The malady was cancer and the dose was 10 g of C per day. The result was no discernable effect—63% of the test group reported feeling better vs 58% of the control. The median survival rate of both groups was "about seven weeks".

One wonders what 10 g/d was supposed to do for patients who were that "terminal" when a garden variety cold can "consume" 50 g/d, flu or mononucleosis over 100 g/d and some severe viral infections over 200 g/d?

The Mayo group, headed by E. T. Cregan, undertook this more positive study because earlier Scottish studies, in which Linus Pauling collaborated, didn't randomize their sample "scientifically".

Checklist

- | | | |
|--|---------------------------------------|--|
| Corporate myths | 71
<input type="checkbox"/> | The ruts we're in often stem from no more logic than some aboriginal taboos, says Pacifico ; but digging out can cost you your head. |
| Quads on campus | 73
<input type="checkbox"/> | Ethics, recently strengthened by law, will bring more handicapped people into the work place. Thus Lipps' rare insight into how the most severely handicapped cope in college is prelude. |
| Symptomectomy with vitamin C.
A chat with Robert Cathcart, M.D. | 76
<input type="checkbox"/> | "I still get colds but now I know what to do about them" (and a lot of other diseases), says Cathcart in this interview that also probes problems of today's medical practitioner. |
| Condensation product and method
of making same | 88
<input type="checkbox"/> | This month's exemplary patent is the one that just got Leo Baekeland elected to the National (U.S.) Inventors Hall of Fame. |
| How to read a patent | 91
<input type="checkbox"/> | If reading our first couple of Landmark Patents has you wondering how best to use patents, Maynard's new book, from which this article is condensed, is the best place to start. |