



Notable Grand Rounds
of the
Michael & Marian Ilitch
Department of Surgery

Wayne State University
School of Medicine

Detroit, Michigan, USA

Dr. Charles Lucas

THE WONDERFUL WORLD OF CALCIUM

December 8, 2021

About Notable Grand Rounds

These assembled papers are edited transcripts of didactic lectures given by mainly senior residents, but also some distinguished attending and guests, at the Grand Rounds of the Michael and Marian Ilitch Department of Surgery at the Wayne State University School of Medicine.

Every week, approximately 50 faculty attending surgeons and surgical residents meet to conduct postmortems on cases that did not go well. That “Mortality and Morbidity” conference is followed immediately by Grand Rounds.

This collection is not intended as a scholarly journal, but in a significant way it is a peer reviewed publication by virtue of the fact that every presentation is examined in great detail by those 50 or so surgeons.

It serves to honor the presenters for their effort, to potentially serve as first draft for an article for submission to a medical journal, to let residents and potential residents see the high standard achieved by their peers and expected of them, and by no means least, to contribute to better patient care.

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The Wonderful World of Calcium

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This paper is based on Dr. Lucas' Surgical Grand Rounds presentation on December 8, 2021

Calcium (Ca) is the most common element in the body. It is present primarily in bone. Non-skeletal ionized Ca (38%) is free, while protein-bound Ca accounts for 50% of the total, and has over 30 protein binding sites. The remaining 12% is tied up in the tissues.

Total serum Ca is easy to measure. To correct for albumin, the formula (which is asked for on the ABSITE test) is:

$$\text{Cor TSCa} = \text{TSCa} + 0.8 (4 - \text{TSCa}) \text{ g/dl}$$

The formula for ionized calcium, corrected for the arterial pH, is also on the test:

$$\text{Cor ICa} = \text{ICa} \times (1 - 0.53 \times 7.4 - \text{pH})$$

The corrected ionized Ca gives the best correlations and is what is meant by "calcium" as used throughout this presentation.

Definitions

A mole or molecule charge of an ion is 6.023×10^{23} of the (atom, ion, etc.) as determined by Avogadro's number, which I did not understand in high school and still don't. Ca has a valence of 2—one equivalent $\text{Ca}^{++} = \frac{1}{2}$ mole. 1 mEq of $\text{Ca} = \frac{1}{2}$ mmol. (Thus, they are interchangeable.) $\frac{1}{2}$ mole $\text{Ca}^{++} = \frac{1}{2} \text{ gm-atomic wt} = 40/2 = 20$; thus, $\text{gm-eqi-wt } \text{Ca}^{++} = 20 \text{ gm}$.

Parathormone

Any discussion of calcium in health revolves around parathormone. A 2000 paper by Jupiter *et al.* published in *Endocrinology* provided the first detailed description of parathormone and its

location in both the intracellular and extracellular spaces (Figure 1.) Parathormone has 84 amino acids with an N terminus and a C terminus. (It was taught that the N terminus is the most active but I suspect that God made both termini active.)

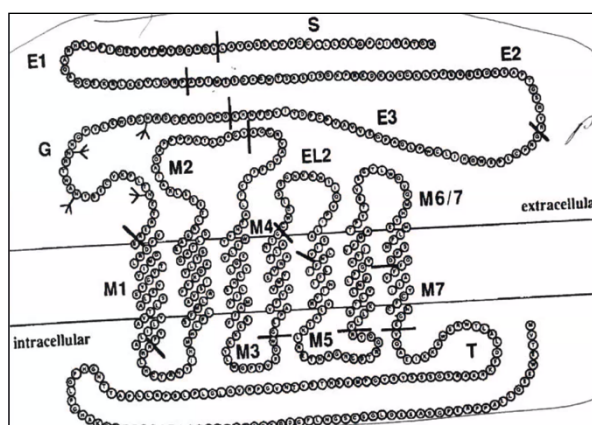


Fig. 1. PTH/PTHrP Receptor
Source: Juppner *et al*; *Endocrinology* 2000

The actions of parathormone are: (1) To reabsorb calcium from the kidneys (increase synthesis $1,25 (\text{OH})_2 \text{ Vit D}$); (2) to reabsorb calcium from the gut; and (3) to take the calcium away from the bone (calcium resorption). It blocks the phosphate reabsorption, and calcium is excreted in the distal tubules. The bone effects are related to calcium resorption so that you get osteoporosis with excessive parathormone.

Hyper Parathyroid Syndromes (Primary, Secondary, Tertiary)

The things we deal with most of the time in connection with calcium (and that is always in the

ABSITE test) are the hyper parathyroid syndromes.

Primary hyper parathyroid: The cause of primary hyper para is about 89% adenoma, 10% hyperplasia, and about 1% cancer, although the Beaumont and the Ford hospitals have higher incidences of cancer, for symptoms we all remember that it's "stones, bones, groans, moans and psychic overtones." (Figure 2 expands on the syndromes.)

Primary
Adenoma: 89%; Single = 95%
Sx: Stones, Bones, Groans, Moans, & Psychic Overtones
Question: OR vs Observe
Groans & Moans
Secondary: Physiologic Response To Renal Failure & Hypocalcemia: Observe
Tertiary: Excess PTH Response to ESRD Increased Ca
Excise 3 1/2 Glands:
Excise 4 glands; implant 1/2 gland in arm

Fig. 2. Hyper Parathyroid Syndromes

It is easy to identify kidney stones, or the cysts which occur in the small wrist bones and in the clavicle, but sometimes it is a little difficult to get into the details regarding the "groans and moans." Back when I used to do more parathyroidectomies and talked to the patient ahead of time about constipation ("groans") and arthritic problems ("moans"), they would describe different medicines they had been taking.

Six months post-op, when asked if they had any constipation or joint pain the fully recovered patient would declare never having had any such problems. I would then read from notes: "This is how many cathartics you took, back before we operated. And this is how many pain medicines you were taking for joint pains before we operated." The patient typically responds that she forgot.

This is not mentioned in the literature on whether to operate or not operate upon an "asymptomatic"

patient with primary hyper para, but from my experience I would recommend taking the groans and the moans seriously because they can be relieved.

Secondary hyper parathyroid is really a normal parathyroid response to patients with end stage renal disease and who have hypocalcemia; these patients are best treated non-operatively.

Tertiary hyper parathyroid occurs when the secondary gets out of control, so that when a patient no longer has renal failure (following transplantation) the patient nevertheless continues to have an increase in parathormone with the result that they become hypercalcemic.

In treating tertiary hyperparathyroidism, there is a big debate in the literature regarding whether to take out three and a half glands (leaving one half gland) or taking out four glands and then re-implanting the fourth gland. I have a strong bias for the three and a half gland approach, being confident that the fourth can be dealt with successfully at a latter date if necessary.

Remember when you transplant—whether it be the spleen is part of the omental after splenectomy after splenic injury or a parathyroid gland - you take away the blood supply and the cells die. And then you have the primary cells that survive and they recreate the splenic tissue within the omental omelet when you do splenectomy, and the same occurs with the parathyroid, which you replant into the arm muscle.

As those cells are growing back they cause tremendous bone hunger for calcium, so patients need huge amounts of it. Again, I recommend (though it is not what the literature recommends) taking out three and a half glands and then going back to the fourth if necessary, due to recurrent hyperparathyroidism.

Albumen Resuscitation and Calcium

Total serum calcium is very easy to measure. In the 1960s it was costly to measure ionized calci-

um and was done mainly for research. Hypocalcemia was commonly seen in patients who had severe injury and also in patients with septic injury. Resuscitation routinely included the administration of calcium chloride, and I was taught as a resident we should give 2 ampoules of calcium chloride for every five transfusions of blood in patients with severe hemorrhagic shock. This was recommended to replace the citrate present in the blood being given to the patients.



Simon Kovalik

Dr. Simon Kovalik looked at the role of albumin versus non albumin resuscitation on calcium. He did the largest randomized study of severely injured patients who required an average of 15 transfusions during ER and OR resuscitation. The study involved two groups of patients: Those that were supplemented with albumin as part of their resuscitation, and those that just got the crystalloid.

As Table 1 shows, the calcium resuscitation in the first half of the fluid uptake phase at 12 hours, the second half of the fluid uptake phase at 22 hours, the first two days of the fluid mobilization phase at 44 hours, and the second two days of the fluid mobilization phase at 86 hours into total calcium was always higher in the albumin patients compared to the balanced electrolyte or crystalloid patients.

However, ionized calcium was always higher in patients who got the balanced electrolyte solution throughout the fluid uptake phase and the

	OR 5hrs	Phase II 12hrs	22hrs	Phase III 44hrs	86hrs	Conv. 24days
TC Alb		8.4	8.7	8.9	9.9	mgm%
BES		7.2	7.5	8.1	8.7	
Ca ⁺⁺ Alb		1.7	1.7	1.9	1.8	mm/ml
BES		1.8	2.0	2.1	2.1	

Table 1. Albumin Resuscitation and Calcium

fluid mobilization phase. What was happening was that the albumin binds with the ionized calcium, reducing the ionized:total calcium ratio. This was associated with an elevated central venous pressure in the group of patients that received albumin.

Dr. Michael Dahn wanted to know the effect of the albumin resuscitation on the heart. He looked at the total calcium and the ionized calcium in the operating room, in phase two and phase three, and then in convalescence (Table 2).



Michael Dahn

	OR 5hrs	Phase II 12hrs	22hrs	Phase III 44hrs	86hrs	Conv. 24days
TC	7.2*	6.7	7.0	7.5	7.6	9.2
* 26 mEq given in OR; N=8.5-10.2 mg%						
Ca ⁺⁺	1.4	1.7	1.9	2.1	2.2	2.5
N=2.1-2.7						
Hypocalcemia Correlates With Shock Time, Initial MAP, Blood Needs and Interstitial Space Expansion [Inulin-RISA spaces] Urine Calcium Low in Phase II						

Table 2. Calcium Dynamics/Trauma

He found that hypocalcemia correlated very significantly with shock time (the number of minutes that the patient's systolic pressure was less than 80 torr), the initial mean arterial pressure, and the amount of blood that was needed during resuscitation. It also correlated significantly with the interstitial fluid space volume, which was measured by looking at the inulin space minus the RISA space. As well, urine calcium was low in Phase II patients.

Looking at the dynamics of the calcium and the heart (Table 3 below), the left ventricular stroke work was decreased in the fluid uptake phase, and did not return to normal until the fluid mobilization phase when the calcium was going higher. So calcium is an inotrope, and reduced ionized calcium is associated with a decrease in left

OR 5hrs	Phase II 12hrs	22hrs	Phase III 44hrs	86hrs	Conv. 24days
	40	43	54	57	NA
N=45-55					

Table 3. Calcium Dynamics: Ionized Calcium and Heart Work (dynes-sec/cm⁵)
Source: L & L J Tr

ventricular stroke work in a very significant manner.



Jon Sennish

In the 1980s, Dr. Jon Sennish wanted to know what the parathyroids had to do with this response to calcium after hemorrhagic shock. He looked at the same group of patients and determined (Figure 3) that the total calcium (orange) and the ionized calcium (yellow) decreased in association with the number

of minutes that the patient had a systolic pressure less than 80. He also found that parathormone levels increased during this period.

This was the first study to demonstrate that the parathyroid gland is an acute responder to the hemorrhagic shock insult, which causes hypocalcemia which then produces hyperparathormonemia, which then normalizes with the patient recovery—as the patient gets better, and the calcium has come back up to normal, the parathyroid goes down to normal.

The well-known trauma surgeon Dr. Michael McGonigal studied the role of the parathyroid in hemorrhagic shock insult. He looked at three groups of animals: Group A had parathyroidectomy done one and a half years earlier; Group B had parathyroidectomy done four



Mike McGonigal

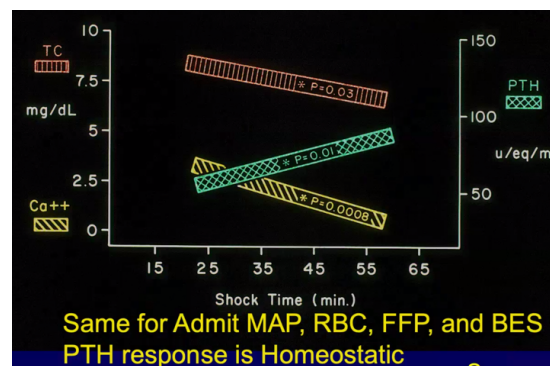


Fig. 3. Calcium PTH and Shock Insult
Source: Surgery: 1984

weeks earlier, and Group C was a normal group. He demonstrated that the ionized calcium decreased following resuscitation in the animals that had had parathyroidectomy a year and a half previously (of course there was no parathyroid to measure—he measured the N terminus) and that the cardiac output, pre shock, was 2.0 and rose with resuscitation to 2.8, which is typical with hemorrhagic shock insult. But there was a slight elevation in pulmonary wedge pressure associated with the resuscitation. (See Table 4—PS = pre shock, PR = post resuscitation.)

Group	TC mg%	Ca++ mg%	PTH-N ng/L	CO L/min	PWP torr
A [PS]	7.0	3.2	00	2.0	8.6
[PR]	---	2.5	00	2.8	9.0
B [PS]	5.6	2.5	00	2.0	9.5
[PR]	---	1.6	00	2.0	11.5
C [PS]	10.1	4.3	24	1.9	8.2
[PR]	---	4.0	74	3.8	8.0

Table 4. Parathyroidectomy and Shock
Source: Am Surg: 1987

Group B showed a decrease in the ionized calcium compared to the animals that were calcium independent. When the resuscitation was done, the ionized calcium went down to 1.6, the cardiac output did not improve with resuscitation, and the pulmonary wedge pressure was elevated during resuscitation. Group C had an ionized calcium which fell to 4 during the shock and resuscitation, the parathormone level increased by

a factor of 3, cardiac output doubled, and the wedge pressure actually decreased. This demonstrates the importance of the parathyroids in the response and treatment to the hemorrhagic shock insult.

Calcium Channel Blockade and Shock

In the 1980s it was generally thought that calcium channel blockers were good for preventing visceral vasospasm from the release of intracellular arachidonic acid. It was thought that calcium channel blockers would protect the brain, kidneys, and heart during ED, OR, and SICU resuscitation. A national champion of this concept was Dr. Blaine White, a dedicated, highly respected, well published, and well-known emergency physician at Wayne State University. But there were some nagging concerns—to some, it just didn't seem right. If parathormones are acute responders to the hemorrhagic shock insult, why are calcium channel blockers better?

Dr. Ronald Denis from the University of Montreal and Dr. Jim Wallace decided to look at calcium channel blockers in a hemorrhagic shock situation to determine whether it was best (a) to supplement with calcium *or* (b) to block *or* (c) to do neither.



Ronald Denis (L) and Jim Wallace

They looked at three groups: One group was supplemented with calcium at 0.5 mEq per kilo, one group was given crystalloid solution plus the calcium channel blocker Verapamil, and one group was given neither. A control group was given anesthesia without operations.

The study generated much data and found that the parathyroids are indeed an acute responder to the hemorrhagic shock insult; that parathyroidectomy is bad; that calcium supplementation helps both groups; and that calcium channel blockers are bad, *bad*, BAD.

Dr. Tomasz Gutowski had a 46 year old patient with bad peritonitis, bowel obstruction, dead bowel, and massive spill. During the operation the patient received 14L of crystalloid. Post-operatively he had multiple organ failure of the kidneys, liver, lung, brain, and abdominal compartment syndrome. They all improved. His creatinine improved with hemodialysis from day 10 (when it was 8.6) to day 19 (when it was down to 1.5). He started having problems with bradycardia in the fourth week, and at that time, the calcium levels were elevated (1.34-1.44 mmol/L). It was thought to be a vasovagal reaction. He was treated with fluids and lasix and given lots of atropine on different occasions. Yet the patient died on day 27. It was frustrating because all of his organs were getting better.



Tomasz Gutowski

I think this is important to remember in life: "He who knows not and knows not that he knows not is a fool to be avoided." I felt like that fool. Why the hypercalcemia? We were totally dumb.

Another "teacher" of mine was a drag racer with multiple injuries, an Injury Severity Score (ISS) of 59 (that's really serious), and multiple organ failures of the lungs, brain, gut, liver and kidneys. He had hemodialysis from days 10 to 19. His creatinine went from 10.6 down to 2.0. All of his other organs improved. But in the fourth week, he started developing bradycardia. He had asystole requiring a chest massage on three occasions. His ionized calcium was elevated.

We assumed it was a vasovagal reaction, treated him with atropine and frequent CPR. Finally it dawned on me to measure the PTH and find out

what was really going on. It turned out he had markedly elevated PTH from days 24-37 at 57-83 (N:13-53). We treated him with bisphosphonate and everything improved. He was discharged on day 107.

Dr. Sachin Shah really drove home the message of the problems with tertiary hyperparathyroidism. He had a patient with a terrible crunch injury: Subarachnoid hemorrhage, a GCS of three, multiple bilateral rib fractures with pulmonary contusion, terrible pelvis (AIS=5), long-bone fractures, and injury to the vascular system in the pelvis. He had an extremely high ISS of 66. The pelvic fracture involved shift of the posterior elements and separation of the pubis (Figure 4).



Sachin Shah

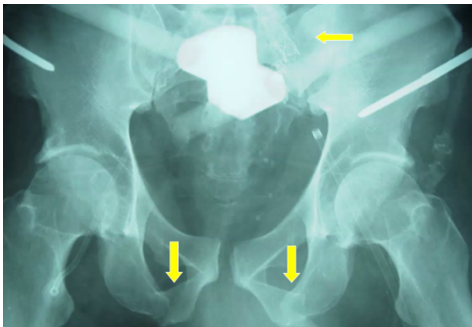


Fig. 4. Pelvic Fracture

He showed evidence of requiring blood over and beyond his many long-bone fractures. We taught at that time, patients with evidence of bleeding in the pelvis who had a positive FAST study would undergo laparotomy and the pelvis would be repaired. A negative FAST study called for angiography (see Figure 5). (The current answer for the ABSITE test might be to do a pre-peritoneal packing, which I think will give a higher incidence of success.)

The patient went to the IR and had active bleeding from the common iliac and the internal iliac arteries. After stenting, he returned to the SICU with terrible problems with his lungs—bilateral

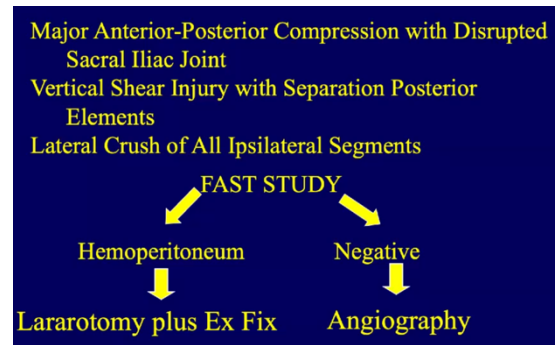


Fig. 5. Severe Pelvic Fractures in the Unstable Patient

contusions, bilateral chest tubes for high respiratory pressures. He had a tracheostomy on day 3, was paralyzed, reversed I/E ratio, and put on high frequency ventilation and antibiotics. He also had terrible liver insult, which is seen with hemorrhagic shock insult.

By day 5, his bilirubin was 18.9 mg/dl. By day 11, total/direct was 39/33 mg/dl. His highest bilirubin was 58.4 mg/dl. All of his hepatocellular enzymes were elevated. He had prolonged adynamic ileus. He also had problems with coagulopathy from every place—the nasogastric tube, the chest tube, the Foley, the rectum. During his stay he received 53 units of red blood cells and 275 units of plasma. He had acute tubular necrosis. The etiology was sepsis, rhabdomyolysis, shock, and antimicrobials.

He was placed on hemodialysis for two weeks then ultrafiltration for another week. Eventually, all of these things got better. God wasn't ready for him. His brain was unresponsive up into week 4 and had decreased responsiveness up to one and a half months, but eventually he woke up. Also in week 4 he had trouble with bradycardia and again was in cardiovascular crisis: He had asystole and was given atropine and CPR. He had placement of a pacer, which didn't work. He had markedly elevated ionized calcium (1.46 mmol/L). Calcium is an inotrope, but you get delayed repolarization, a shortened Q-T interval, all

	OR 5hrs	Phase II 17hrs	Phase III 56hrs	All Studies
Plts	+0.15	+0.03	+0.02	+0.02
B Time	-0.7	-0.3	-0.05	-0.4
MA/adp/%	+0.07	+0.8	+0.2	+0.04
MA/col/%	+0.04	+0.9	+0.5	+0.001

Table 6. Calcium and Platelet Function: Correlation Coefficients

sorts of dysrhythmias, bradycardia and A-V node delay, and cardiac arrest.

We treated the patient with fluid boluses for hydration, lasix (furosemide) to facilitate calcium excretion from the kidney, and bisphosphonate (pamidronate disodium [Aredia]) to drag the calcium back into the bones. Eventually the PTH came back to normal and the patient did well.



Chris Jeffries

Dr. Chris Jeffries put all of these data together and demonstrated that tertiary hyperparathyroidism can occur with both trauma and sepsis. Hyperparathyroidism of multi-system organ failure in acute injury and sepsis leads to bradycardia and death.

The Future: The Calcium Effect on Coagulation

When I was a medical student, calcium was called Factor IV, but later it was found that calcium is not really an independent Factor—rather, it activates Factor V. It promotes aggregation and stimulates both collagen and ADP aggregation including maximal aggregation, T1/2 aggregation, and the rate of maximal aggregation. It also enhances platelet release factors beta-thromboglobulin (BTG) and Platelet Factor IV. It also contributes to the coagulation cascade (secondary hemostasis) and is responsible for stimulating Factors I, V, and VIII at least, and probably more.

Platelets accumulate at the site of injury and plug the hole (Figure 6 outlines the process). They also have a very important role in wound healing

Accumulate at Site of Injury: Plug Hole in Vessel
 Platelet Adhesion
 Release Reaction: Entrap Clotting Proteins
 Aggregation: Collagen & ADP
 BTG: Increase Megakaryocyte Maturation
 PF-4: Inhibit Antithrombin; Promote Clot
 Facilitate Fibrin Clot (Secondary Hemostasis)
 Help Activate Factors I, II, IX, X, XI & XII
 Late Effects: Wound Healing; Immune Response

Fig. 6. Primary Hemostasis: Formation of a Platelet Plug

and in subsequent immune responses in patients who become infected. In 2020, Matthay *et al* looked at calcium and platelet activation following trauma. They had a large sample (538) of injured patients, with an ISS of 10. They found that calcium therapy before resuscitation increased the percent of ATP and collagen-stimulated aggregation but was inversely related to the number of transfusions and the shock the patients had. Their Rotem studies demonstrated the same type of relationships. They recommended correcting hypocalcemia in injured patients.

Their paper stimulated me to examine the relationship of calcium to some of the things involved with coagulation, using data we have. The ionized calcium, corrected for PH, is presented in

	OR 5hrs	Phase II 17hrs	Phase III 56hrs	Conv. 24days
Plts	110/49	118/94	96/44	563/197
ClCa	1.6/0.3	1.8/0.2	2.1/0.2	2.4/0.2
B Time	15.4/2	13/2	11/3	7.2/2
MA/adp/%	41/16	58/18	57/20	79/13
Rate/adp	25/15	36/13	37/19	67/18
T1/2 adp	17/10	22/11	37/12	36/13
MA/col/%	72/15	82/9	84/7	90/9
Rate/col	18/9	19/6	29/10	35/13
T1/2 col	154/53	158/50	133/35	100/21

Table 5. Calcium and Platelet Function

Tables 5-10, which show a significant relationship during phase II, phase III, and in convalescence, with the number of platelets. We saw significant relationships to collagen-stimulated aggregation and ADP-stimulated aggregation. All of the oth-

ers were trends, because the numbers in the subcategories were not large enough to show statistical significance.

Tables 6 and 7 show that the calcium is directly related to the platelet number, inversely related to the bleeding time, and directly related—significantly—to ADP-stimulated aggregation and collagen-stimulated aggregation—maximal aggregation as well as T1/2 aggregations and percent aggregations. They all showed the same pattern.

The platelet release factors (Table 8) were off the wall and did not return to near normal until convalescence at 28 days. There was a tremendous

Platelet Level:	+0.02
Bleeding Time:	-0.4
Max Aggreg/adp/%	+0.04
Max Aggreg/col/%	+0.001

Table 7. Calcium and Coagulation Correlations—All Studies (555 in 289 Patients)

increase in BTG and Platelet Factor IV. Urine levels are usually not measurable unless you have huge levels within the plasma. The marked increases in the release factors correlated with the calcium.

Secondary hemostasis is the formation of a fibrin clot. We know that Factor IV (calcium) promotes Factor V and platelet aggregation. Table 9 shows that ionized calcium, corrected for PH, correlates significantly with Factor I, Factor V, Factor VIII, and inversely with INR, with PTT and TT. These are all significant relationships. It is clear that calcium plays a very important role in all of these Factors.

Taking all the studies together, Table 10 summarizes the total relationship that the calcium increases the platelet count. The mechanism is that the megakaryocytes have calcium channels which, under the stimulus of ADP, allow for calcium to enter into the cell, forming so-called vesicles which are then released as platelets. Thus, the increase in the platelet level is due to the ef-

	OR 5hrs	P II 17hrs	P III 56hrs	Conv. 24d
Plasma BTG(ng/ml)	415/68	129/71	54/36	36/10
Plasma PF-4(ng/ml)	36/18	26/17	12/8	9/5
Urine BTG(ng/ml)	30/56	23/14	0.3/0.2	N/A
Urine PF-4(ng/ml)	18/18	10/12	10/17	N/A
Normal Plasma BTG=25.2 (8.6-41.8)				
Normal Plasma PF-4=2.98 (1.86-6.7)				
Normal Plasma & Urine BTG & PF-4=None				

Table 8. Calcium and Platelet Release Factors

	OR 5hrs	Phase II 17hrs	Phase III 56hrs	Conv. 24days
ClCa	1.6/0.3	1.8/0.2	2.1/0.2	2.4/0.2
F I (mg/dl)	131/40	241/127	429/166	469/133
F V (%)	43/23	65/25	125/40	177/45
F VIII (%)	61/40	101/52	151/71	217/41
INR	1.5/0.5	1.27/0.2	1.2/2	1.1/1
PTT (sec)	36/14	35/13	28/10	25/2
TT (sec)	8.4/4	4.7/3	0.5/1	0.08/1
FSP(ug/ml)	10/5	20/7	44/11	53/6
Mono	0.04/0.1	21/30	37/43	N/A
Antithr	14.6/2.7	15/5	17/5	N/A

Table 9. Calcium and Coagulation Cascade

fect of calcium on the megakaryocytes and works together with ADP.

Consider the patient with hemorrhagic shock who gets multiple transfusions: We know that with the shock insult and mean arterial pressure less than 60 there is cell injury, release of acid products, and changes in the cell membrane potential, increasing the intracellular sodium from 9 to 15 and the cell membrane potential from -90 mV down to -60 mV. This change is so predictable that some people have used it to moni-

Platelet Level:	+0.01
Bleeding Time:	-0.001
Max Aggreg/adp/%	+0.04
Max Aggreg/col/%	+0.001
Factor I	+0.001
Factor V	+0.001
Factor VIII	+0.001
INR	-0.001
PTT	-0.001
FSP	+0.001

Table 10. Calcium and Coagulation Correlations—All Studies (543 in 289 Patients)

tor shock insult.

All this occurs because of the sodium–potassium ATPase pump. Today we are talking about calcium entering into the cell under the influence of the same ADP. What, then, is the exchange ion? Is this a calcium–phosphorus exchange? (Perhaps a resident attending Grand Rounds 15 years from now will be teaching us about the calcium–phosphorus ATPase pump that alters the movement of calcium into the cell in patients with severe hemorrhagic shock.)

Bolus vs. Infusion

Having decided to give calcium, should it be given as a bolus or as an infusion? To find out, Dr. Don Porter gave a group of hypocalcemic patients a calcium infusion of 13.7 mEq from 0 to 30 minutes, then monitored the calcium cardiac output and systemic vascular resistance. He demonstrated (Table 11) that infusion started at 0 time by 15 minutes caused an increase in ionized calcium, an improvement in cardiac output, and a decrease in systemic vascular resistance.



Don Porter

This continued to be about the same at the 30-minute level, when the infusion was stopped. By 60 minutes, cardiac output had gone down to below what it was at the beginning, and systemic vascular resistance went up again. Evidently, to supplement hemorrhagic shock, calcium infusion is better than a calcium bolus.

Protein Resuscitation and Free Calcium

Prior studies from WSU have compared albumin vs. balanced electrolyte solution for traumatic hemorrhagic shock. We noted that albumin supplementation binds with ionized calcium and leads to problems—increasing total Ca but de-

Ca ⁺⁺ :	1.9	2.2	2.2	2.1
CO:	4.8	5.2	5.1	4.5
SVR:	1250	936	953	1231
Calcium Infusion 13.7 mEq				
	0	15	30	45
				60
			Minutes	

Table 11. Calcium Dynamics: Short-Term Benefit

creasing ionized Ca. How, then, do we handle the current recommendation of a 1:1 FFP/RBC resuscitation ratio, or as we follow a 0.5:1 resuscitation ratio?

Recommended Calcium for Injury

Our data (from the study discussed above) show an inverse correlation between ionized calcium and the amount of plasma given in patients resuscitated in the ED and in the OR. That means we should give at least one ampoule of CaCl (13.7 mEq) for every 5 units of red blood cells in the severely injured patient (as a continuous infusion, not as a bolus). In the early post operative period, the patient should be monitored and supplemented with additional infusions as needed.

One of the areas where there is ignorance has to do with how much calcium leaves the extracellular space and enters into the cell through the calcium channels. All we know is that in hemorrhagic shock the intracellular Na goes from 9 to 15, so we can predict how many mEq of Na are going to be within the cell and not part of the interstitial space; but we have no idea how much Ca is going to get into the cell so we have to do our replacement based upon the expansion of the interstitial space calcium and the intracellular calcium. One of our students will probably answer that unknown by 2035.

Thank you for your attention.
