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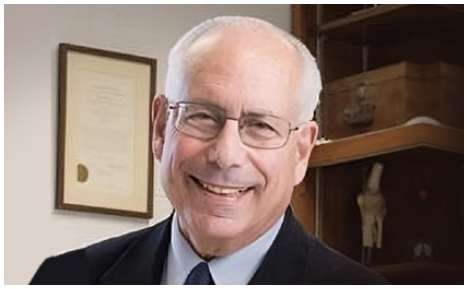
Orthopedics This Week

WEEK IN REVIEW



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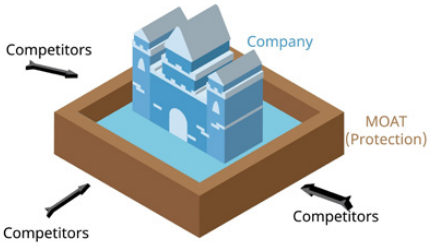

BREAKING NEWS

For all news that is ortho, read on.

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Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

THIS WEEK: Throughout the just completed 2023 and Q4 sales and earnings reporting season, the common refrain was better than forecast procedure volumes, sales and earnings. That theme was echoed by Goldman Sachs this morning where strategists boosted their S&P 500 forcast for the second time, reflecting Wall Street's optimistic outlook for corporate earnings. Goldman's 12-month forward earnings expectations are at a record high. Goldman strategist David Kostin originally set his 2024 S&P forecast at 4,700. He's now expecting it to reach 5,200 by the end of the year.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	2	Smith & Nephew	10.06%	2.37%	SNN is set to release its 2023 full year sales and earnings results on February 27, a week from now. Most analysts expect SNN to beat expectations and raise guidance for 2024.
2	4	Integra LifeSciences	17.32	7.52	Buyers are signaling that IART's February 28th sales and earnings release will also beat the current modest 0.30% sales growth forecast and $0.90 EPS estimates for 2023.
3	3	Orthofix	(8.51)	3.68	We spent time at the OFIX booth and new CEO Massimo Calafiore is bringing stability and forward momentum to OFIX after a tumultuous 12 months.
4	1	Zimmer Biomet	19.31	2.03	Under new CEO Ivan Tornos, ZBH had one of its best academies in years. The team seemed to be hitting on all cylinders with a new sense of energy and vitality. 2024 should be good year.
5	6	Pacira Biosciences	12.86	(8.09)	PCRX presented data showing EXPAREL effective treating sciatic pain after bunionectomies. 350k procedures annually. Major announcement. At these prices investors should be excited.
6	8	Axogen	(9.75)	35.64	Again, this supplier of nerve grafts, is the #1 stock performer in the Power Rankings. What's fueling buying? Axoguard Nerve Cap to manage chronic neuropathic pain. Strong study data.
7	5	Medtronic	19.26	(1.89)	MDT is the 9th cheapest equity in our universe. Its 5 most recent press releases are about inclusion, diversity, and equity. Laudable goals, but how is MDT improving spine care and more? Any updates?
8	7	Bioventus	(5.33)	(6.60)	New CEO Claypoole is on board and the new announcement is a loan amendment with creditors—highlighting BVS's most urgent needs. Also, won't be reporting 2023 for another month or so.
9	NR	Stryker	24.47	11.36	SYK had a solid AAOS after a record breaking sales and earnings report. Sales were a whopping $213 million higher than Wall Street's forecast. And management expects Ortho to stay strong in 2024.
10	NR	JNJ	19.22	(2.41)	JNJ is finishing its 2023 ortho restructuring program, exiting certain markets and products. So sales last year and this year will be down. But, management hopes, peak benefits show up by 2027. All we know is that the risk reward favors purchase.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	AxoGen	AXGN	$10.60	$456	35.64%
2	ZimVie	ZIMV	$20.69	$549	23.45%
3	MicroPort Scientific	853	$0.93	$1,705	13.41%
4	Stryker	SYK	$349.30	$132,826	11.36%
5	SI-BONE, Inc	SIBN	$20.92	$847	11.34%
6	Anika Therapeutics	ANIK	$24.21	$354	7.89%
7	Integra LifeSciences	IART	$45.04	$3,521	7.52%
8	OrthoPediatrics Corp	KIDS	$29.46	$688	4.95%
9	Medacta	MOVE	$148.73	$2,975	4.31%
10	Orthofix	OFIX	$13.79	$507	3.68%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	SINTX Technologies	SINT	$0.14	$3	-51.57%
2	ConMed	CNMD	$81.02	$2,492	-26.03%
3	Aurora Spine	ASG.V	$0.24	$17	-10.86%
4	Dynatronics Corp	DYNT	$0.48	$2	-10.54%
5	Pacira Biosciences	PCRX	$29.08	$1,350	-8.09%
6	Bioventus	BVS	$4.53	$357	-6.60%
7	Nevro Corp	NVRO	$17.32	$628	-5.87%
8	Xtant Medical Hldgs	XTNT	$1.06	$138	-2.75%
9	Johnson & Johnson	JNJ	$156.55	$377,093	-2.42%
10	Globus Medical	GMED	$53.82	$7,567	-2.00%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Johnson & Johnson	JNJ	$156.55	$377,093	18.84
2	Integra LifeSciences	IART	$45.04	$3,521	19.50
3	Medtronic	MDT	$84.42	$112,249	20.03
4	Zimmer Biomet	ZBH	$124.71	$26,062	26.21
5	Globus Medical	GMED	$53.82	$7,567	27.64

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Medacta	MOVE	$148.73	$2,975	56.87
2	Smith & Nephew	SNN	$28.06	$12,267	55.01
3	Stryker	SYK	$349.30	$132,826	37.59
4	Pacira Biosciences	PCRX	$29.08	$1,350	37.14
5	ConMed	CNMD	$81.02	$2,492	36.06

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Smith & Nephew	SNN	$28.06	$12,267	-6.88
2	ConMed	CNMD	$81.02	$2,492	1.42
3	Medacta	MOVE	$148.73	$2,975	2.04
4	Globus Medical	GMED	$53.82	$7,567	2.04
5	Integra LifeSciences	IART	$45.04	$3,521	2.19

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Medtronic	MDT	$84.42	$112,249	5.94
2	Johnson & Johnson	JNJ	$156.55	$377,093	4.01
3	Zimmer Biomet	ZBH	$124.71	$26,062	3.78
4	Stryker	SYK	$349.30	$132,826	3.41
5	Pacira Biosciences	PCRX	$29.08	$1,350	3.23

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Dynatronics Corp	DYNT	$0.48	$2	0.06
2	ZimVie	ZIMV	$20.69	$549	0.60
3	Bioventus	BVS	$4.53	$357	0.70
4	Aurora Spine	ASG.V	$0.24	$17	0.88
5	Orthofix	OFIX	$13.79	$507	1.10

HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	SI-BONE, Inc	SIBN	$20.92	$847	7.96
2	Globus Medical	GMED	$53.82	$7,567	7.40
3	Medacta	MOVE	$148.73	$2,975	6.80
4	Stryker	SYK	$349.30	$132,826	6.48
5	Alphatec Holdings	ATEC	$15.52	$2,115	6.03

PSR: Aggregate current market capitalization divided by aggregate sales and the calculation excluded the companies for which sales figures are not available.

What Effect Do Industry Payments Have on TJA Costs or Outcomes?

BY ELIZABETH HOFHEINZ, M.P.H., M.ED.

Do industry payments (consulting or clinical trial work) to total joint arthroplasty (TJA) surgeons or their institutions affect TJA costs or outcomes and, if so, how much?

A new study from Stanford University Medical Center compared data for more than 360,000 total joint arthroplasties with industry payment data and their results "Costs and Outcomes of Total Joint Arthroplasty in Medicare Beneficiaries Are Not Meaningfully Associated with Industry Payments," was published in the November 22, 2023, edition of *The Journal of Bone and Joint Surgery.*

Total joint arthroplasty is one of the most commonly performed surgical procedures around the world. As the global population ages, the number of total joint arthroplasties is expected to continue to increase. At the same time, caregivers continuously seek to improve costs, efficiencies, and patient outcomes.

To what extent do industry payments affect TJA efficiency and patient outcome? To answer this question, the Stanford team collected data from a 20% sample of Medicare-insured patients undergoing primary elective total hip arthroplasty (THA) or primary elective total knee arthroplasty (TKA).

From the dataset, the team collected 130,872 THAs, performed by 7,539 surgeons and 230,856 were performed by 8,977 surgeons from 2013 to 2015.

Source: Shutterstock

Co-author Derek Amanatullah, M.D., Ph.D., associate professor of orthopedic surgery at Stanford University Medical Center, told *OTW*, "Higher total industry payments were associated with increased total costs and operating room costs of THA in Medicare patients, but the cost increase was minimal (between $0.20 and $0.50 increase for each $1,000 of payments).

Higher total industry payments were associated with a decreased length of stay after both THA and TKA.

Higher total industry payments were not associated with 30-day mortality after THA or TKA.

Higher total industry payments were associated with an increased 30-day readmission rate after THA. However, the magnitude of this relationship was very small; for each $1,000 increase in industry payments, the odds of 30-day readmission increased <0.1%.

Higher total industry payments were not associated with 30-day readmission after TKA.

While the team concluded that arthroplasty costs and outcomes were not meaningfully affected by industry relationships, Dr. Amanatullah did add, "We did not analyze the impact of the individual types of payments (particularly the specific influence of royalty payments as distinct from other forms of industry payments), and the accuracy of Open Payments data has been disputed because many deidentified payments are classified as research, but the outcome of that 'research' cannot be verified." ♦

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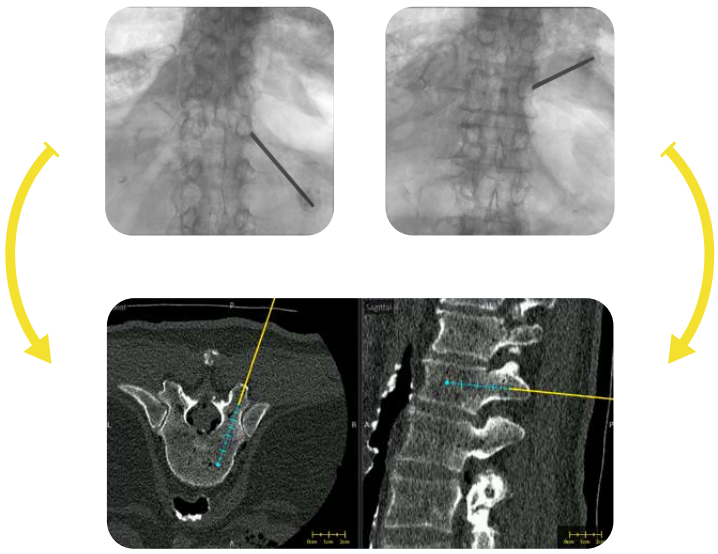

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Arnold Caplan: Becoming the Father of Regenerative Medicine

BY ROBIN YOUNG

Dr. Arnold Caplan, "Arnie" to his thousands of colleagues and friends around the world, died at age 82 on January 10, 2024.

Dr. Caplan's was professor of biology and director of the Skeletal Research Center at Case Western Reserve University. He also was the lifetime achievement award winner from the Tissue Engineering and Regenerative Medicine International Society.

Dr. Caplan's unifying vision of regenerative medicine lived within an exceptionally creative, warm, and generous mind. His legacy will drive musculoskeletal care for generations to come.

Arnold Caplan spent 54 years at Case Western Reserve University. In that time, he mentored and touched the lives of 150+ researchers. He was a fixture at scientific meetings throughout the world and received many awards including The Marshall R. Urist Award; The Tissue Engineering and Regenerative Medicine International Society Lifetime Achievement Award; and the Case Western Reserve University Faculty Innovator Award.

In 1992, he founded Osiris Therapeutics, Inc., to bring these reparative cells to patients. Among the early staff members at Osiris was one of Dr. Caplan's most promising young doctoral students, Scott Bruder Ph.D. At least a couple dozen other companies have been founded on the basis of Caplan's work.

His more than 400 published papers, 104,000 aggregated citations and 20 patents stands as one of the greatest bodies of work in the history of regenerative medicine.

Arnold Caplan, Ph.D. / Courtesy of The Family of Arnold Caplan

But, to understand the effect more fully, the reach and enduring importance of Arnold Caplan, which ultimately led to the moniker "father of regenerative medicine," we turn to Dr. Caplan's closest friends and colleagues.

Marc Penn, M.D.

Dr. Penn is a cardiologist and director of research at the Summa Health Heart and Vascular Institute (Akron, Ohio), as well as director of the Institute's Cardiovascular Medicine Fellowship. He is also professor at Northeast Ohio Medical University where he leads the Skirball Laboratory for Cardiovascular Cellular Therapeutics (Rootstown, Ohio).

"I first met Arnie when I was at the clinic. I got to know him at the Center for Regenerative Medicine. We became really good friends. I'm going to miss him dearly. He was a friend, a mentor, a lot of things to me.

Arnie, I genuinely believe, wanted what was best for each individual. Arnie made me a better scientist, a better Jew, a better father, a better person. He was really a wonderful person to spend time with.

Arnie's the father of what is currently considered regenerative medicine. Mesenchymal stem cells are the foundation of almost everything. What was great

about Arnie is the way he evolved with the science. So many of folks in the field don't adapt, don't look at the data.

Arnie was absolutely data-driven. He followed the data, adapted to the data, and didn't argue against the data—even if he didn't like it.

There's no question the field of regenerative medicine is better off because of Arnie. He was its epicenter where everybody who wanted to be in the space could freely collaborate with him and gain the expertise.

Arnie was so much more than what we knew about him as a scientist. Young students at Case who needed advice I would send to him. And he was always very open to talking to them and always really resourceful and insightful to help them.

Arnie moved things forward. He wanted to see things be successful and funded to the day he died. He wasn't done, sadly.

He was incredibly satisfied with where he ended up in life and was at peace with all he had achieved."

Bruno Peault, Ph.D.

Professor and Chair of Vascular Regeneration, Centre for Cardiovascular Science University of Edinburgh; Professor, Orthopaedic Hospital Research Center, University of California Los Angeles

"Arnie was very inventive. He had great ideas, frequently 'out of the box,' and was always keen to theorize and propose new experiments. He was one of the most thoughtful and creative people I have interacted with in the field of MSCs. He also had a special talent to communicate scientific knowledge to broad audiences.

Arnie had this accurate vision of stem cells, which probably came from his background in developmental biology. He coined the term mesenchymal stem cell. He worked on the emergence of mesodermal tissues in the embryo. By analogy, he proposed that similar mesodermal stem cells are also present in adult tissues.

My original interest and expertise is in hematopoietic stem cells, which have been directly and prospectively identified. It was not the case for MSCs which

were produced retrospectively in long-term culture.

We explored this issue and found that MSCs are derived from perivascular cells notably pericytes.

Arnie liked the idea. In all of his presentations, he would talk about the pericyte as the native, tissue resident MSC that can be recruited into tissue regeneration after being shed from blood vessels.

Every time I would see Arnie at a meeting, he would always come with a big smile, and he would say, 'Bruno, each time I hear you, I hear new things'. That was very nice to hear. But I can say that it was reciprocal. I always learned a lot also from Arnold."

Rodrigo Somoza Palacios, Ph.D.

Research Associate Professor, Skeletal Research Center
Project Lead, TR&D-1
Director, Cell Culture Facility
Case Western Reserve University, Cleveland, Ohio

"I had read most of his work before I met Arnold Caplan. Arnold is why I've been working with MSC since I was an undergraduate student. I was lucky enough to get a scholarship and come from all the way from Chile to attend his three-day short course in 2011. That was the first time I met Arnold in person. He was very interested in me and knew people from Chile including people I knew too. He asked me a lot of questions. He was very nice. I asked him if there was a possibility that I could work with him. He was open to that idea. He never closes any doors.

At that same course in 2011, I met Diego Correa, who was already working with Arnold. He was from Colombia. I actually was born in Colombia.

Diego was working on a project about how MSCs can control bone metastasis. Diego was submitting an NIH funding application for this project. I was lucky enough to finish my Ph.D. at about the time that grant got funded. Arnold and Diego were kind enough to offer me the position of a postdoc in the lab.

Working in Arnold's lab was a very good experience for me. Arnold met with me probably two, three times a week. Every week he asked me for a new idea. We discussed those ideas, hypothesis, objectives, and how I was planning to do those experiments. Some ideas he hated, some he liked.

Arnold is a big name. Every time I had a meeting with him, before that meeting, I dedicated hours and hours getting prepared. But he always had a question I couldn't answer. He was always really polite and professional and made me feel like a colleague, not just a postdoc.

He also talked about family. That's something that really impressed me. Arnold loved his family. Sometimes half of the meeting was about family and travel and other things beyond science. So, I really felt connected to him.

I learned how to achieve scientific excellence from Arnold. I learned how to solve problems. MSCs are not easy to work with. He taught me all the details and tricks to effectively work with MSCs. I also learned how to write grants; we were successful in getting funded.

He had a great impact on me and my career. We were always talking about ideas and experiments. Always he agreed with my ideas, and I agreed with his ideas. I really felt connected with Arnold.

In November, Arnold talked to us about his cancer and the surgery and that it was risky. He was calm about it. He said, 'I know it's risky but I'm happy with my life. My family is happy, I'm happy with everything that is happening around me.'

He was very brave.

My goal is to continue Arnold's legacy. He left our lab with very excited projects going on, how MSCs control cancer metastasis, how MSCs are involved in pain management and, of course, teaching. We are going to continue on that same path."

David Mooney, Ph.D.

Dr. David Mooney is the Pinkas Family Professor of Bioengineering in the Harvard School of Engineering and Applied Sciences, and a Core Faculty Member of the Wyss Institute. His laboratory designs biomate-

rials to promote regeneration and immunotherapy. He is a member of the National Academy of Engineering, the National Academy of Medicine, and the National Academy of Inventors. His inventions have been licensed by over 15 companies, leading to commercialized products. He has founded companies and is active on industrial scientific advisory boards.

"Dr. Caplan was 20 some years older than me and he was an inspiration for me in terms of the work that he did, the accomplishments he had, his vision, his pioneering research.

As I got to know him personally, I recognized quickly what a great role model he was in terms of how to succeed with all the accomplishments but still continue to engage and interact with others, including the next generation, which he tried to encourage and help.

I had read once that a measure of a true friend is how you feel when you see that person. And every time I would see Arnie, I would smile. He was a good man.

I learned a lot of things from Arnie. Scientifically, he was not afraid to go out on a limb. He would do science very rigorously. He would follow the data and if the data took him in a certain direction, he would follow it and put a stake in the ground and say, this is what I'm finding and this is what I think this means, and here's how this is going to change how we think about things and how we do things in our field.

Sometimes with all of us, some of our ideas will get refuted by our own work as we go deeper into the science. As time went on, Arnie started saying that these cells mainly work by secreting different molecules that impact the biology around them. That these MSCs are probably not the builders, but rather the ones controlling the other cells.

He went with the science and went with the data and would not get locked in.

Arnie's work inspired and led to just an incredible amount of research by others. It really is just phenomenal. Arnie had a huge impact. So many people got into this field because of his work. So many people."

C. Randal Mills, Ph.D.

Randy Mills, Ph.D., co-founder and director of Elutia, former CEO of Osiris Therapeutics, which commercialized five

cell-therapy products responsible for $1.5 billion in sales. Sold to Smith & Nephew for $660 million. Dr. Mills also co-founded Regeneration Technologies. Randy later served as president of the $3 billion California Institute for Regenerative Medicine and CEO of the National Marrow Donor Program.

"When I became the CEO of Osiris Therapeutics, it was a pretty hard time for me. I was a first-time CEO; I was 31 years old and was the seventh CEO the company had hired over the past 4 years. The previous one only lasted 6 weeks! Not great odds.

Right away, all I heard was that I wasn't going to last very long either, and exhibit A was that Osiris's founder, Arnold Caplan, hates us.

I sat and thought, 'Well, that sucks'!

At the time I was trying to figure things out and piece together a business plan. I saw some really phenomenal opportunities for Arnie's MSCs and the ability to build a great company, but it also required that we make a big cultural leap from Osiris University to Osiris Therapeutics.

But as the plan started coming together, I kept hearing that the guy who founded the company still hates you. I thought, 'If he's not on board, how can anyone believe what we are doing?' So, I just called Arnie out of the blue. And to my shock he answered the phone.

I said, 'Dr. Kaplan, I'm Randy Mills, and I am the new CEO of Osiris Therapeutics.' And there's this uncomfortable pause. So, I just kept talking.

I said, 'Look, you don't know me from Adam, but I gotta tell you, I see so much potential in your discoveries. And I think Osiris is gonna become a really, really iconic company in the field of medicine. And I can't for the life of me figure out why this great company and its founder should be estranged. I'd love to come talk to you about what we're doing.'

And again, silence. Then Arnold says 'Yeah, Randy. I'm free next week'.

I said, 'perfect! I'll be there.'

It was the winter of 2004 in Cleveland, Ohio, which is not a fun place for a Florida boy. I'm scared to death because Arnold Caplan is not only this guy who founded the company but also the guy who discovered the very principles behind this thing I've now fallen in love with. I feel like I'm defending my dissertation again! But instead, I find a man who is so warm and gracious.

He said to me, 'tell me what you're going to do.' And so, I tell him the plan. He says 'that sounds great. It sounds exactly like what the company needs right now, and what I've been hoping Osiris would do. And I can't wait for you to pay my grandkids college 'cause I've given them shares in Osiris!'

So, like, no pressure. And then he took me around and introduced me to everybody, invited me to his lectures, gave me a platform, and over the next decade, lent me his credibility. And became a dear friend.

I'll never forget that. His grace and generosity forever left an impression on me. We wouldn't have been successful at Osiris if he had not done that.

Arnold Caplan literally and figuratively put his arm around me, said, 'You're onto something, and I'm here for you.' We lost a lot, and I'm going to miss him."

Robert Harman, M.D.

Co-Founder, CEO, and Chief Scientific Officer of Personalized Stem Cells, Inc. Dr. Robert Harman is a Doctor of Veterinary Medicine, with a Master's in Preventive Veterinary Medicine, which focuses on epidemiology. For the majority of Dr. Harman's career, he has worked as a biotechnology entrepreneur. He and his partners successfully founded, expanded, and sold two biotech companies. He currently serves as CEO for PSC and VetStem, Inc, a veterinary regenerative medicine company.

"I was a young investigator, 15 years Arnie's junior, just starting in the field. David Fink, one of Arnie's good friends, introduced me. I told him 'I'm hugely honored to meet you and I'm embarrassed with what we're doing in veterinary medicine without really understanding how these cells function.'

He said, 'Harman, I know you already and you just have to keep doing this work. It is hugely important.' Then I said, 'But Dr. Kaplan, I don't even understand how these cells work.'

Then he goes, 'I don't give an F how they work. I'm telling you they work and go forward. You have the opportunity to create data that we can only dream about on the human side because you're going to be able to treat lots of patients.'

This was when I had treated 10 horses. And of course he was correct. The next

year at ORS, he sees me down the hall and says, 'So, Harman, was I right?' And of course he was. We had treated 300 or 400 horses.

Literally everything I did from there forward, had Dr. Caplan's fingerprint on it.

The thing I admired most about Caplan was his ability to see when things had changed, when there was new data, better data, more insight.

At the beginning, Arnie said here is how these cells work and differentiation was the correct pathway. Five or ten years later, he is lecturing that differentiation is probably not the major mechanism but, rather, these cells are signaling drugstores. And we started looking at how cytokines would be produced and that, wait a minute, maybe they're not even the stem cells, maybe they're getting eaten by macrophages. And the macrophages are tissue resident and begin to express the same phenotype as the stem cells.

I think of the fourth generation of these insights from Arnie's work is not a change in the paradigm, but the additions of pain and antibacterial and antiviral effects of these cells.

Each one of these changes in the view of what these cells do had a profound impact on how we developed veterinary cellular therapies.

I would call Arnie periodically and say, we just used cellular therapies with a northern white rhino, we just did a giraffe. Now we're working with marine mammals, we've done turtles. And we would talk about it and if there's one thing in my entire career in regenerative medicine that stands out, it is how these cells work across all these species. It's amazing. Amphibians, reptiles. I did a condor a couple months ago, birds, dolphins, orcas. They all respond the same way.

Arnie's views were constantly evolving. I must've listened to his MSC talk a hundred times over the last 15 years. I know people would just roll their eyes and go; it's the Caplan talk again. But it never was. Arnie's talk always had a little evolution. If you paid attention, it was profound.

Arne was larger than life, strong and a little bit stubborn. Finally, he had more clinical compassion than anybody I could ever imagine. I mean, he just cared about the patients and getting this technology. I hope nobody forgets. He impacted so many of us."

Steven Goldstein, M.D.

Professor Emeritus, Mechanical Engineering
Professor Emeritus, Biomedical Engineering
Henry Ruppenthal Family Professor Emeritus, Orthopaedic Surgery and Bioengineering

"Arnie was always present. Besides being prolific in publishing, he was prolific in being present in the scientific community. He was on the podium, in the audience, at the meetings and he was nonstop.

Arnie Caplan was relentless in terms of making sure that he provided the findings of his science, his perspectives, his predictions of how mechanisms worked. Although he was immensely confident, he wasn't afraid of being wrong.

He was tenacious. If he was still here, he would be working on new grants and ideas. He would be traveling the world lecturing, and he would be pushing entrepreneurial limits.

Arnie always knew he wanted he was always 'in charge'. He had a kind of fearlessness which, I think, influenced how he did science—with tenacity and fearlessness.

Perhaps his most significant contributions related to regenerative healing and regenerative medicine. It was this work that we shared in common and resulted in collaborations. His work identifying the role of mesenchymal stem cells and the interactions among the multiple factors associated with the cascade of events directing tissue formation, repair and regeneration influenced all in the field. It was critical to my own work investigating the interplay between mechanical and biologic regulators of bone metabolism.

Our approach to life science and family were so similar that we sort of had a natural and very personal connection. I didn't have enough time, personal time, with Arnie. We always tried to get together, get our families together. That remains far too unfulfilled. My last wish to Arnie was for him to be at peace. My wish was for more time with him."

Stan Gerson, M.D.

Stan Gerson, M.D., is the Dean and Senior Vice President for Medical Affairs at Case Western Reserve University School of Medicine, where he is the Asa and Patricia Shiverick–Jane Shiverick (Tripp) Professor of Hematological Oncology and Case Western Reserve University Distinguished University Professor. In 2012, he was the recipient of the Case Western Reserve Medal for Excellence in Health Science Innovation, the highest honor bestowed by the School of Medicine to those advancing research, education and health care. He is the past president of the Association of American Cancer Institutes (2016-2018) and a member of the American Association of Physicians since 1997 and has been a member and Chair of numerous NIH study sections, including the National Cancer Institute (NCI) Board of Scientific Advisors. He serves on the Executive Advisory Board of 11 NCI-designated cancer centers.

"I think the field has lost its convener and synthesizer.

He was infectious in his collaborative engagements. We had a celebration of Arnie's 50 years at Case four or five years ago and the number of international colleagues who flew in on their own volition to be there was really quite astonishing.

Arnie's aptitude for engagement and attentiveness was quite remarkable. Which wasn't just a social engagement, he would connect people in science and give them something new to think about.

Arnold Caplan was a simulant for discovery.

Arnie's fundamental intellect was to broadly reassess his own inventiveness and perceptions and to be as inclusive, as engaging as he could to build a comprehensive model.

Arnie could also drive everybody crazy because every time you talked to him, he'd have a new idea that he was just as confident of as he was of the prior rule.

Within the first few months of my joining Case in 1983 I heard Arnie talking about cartilage in eggshells or the ceramic matrix of eggshells, something like that. I was fascinated with his approach and style. I'm a hematopoietic stem cell person. Always have been. My area of interest is DNA repair of hematopoietic stem cells.

My involvement with Arnie was in the therapeutic application of these cells. What do these cells do? How do they contribute to the physiology of the body of the tissue? Can they be manipulated,

utilized, resurfaced, repurposed for a therapeutic value?

Thirty years ago, we showed that if you stimulated mesenchymal stem cells, they would produce 30 or 40 massive increases in cytokines. Refining that crude observation from 30 years ago was frankly something Arnie spent 30 years studying. And Arnie really pushed hard on the breakthrough versus the incremental science."

Scott Bruder Ph.D.

Scott P. Bruder, M.D., PhD, is the Founder and CEO of the Bruder Consulting & Venture Group, providing product development, regulatory, compliance and commercialization support for companies and HCPs engaged in tissue repair and regeneration. He is the former Chief Medical and Scientific Officer of Stryker Corporation, and Member of FDA's Advisory Panel on Human Cell, Tissue and Gene Therapy. Over the last 25 years, he has launched numerous orthobiologic products, published over 125 papers, abstracts, and chapters, and received the highest scientific awards from the AAOS, ORS, ABJS, and AIMBE. His landmark patents on the use of MSCs for treating orthopedic conditions moved the entire platform from autologous to allogeneic cell therapy in a variety of companies around the world.

"That first week I was in Arnie's lab in 1984, he said, 'give me all the papers and everything that you wrote as an undergraduate for your thesis.' So, I brought it in and gave it to him the next morning. He came back the next day. He read it all that night. He's got good technical questions for me, and then he asked me something…something that he has since always asked me…the question that was the turning point in our relationship…he asked me: 'What's the next experiment? Tell me the experiment you want to do. And what's the next experiment after that?'

In other words, Arnie was telling me to design my investigation and experiments in such a way that, no matter the outcome you learned something.

My dad died 3 years before I entered Arnie's lab. I was 19 years old. Arnie was very paternalistic, and I viewed him as my scientific father and in many ways a surrogate father. I became very close with the whole family, Bonnie and Aaron and Rachel. He was in the restaurant the night I proposed to my wife.

They sent over a bottle of champagne. He celebrated my wedding and has been a part of my children's lives growing up. He was at both of their Bat Mitzvahs, and Hannah's wedding last year.

The thing that made him a good scientist is he was always asking questions. He wanted to understand the next implication of the observation and how that tied to other things that some people might not find an affiliation or association with. Things like immunology, and then what he'd learned about embryology and cell therapies.

At the time that we first identified MSCs, everybody thought we were full of shit. Many serious scientists didn't believe us, until they eventually reproduced the results, and then they became converts. Which is another interesting story because Arnie had this nickname when I started in the lab. He was the 'Full of Bull' Professor. He would say things that people thought were preposterous. Eventually though, most of it turned out to be true.

Another thing that made him a very good scientist was—and it's a double-edged sword here—he was very dogmatic about things. This is the way he was, sometimes to a fault, but eventually, when presented with compelling data, he had the humility to say, 'I was wrong.'

He came to the view that MSCs were not stem cells in the classical way of hematopoietic stem cells. So, he began calling them Medicinal Signaling Cells, because the way that they work, and he pleaded with everyone to STOP calling them stem cells.

The last time I saw Arnie was at his birthday, January 5. His caregivers at the hospice center brought him to a common space, where his closest friends and family waited to share their parting thoughts with him. I waited patiently until the end because Bonnie, his wife, said 'I want you to have some extra time there, because you're 'the favorite son.'

I approached him and took his hand. One of the things that I asked him in our last moments together after 4 decades of weekly discussions was, 'Boss, what do you want me to do next?' And he said, 'Help everybody bring products to market. You can do it.' Then I said to him. I am just so happy to see that you had an incredible 82-year run, and I've been blessed to be part of it for the last 40 years. You've travelled the world. You've impacted science.'

Then Arnie said., and this is the part that chokes me up, he said, 'It's been an incredible role reversal. I was your teacher for the first 20 years, and you became my teacher the last 20 years. Help get this science into people!' Then he said, 'so keep developing products. Get your clients, get your peers, and get your colleagues aligned to impact healthcare, help them get these things into market.'

But that was our relationship.

What's the next experiment, and the one after that? Why are you doing that experiment? The other thing he used to say is: 'Do the hard experiment first. And try, you know, try to do the heroic things. Make a difference.' I plan to honor his wishes with as many people and technologies as possible."

Cheryl Blanchard, Ph.D.

Dr. Cheryl Blanchard is President and Chief Executive Officer of Anika Therapeutics, Inc. Prior to her work at Anika, she served as the President and Chief Executive Officer of Microchips Biotech, Inc. Previously she served as Sr VP, Chief Scientific Officer of Zimmer and GM of Zimmer Biologics. During her 12 years with Zimmer, she had global leadership of R&D, advanced technologies, clinical, quality, medical and regulatory affairs, medical education, health economics, reimbursement, and general management. She created and led the biologics business at Zimmer through R&D, partnering and business development. Prior to Zimmer, Dr. Blanchard built and led the medical device practice at Southwest Research Institute and was an adjunct professor at the University of Texas Health Science Center, in San Antonio, TX. She holds a BS in Ceramic Engineering from Alfred University, and an MS and PhD in Materials Science and Engineering, from the University of Texas at Austin. She is a member of the National Academy of Engineering.

"I first met Arnie when I was the Chief Scientific Officer at Zimmer years ago. He was what I would consider to be the quintessential professor—challenged thinking and asking questions. Arnie was a real role model for me about how to just keep asking the right questions. What we do is hard. There are no easy answers.

He had a way of tying science to business. He understood that at the end of the day, patients get therapies because a business develops them. I think he saw how that ecosystem worked very early on.

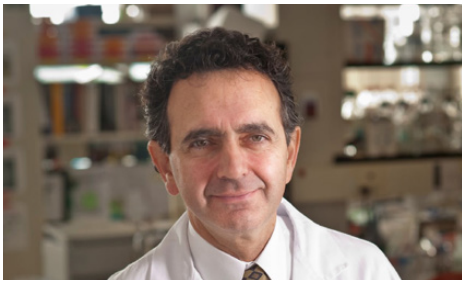
I don't know that Arnie ever got his full credit due for the science he pushed forward that frankly resulted in so many therapies used ubiquitously today. People kind of tend to forget that there was a foundation laid for our clinical success today.

The seminal work that Arnie did around mesenchymal stem cells had an impact across many therapeutic areas. He really got clinicians and researchers thinking about what biologics could mean in the field of orthopedics.

I think the biggest thing he did for me is he would listen, go through my thinking with me. He had this way of saying: 'Let's ask a whole bunch of questions, you don't have to get four answers out of your mouth before we've had a chance to think about things.'

Arnie was a very giving person. He viewed it as his place on earth to give and challenge, and so he did."

Anthony Atala, Ph.D.



Anthony Atala, M.D.,is the G. Link Professor and Director of the Wake Forest Institute for Regenerative Medicine, and the W. Boyce Professor and Chair of Urology. Dr. Atala is a practicing surgeon and a researcher in the area of regenerative medicine. Sixteen applications of technologies developed in Dr. Atala's laboratory have been used clinically. He is Editor of 25 books and 3 journals. Dr. Atala has published over 800 journal articles and received over 250 national and international patents. Dr. Atala was elected to the Institute of Medicine of the National Academies of Sciences, to the National Academy of Inventors as a Charter Fellow, and to the American Institute for Medical and Biological Engineering.

"Arnold Caplan and I met several decades ago. He was an amazingly warm, charismatic individual—truly one of a kind. We formed an instant and wonderful life-long friendship. Our mutual scientific interest involved stem cells and their potential.

Arnie's groundbreaking work with bone marrow derived mesenchymal stem cells (MSCs) formed the basis for our own work, enabling us to find highly multipotent stem cells in amniotic fluid and placenta which can be directed to all three germ layers, endodermal, mesenchymal, and mesodermal. We had ongoing discussions about different stem cells.

Every time I'd see Arnie, he'd have something new. He'd say, 'I'm working with these cells and now they're doing this. I'm working with this now.' He was always advancing the field. He was not satisfied with the status quo. He just wanted to keep moving forward.

Over time, new discoveries are made and our understanding in science advances. Arnie saw the stem cell field evolve and felt a personal responsibility to advocate for the most current science. He highlighted a paradigm-shift regarding MSCs, proposing a new nomenclature of Medicinal Signaling Cells instead of Mesenchymal Stem Cells, further defining their expansive potential.

The body of work he accomplished in his lifetime was monumental." ♦

Why Such Low Rates of Pre-Op Nutritional Testing?

BY ELIZABETH HOFHEINZ, M.P.H., M.ED.

Source: Shutterstock

A new multicenter study has documented a surprising and concerning lack of pre-op nutrition testing for total knee arthroplasty (TKA) patients.

Indeed, only 2 out of 10,000 TKA patients (0.02%) are tested for zinc despite, as this study demonstrated, orthopedic residents specifically asking for zinc pre-op testing.

- Prealbumin test? 2.2 out of 100 TKA patients
- Transferrin? 1.9 out of 100
- Vitamin D? 10.2 out of 100
- Zinc? 2 out of 10,000

This new multicenter study, "Nutritional Laboratory Studies Prior to Total Knee Arthroplasty: Practice Versus Publication," appears in the December 20, 2023, edition of *The Journal of Bone and Joint Surgery.*

If, as the study authors maintain, a large percentage of orthopedic surgeons are restricting access to arthroplasty when malnutrition is an issue—then why are there not more surgeons ordering nutritional lab studies before total knee arthroplasty?

Co-author David C. Landy, M.D., Ph.D. explained the issue to *OTW,* "While there is some low to moderate quality evidence to suggest an association between various markers of nutrition and complications following hip and knee replacement type surgeries, there is little information on how effective nutrition optimization may be at modifying this risk. So, while some articles have recommended assessing nutritional status prior to surgery, it's unclear how valuable this may be at present. Given this, we were curious if these labs are really being ordered in practice."

"We were reviewing Orthopaedic In-Training Examination questions with our residents and this question came up on which labs are needed prior to surgery for medical optimization," said co-author Stephen Duncan, M.D., associate professor, department of orthopaedic surgery, University of Kentucky. "Zinc was the answer and we questioned how often this test was actually performed prior to surgery."

The researchers looked at 557,670 patients undergoing primary TKA from 2011 to 2020 with a metabolic panel

or blood cell count claim within 90 days prior to TKA. They gathered data on prealbumin, transferrin, vitamin D, zinc, blood cell count, and metabolic panels.

The team found that within 90 days before TKA, studies for prealbumin were done in 2.2% of patients; transferrin, 1.9%; vitamin D, 10.2%; and zinc, 0.2%.

From 2011 to 2020, there was a moderate but steady increase in the proportion of patients with claims for prealbumin (change from 0.8% in 2011 to 3.4% in 2020), transferrin (0.8% to 2.7%), and vitamin D (7.6% to 9.4%) laboratory tests but there was less of a change for zinc (0.1% to 0.2%). There were weak-to-absent associations of age, gender, obesity, diabetes, and anemia with laboratory claims.

Dr. Landy noted, "The finding that nutrition labs are rarely ordered prior to knee replacement suggests that we need to better understand how nutrition can be optimized and the extent to which this improves outcomes following hip and knee replacement in order to justify surgeons further incorporating this into practice. While optimizing patients as best possible prior to surgery is important, it is also important that we provide efficient care and do not unnecessarily delay care."

"The percentage of patients actually getting the nutritional labs performed prior to surgery was extremely low. As we try to optimize patients with obesity, diabetes mellitus, and smoking cessation, we often overlook nutritional deficiencies that need to be addressed to avoid complications such as wound healing or PJI."

OTW asked Dr. Duncan why so few studies are ordered before TKA. He said, "Education on nutritional optimization is often lacking in our training. We focus on albumin, WBC [white blood count] level, and Hg [hemoglobin]. However, we need to educate clinicians better on obtaining these labs. Also, insurance companies do not require these prior to surgery and until the payers require this, there may not be a huge shift in the number of patients getting evaluated prior to surgery."

"Physician education is important on this topic both at national meetings and in publications. Correlating treatment of deficient nutritional labs to outcomes will help to drive further adherence to obtaining these on a more consistent basis in the future." ♦

COMPANY

icotec ag Raises $30M

icotec ag, a Swiss medical device company focused on non-metallic spinal implants for cancer treatment of the spine, has successfully raised $30 million in growth financing from MVM Partners.

The financing comes from icotec and MVM Partners forming a strategic partnership. MVM Partners is a venture capital firm focused on healthcare businesses.

icotec ag Group CEO Roger Stadler expressed excitement about the partnership commenting, "We are thrilled to partner with MVM, whose deep understanding of the healthcare landscape aligns seamlessly with our vision for the future."

Source: icotec ag

Stadler continued, "This partnership marks a pivotal moment for icotec, supporting us to advance our mission of improving patient outcomes by offering a convincing alternative to the 100-year-old material technology of metal implants."

The funding will be used to support icotec's efforts to commercialize its BlackArmor® Carbon/PEEK products. In 2019, the U.S. Food and Drug Administration (FDA) granted 510(k) clearance to icotec's VADER®one pedicle screw system. According to the 510(k) summary document, the "VADERone Pedicle System MIS and LightMore Pedicle System 6.0 can be used for single or multiple level fixations in the non-cervical spine." The VADERone system is made from icotec's BlackArmor material.

The 2019 clearance has enabled a number of cancer centers in the United States to utilize icotec's BlackArmor products. The investment, per the press release, "will enable icotec to continue

its impressive growth and strengthen its research and development capabilities to expand the portfolio into the underserved indications of spinal infection and osteoporosis."

MVM Partner Thomas Casdagli commented, "We are excited to support icotec in its mission to revolutionize the spinal implant industry."

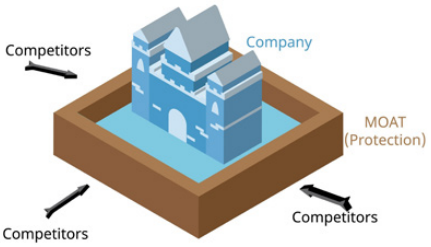
Casdagli continued, "icotec's BlackArmor® Carbon/PEEK implants represent a huge step forward in the treatment of complex spine disease. For the first time clinicians have the choice to be able to accurately visualize and treat patients after surgery without the artifacts and limitations of traditional metal implants. We see this as a big step forward for patient care. We look forward to working closely with the icotec team to drive continued success and growth." — *KD*

Do You Have an Effective "Moat" Around Your Business?

I read a recent blog post that discussed "moats", competitive advantages or barriers to entry, that protect a company from its competitors.

In 2007, at a Medtronic investor and analyst meeting in which management addressed the numerous "ankle biters" that were taking market share, management touted all the PMA [premarket approval] products in their pipeline. That was their "moat." Management said that those "ankle biters" could not compete long-term because "this is a whole different ballgame."

Medtronic projected that in 2012, 50% of their sales would be from PMA or



Source: Shutterstock

IND [investigational new drug] products. It never happened. All the PMA products noted on slides that day were never commercialized in the US. Their "moat" never materialized.

Which current companies appear to be building truly effective "moats" in spine?

Tech "Moats"

Are robotics, imaging, navigation, AI [artificial intelligence], augmented reality ecosystems a "moat" in spine?

Medtronic and Globus Medical, Inc. are the primary movers in this area, but most of the mid to large spine companies are working to add some element of enabling technology to their portfolios, and numerous independent technology companies are developing open platforms that can be used by any implant manufacturer.

I analyze U.S. patents related to the spinal implant market and publish an annual Patent Power Ranking.

I found that the number of enabling tech patents has grown from 2% of issued spine-related patents 10 years ago to approximately 20% in 2023.

Medtronic and Globus credit pull-through from their respective ecosystem for growth in implant sales, and at present they have benefited from being first-movers. It remains to be seen how durable these enabling tech moats will be as more spine companies enter the market and independent, open platforms expand their user base.

Procedural "Moats"

NuVasive, Inc. [NUVA] built a long-lived moat with the XLIF lateral procedure. Lateral continues to grow more than two decades after NuVasive pioneered it, and the barriers to successful entry have been durable. I spoke with an executive at NASS [North American Spine Society] who shared that their company was abandoning lateral because it was too costly and not profitable. NUVA's market share has declined, but remained double its nearest competitor in 2023, and the combined Globus/NuVasive will hold more than 50% market share in lateral*.

Tried and True Intellectual Property "Moats"

Globus filed their first patent for expandable interbody in 2009 and received 510(k) clearance for the Caliber expandable interbody in January 2011.

At that time, Spine Wave's StaXx was the only fully expanding device on the market. Through the third quarter of 2023, expandable devices represented approximately one-third of the ~ $1.7 billion U.S. thoracolumbar interbody market and Globus/NuVasive held ~ 40% market share.

Globus currently has more than 150 issued U.S. patents related to expandable devices and appears to have created an effective moat that has significantly delayed and/or prevented larger competitors from entering the space.

Following Globus' Caliber launch, it took four and six years respectively for Medtronic and NuVasive to successfully launch an expandable device in the U.S. Stryker Corporation and DePuy Synthes currently do not own the expandable devices they distribute.

Regulatory "Moats"

Medtronic received PMA approval for Infuse more than 20 years ago and sales of this product exceed $10 billion over this time period. The product remains the only biologic with PMA approval for use in the lumbar spine.

Sales peaked in 2008-09 but Infuse remains by far the best-selling biologic/bone grafting product in spine. Cerapedics, Inc. filed for their cervical P-15 IDE [investigational device exemption] study in September 2005 and received PMA approval 10 years later. The final modules for their TLIF PMA were just filed and approval will likely be forthcoming.

Reimbursement "Moats"

SI-BONE, Inc. is the 800-pound gorilla in SI fusion. The company really pioneered the procedure and invested heavily in clinical studies and education to create this market. As new companies entered the space, SI-BONE was successful in gaining exclusive coverage from payors for the use of iFuse.

The company also realized a significant benefit in 2023 due to the Category III coding requirement for dorsal allograft procedures. These are examples of an individual company gaining an advantage over the competition through reimbursement.

There are other examples where companies have successfully created a regulatory moat only to be restrained by reimbursement challenges. I'm reminded of a discussion at ISASS [International Society for the Advancement of Spine Surgery] last year in which the surgeon attendees agreed that continued growth in the use of cervical disc was stymied due to greater reimbursement for fusion procedures.

Future "Moats"

Alphatec Spine (ATEC) has included a slide in recent presentations that contrasts the revision rates in spine vs. hip and knee.

The slide highlights the fact that although spinal implants themselves are viewed as commoditized, there is tremendous opportunity to improve outcomes.

Enabling tech will likely assist in that regard through better surgical pre-

planning, less invasive procedures, and more precise implant placement.

As procedures become more standardized and reproducible, we will at some point reach the limits of what enabling technology can provide in improving outcomes and new implant technology moats will emerge.

Lateral defined as interbody spacers designed for transpsoas or direct lateral that can also be used for an antepsoas or OLIF approach.

I'm interested in your thoughts, especially as it relates to enabling tech. What companies do you think are creating or have created a sustainable moat in spine? — *RP*

For more information: contact Rick Phillips: Email: Rick.Phillips@spine-market.com Website: spine-market.com

LEGAL

FDA Issues Draft Metallic and/or Calcium Device Coating Guidance

The U.S. Food and Drug Administration (FDA) has issued draft guidance for premarket submissions for orthopedic devices with certain coatings.

In the draft guidance, the FDA provides "recommendations for premarket submissions for orthopedic devices that contain metallic coatings and/or calcium phosphate coatings on the surface." Specifically, the guidance applies to class II and class III devices intended for orthopedic applications that contain "metallic coatings, calcium phosphate coatings, or metallic and calcium phosphate dual coatings."

The FDA recommends that the following information be included with submissions:

Source: FDA.gov

- coating description,
- sterility,
- pyrogenicity,
- shelf life and packaging,
- biocompatibility,
- non-clinical bench testing,
- non-clinical animal testing,
- clinical performance testing, and
- labeling.

The coating description should include:

- the name of the coating,
- coating method,
- starting materials,
- physical structure of the coating,
- the location of the coating and
- its coverage of the device.

The agency also recommended that manufacturers sterilize all coated orthopedic devices and if a coated device is provided non-sterile additional justification should be provided. In addition, the agency recommended that coated orthopedic devices meet applicable pyrogen limit specifications to address certain associated risks. Additional details regarding the information that is being recommended can be found in the draft guidance.

The draft guidance does not apply to other types of coatings such as other calcium-based coatings and other ceramic coatings. The guidance also does not apply to surface modifications such as surface etching and surface anodizing.

Under the draft guidance, sponsors may also be required to submit a new 510(k). This would be required if certain changes or modifications are made to the coating method, coating vendor, coating layer, another substrate material, or the surface treatment.

Draft guidance, when finalized, represents the current thinking of the FDA. It does not establish rights and is not binding. Once finalized, the guidance will supersede the 1995 510(k) Information Needed for Hydroxyapatite Coated Orthopedic Implants and 2000 Guidance for Industry on the Testing of Metallic Plasma Sprayed Coatings on Orthopedic Implants to Support Reconsideration of Post market Surveillance Requirements.

The deadline to submit comments is March 22, 2024. — *KD*

LARGE JOINTS

What NON-Medical Factors Affect TKA Outcomes?

Source: Shutterstock

A team of researchers from Henry Ford Hospital in Detroit, Michigan have published a new study which sets out social determinants of health—defined as the non-medical factors that influence health outcomes. These are the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life.[1]

The authors collected data from 19,321 total knee arthroplasty (TKA) patients. They found that socioeconomic status, housing type, and transportation access were the most predictive of emergency department visits, readmissions, and complications following total knee arthroplasty.

According to co-author Craig D. Silverton, D.O., vice chairman of the Department of Orthopedics at Henry Ford Hospital in Detroit, Michigan, "By practicing in a large academic hospital system within metro Detroit, we have the opportunity to help a wide array of patients from all backgrounds."

"As social determinants of health have come into the spotlight recently in orthopedics, we could not help but

acknowledge how these factors affect our immediate populace. So, we sought to better understand social determinants of health objectively by associating well-studied neighborhood deprivation indices to outcomes following TKA."

OTW asked Dr. Silverton to explain why he and the research team selected TKA patients for their study. He said, "TKA is a broadly performed procedure that allowed the study of surgical outcomes in relation to neighborhood deprivation. Furthermore, TKA is unique from total hip arthroplasty in that we still do not understand why 20% of patients have sub-optimal outcomes. While some evidence points towards technical aspects of the surgery, we hypothesized that at least a portion of the 20% could be explained by poor optimization of patients from the most deprived neighborhoods."

Money and Housing Stand Out

"Based on the results of our investigation, it was clear that the composite Social Vulnerability Index and Area Deprivation Index were the most predictive of emergency department visits, readmissions, and complications following TKA."

"Of the studied Social Vulnerability Index subthemes, socioeconomic status and housing type/transportation access were the most important. These findings may comment on particular patients not having adequate access to postoperative care and patient education."

"Our most important results certainly were that across most Social Vulnerability Index sub themes, Social Vulnerability Index, and Area Deprivation Index ranks, greater deprivation associated with greater emergency department visits. Certainly, this would suggest greater costs of care for these patients, highlighting the importance of further investigating optimization options as well as policy changes to better treat TKA patients."

As for how to operationalize these findings, Dr. Silverton explained to *OTW*, "These variables should be readily integrated into the preoperative phase of care. Automatic extrapolation of these variables using patient addresses at intake can help identify potential at-risk patients, allowing for early discussion with patients and prompt intervention should a pertinent problem be noted. The steps after identification, however, remains the challenge."

Societal Issue, Societal Solutions

"Definitely, it is important to provide access to a social worker and informa-

tion regarding neighborhood resources, but our study highlights societal issues that need policy level changes. Some success has been demonstrated outside of orthopedics in incentivizing practitioners for reducing disparate care outcomes, but implementation of such policies can be challenging."

And in the end, physicians are supposed to be patient advocates.

"The next steps," said Dr. Silverton to *OTW*, "will be to study how automated collection of these variables affect clinical practice prior to TKA or THA. Most importantly, we need to devise a strategy of optimizing patients with known social risk factors. While a part of our work is in the clinical setting, for true societal change, we must do our part on the health policy and advocacy front." — *EH*

[1] https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1

Elevated Glucose Levels in Non-Diabetic Patients =Higher PJI Risk?

While diabetic total hip arthroplasty (THA) patients are associated with higher levels of periprosthetic joint infection (PJI), does that, therefore, imply that non-diabetic patients with elevated glucose levels are also at higher risk of PJI?

A research team from the University of Southern California (USC) Keck School of Medicine designed a 90,830-patient study to answer that question. Their work, "Higher Blood Glucose Levels on the Day of Surgery Are Associated with an Increased Risk of Periprosthetic Joint Infection After Total Hip Arthroplasty," appears in the December 21, 2023 edition of *The Journal of Bone and Joint Surgery.*

"It is well accepted that total joint arthroplasty patients with uncontrolled diabetes and diabetics with elevated perioperative glucose levels have increased wound healing problems and elevated infection rates," co-author Jay Lieberman, M.D., chair of the Department of the Keck School of Medicine of the University of Southern California (USC), told *OTW*. "The hypothesis has been that the elevated blood glucose in some way impacts polymorphonuclear leukocyte activity. Our thought was that this could be true in other patients with elevated glucose levels."

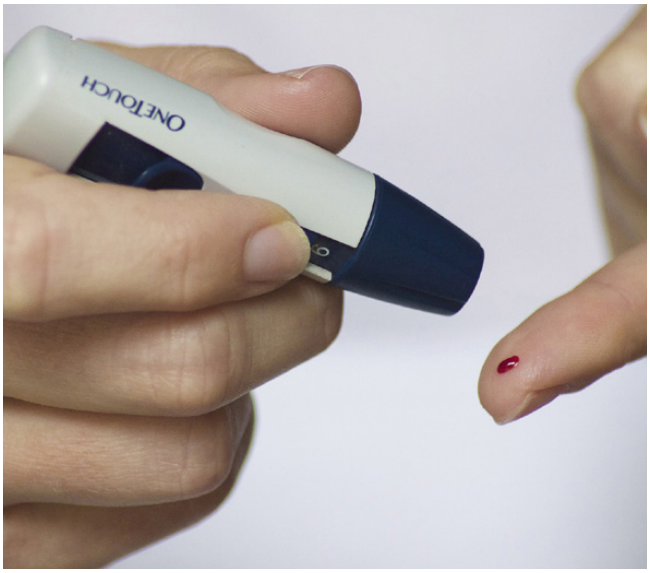
Nathanael Heckmann, M.D., an orthopedic surgeon with Keck Medicine of USC, was also an author and commented, "There has been no consensus on this topic because the results in the prior literature have been inconclusive. In addition, arthroplasty surgeons are focusing on medical optimization of diabetic patients. However, there are pre-diabetic patients and unrecognized diabetic patients that are at increased risk for elevated pre-operative glucose levels."

The team evaluated 90,830 THA patients whose day-of-surgery pre-operative blood glucose levels were measured (January 1, 2016, to December 31, 2021). They evaluated the association between pre-operative blood glucose levels and 90-day PJI risk.

Dr. Heckmann told *OTW*, "The most important results include:

- There is an independent association between elevated pre-operative blood glucose levels and periprosthetic joint infection risk in both diabetic and non-diabetic patients undergoing a THA;
- In patients with diabetes the odds of superficial and deep wound infections were increased in patients with elevated pre-operative blood glucose levels;
- It is important to note we are not stating that a single metric be used to determine care. A global approach to medical optimization is necessary in order to balance risks and access to care."

Dr. Lieberman added, "The influence of pre-operative and perioperative glucose levels needs further study to better identify appropriate glucose levels. In addition, there is very little data on glucose control in same day surgery patients." — *EH*



Blood sugar level test / Source: Wikimedia Commons and Reversing Your Diabetes Today

SPINE

Better Ergonomics, Digitally Enhanced Cinematic Vision in Spine Surgery

Dr. Leonel Hunt and the DigiLoupe AR/XR headset / Courtesy of Ocutrx Technologies, Inc.

Laguna Beach, California-based Ocutrx Technologies, Inc. has announced the latest version of its ORLenz™ headset, which features a stand-alone digital magnifying eye glass (brand named DigiLoupe™).

DigiLoupe is an advanced digital loupe system for spine surgery. Ocutrx incorporated ORLenz into the DigiLoupe AR/XR headset. The company initially developed Ocutrx for demanding ophthalmic applications but has applications for equally demanding spine and neurosurgery applications.

According to the company, traditional loupes are an "ergonomic nightmare." By contrast, the DigiLoupe AR/XR headset features cameras that tilt and look down during surgeries—instead of forcing the surgeon to look down. It also displays 3D holographic images with up to 10x magnification and cinematic quality resolution.

Ocutrx Global Director of Surgical Applications Simon Prosser, commented to *OTW* on the development phase: "It was interesting to determine how practical operative needs play such a crucial role in the hardware design and configuration."

"There are two main goals at play here and both are equal in their value: the first is to improve ergonomics and the second is to transition from an optical to a digital solution."

"The merits of ergonomics are easy to understand with every surgeon recognizing the toll the unergonomic posture has on their long-term health. Over time, this reduces the number of surgeries they are able to perform and at some point, more often than not, determines when they remove themselves entirely from the OR."

"The merits of transitioning from an optical to a digital solution are more complex and not immediately recognized by many surgeons. Greater magnification is already a gain. But even more exciting are the benefits of making the 'unvisible visible'."

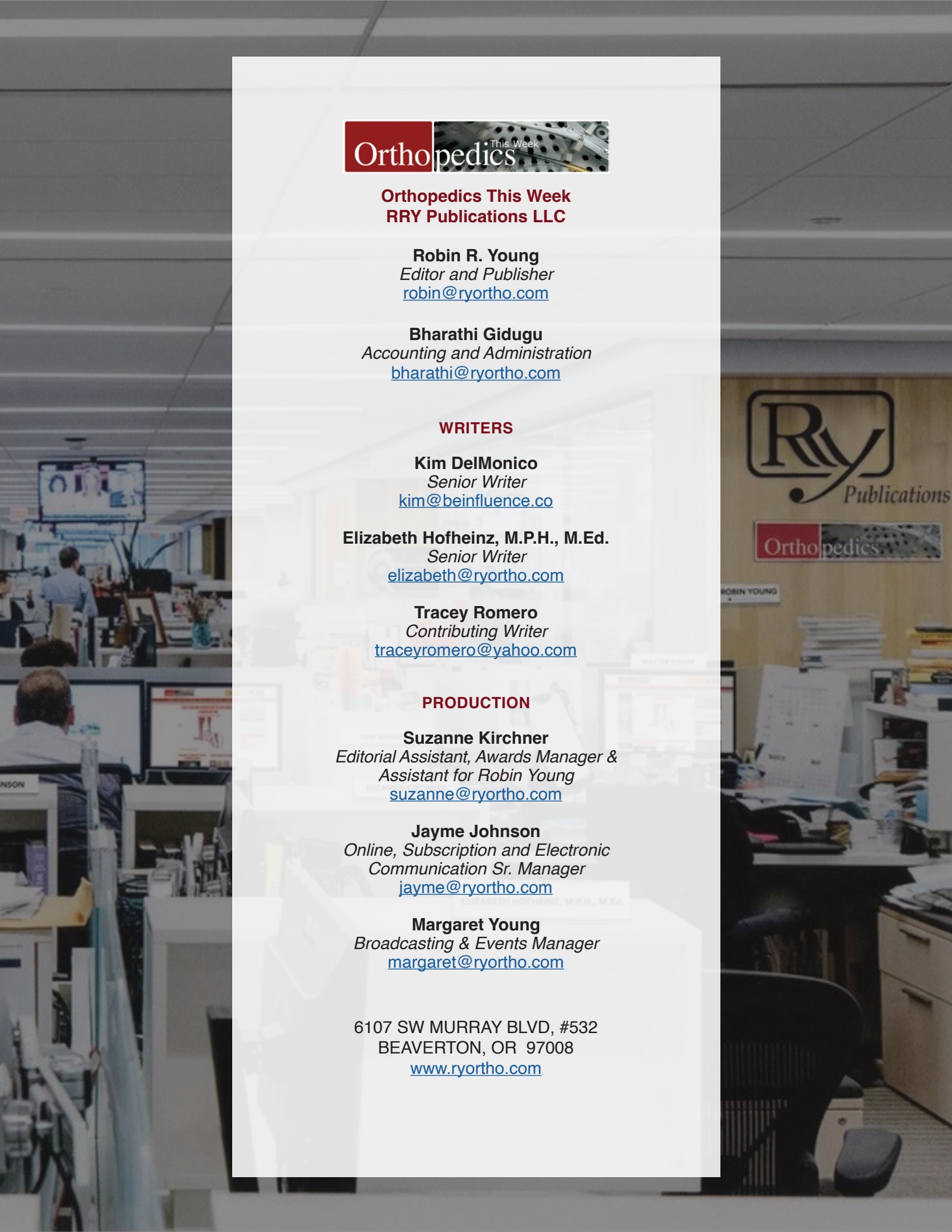
"The capabilities here are almost endless. And with digitalization, the integration of the device becomes a reality that allows surgeons to access real time data and be able to control much more of his working environment."

Dr. Leonel Hunt, M.D., an attending surgeon at both the Cedars-Sinai Spine Center and Cedars-Sinai Orthopedic Center, has recently joined Ocutrx's International Surgical Steering Committee.

OTW asked Dr. Hunt what he might say to someone who is hesitating about trying this headset with the DigiLoupe. He said, "We are designing this headset to not only give better illumination, magnification, and overall visualization when compared to traditional loupes and headlight, but to also place the surgeon in a better ergonomic position that should cause less issues with neck and back due to improved mechanics."

"Now if that isn't convincing enough, there are many features planned with MedTiles application that will have functionality unmatched by any other system to improve our ability to provide the safest and most exceptional care while also creating a platform to communicate and share our experiences in real time."

"MedTiles will allow us to have imaging, image guidance, records, etc. in full view at the speed of a blink of an eye. I anticipate that this is just the beginning, and the applications will evolve beyond what we think is possible. This is the next generation med tech that I feel will be the future of the surgeon-tech dynamic as we move into the robotic and AI phase of healthcare delivery." — *EH*



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