

Dr. Solez has nothing to disclose.

Outline of Presentation

- The NKF cyberNephrology program has existed now for 12 years, the NEPHKIDS discussion group for 11.
- When we began in 1997 there were speculations about the benefits and risks of the Email discussion groups we were creating, the ethical dilemmas.
- Now in 2009 we can see which of those benefits and risks and dilemmas are real, and which are imaginary.
- We can also imagine the future, the way medical communications are evolving, how things will be 12 years from now in 2021.

EMAIL DISCUSSION GROUPS FOR NEPHROLOGY PROFESSIONALS

- Email discussion groups for Nephrology Professionals – Physicians
- NEPHROL general nephrology, all subjects, 1,045 subscribers, 54 posts a week.
- o NEPHDEVEL discussion of humanitarian projects
- NEPHNPPT discussions of renal pathology
- o NEPHHIST history of renal medicine
- IFKF-L discussion relating to the International Federation of Kidney Foundations_

EMAIL DISCUSSION GROUPS FOR NEPHROLOGY PROFESSIONALS

- Email discussion groups for Nephrology Professionals – Non-Physicians
- RENALPRO e-mail list for nephrology professionals - nurses, technicians, dieticians, social workers, administrators, physicians, engineers, etc.
- RENALRD a listserv primarily for those in renal nutrition. 1,691 subscribers, 170 posts a week.
- PEDSRENALRD An unmoderated on-line discussion group for those with an interest in renal pediatric nutrition and related issues.

EMAIL DISCUSSION GROUPS FOR PATIENTS AND PATIENTS' FAMILIES

- Email discussion groups for Nephrology Patients and Families
- o IGAN IgA Nephropathy
- KidneyDisease for adult patients with renal disease
- NephKids for parents of children with renal disease, 454 subscribers, 16 posts a week.

CYBERNEPHROLOGY GROUPS REACH ABOUT 8,000 PEOPLE IN TOTAL

- o Large impact in nephrology.
- Small in comparison to a site for the general public like ThinkerNet Blog <u>www.internetevolution.com</u> which reaches about 300,000 people a month.
- o My posts there often "editor's pick", examples:

Medicine & Web 2.0 Go Well Together
Prehistory Prefigured Internet Use
In Search of Reality: Where Virtual Fits In
Virtual Flying Doctors
Expanding Time in the Digital Age
Searching for Women Leaders in the Age of

Singularity
The Emerging Digital Intelligence

Communications - Getting the Word Out

- Since 1997 I have headed NKF cyberNephrology with resources, email discussion groups and websites, that reach 8,000 people.
- Writing a book for the general public <u>Digitality</u>, autobiographical stories dealing with the future of technology and the digital age, the "merger" of humans with machines while maintaining the higher elements of the human spirit.
- The book is serialized and related material published on ThinkerNet Blog http://www.internetevolution.com that receives 300,000 visitors a month. My pieces have been the "editor's pick" there.



NEPHKIDS

- o "We are a group of concerned families, patients and medical caregivers sharing information and experiences with the purpose of helping children and adolescents with kidney disease. We are open to adult family members, mature adolescent patients, physicians, nurses and other members of the care team. Watching over this group is Dr. Susan Conley, a pediatric nephrologist with over 25 years of experience in the field."
- "Individual medical advice will not be given nor will specific physicians be recommended."

A DISCUSSION GROUP IS NOT LIKE A MOVIE

- In a movie actors and actresses chosen for their skills and effect are hired to obtain a predictable result from audiences.
- In a discussion group, the actors and actresses are also the audience, are mostly not chosen but are self selected, and their personalities heavily influence what happens. So the result is highly idiosyncratic. It is hard to generalize. Many of the anecdotal stories one ends up telling are about events unlikely to be repeated.

REFLECTING ON NEPHKIDS

- The NEPHKIDS group has been a stunningly successful unique resource, giving parents of children with renal disease a way to share experiences and advice with each other, while having the opportunity to ask questions of an experienced pediatric nephrologist moderator.
- It has also created conflict with local treating physicians by causing some parents to resist treatment suggestions based on ill informed opinions conveyed online by non-physicians.

UNIQUENESS OF THE MODERATOR

- Those who enjoy being physician moderators and spending a large part of every day managing online resources are special people. There are not very many such people.
- When Dr. Conley became too busy to participate in the group some years ago no one could be found to replace her despite much searching. Now she is back.

ALL THE OTHER PROBLEMS WE HAD ANTICIPATED DID NOT MATERIALIZE

- o There were no threatened lawsuits.
- The disclaimer on each message seemed almost unnecessary: "Individual medical advice will not be given. Please communicate any thoughts or concerns you may have, that are generated by this listserv, with your doctor. ... Group members are cautioned not to interpret any information or opinions posted on NEPHKIDS as a second opinion. If a second opinion is desired, it is best pursued via your current primary doctor (or treating physician) and/or your health insurer."

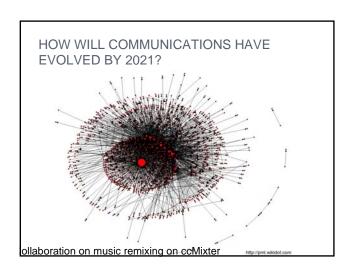
GREATER SENSE OF COMMUNITY THAN IN IF DATA WERE ANONYMIZED

- Understand arguments about making postings anonymous.
- o But it has not proven to be necessary for us.

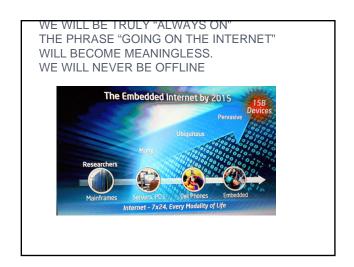
OTHER OBSERVATIONS

- Groups which mix patients, parents, and health professionals highly successful and unique.
- "Ethnic cleansing" to remove patients from physician groups not necessary. No disruptions ever caused by patients, only by physicians.
- Face to face meetings with those who misbehave online in our Email discussions groups very informative. I learned a lot!



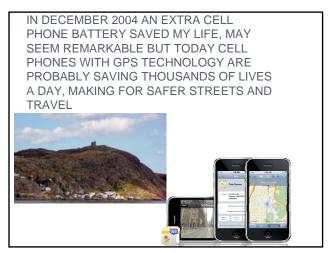












WE ARE LESS AND LESS TRULY ALONE AND WE ARE MORE AND MORE WATCHED, MOST OF US APPEARING ON SEVERAL DIFFERENT SECURITY VIDEOS A DAY, IN THE FUTURE TRUE SOLITUDE AND UNWITNESSED ACTS WILL BE MUCH MUCH MORE RARE THAN THEY ARE TODAY.



THERE ARE SOME INTERESTING CHALLENGES IN THE FUTURE, BUT IN GENERAL THE POSITIVE POSSIBILITIES FAR OUTWEIGH THE PROBLEMS!



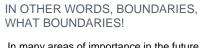
COMMUNICATION TECHNOLOGIES OF 2021: DON'T KNOW EXACTLY WHAT THEY WILL BE BUT WE WILL BE USING THEM CONSTANTLY, LANGUAGE NO BARRIER, OUR LIVES RICHER.



THE END RESULT WILL BE UBIQUITOUS HEALTH, THE END OF WAR, PEACE AND HAPPINESS EVERYWHERE, ETERNAL YOUTH.

- UP UNTIL SHORTLY BEFORE HIS DEATH AT 72, ISAAC ASIMOV REFERRED TO HIMSELF AS BEING "IN MY LATE YOUTH".
- A SIMILAR SITUATION FACES ALL OF US BUT THE "YOUTH" WILL CONTINUE WELL BEYOND AGE 72 AND ENHANCED COMMUNICATIONS BROUGHT ABOUT BY TECHNOLOGY WILL BE AN IMPORTANT PART OF WHAT SUSTAINS IT!





In many areas of importance in the future, the boundaries, limits you may be thinking of may not exist.



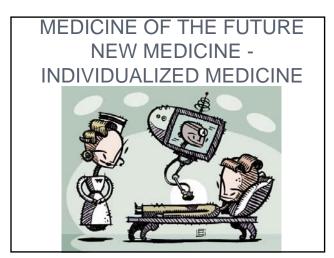
HUMAN CENTERED

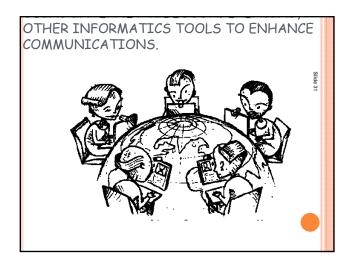


Fostering nephrology's embrace of the Internet and new technology since 1994 with Email and web resources. Websites which allow virtual attendance at meetings, education.

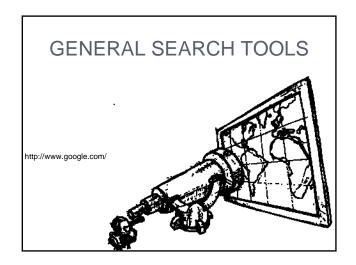
www.cybernephrology.org www.cyber-medicine.org

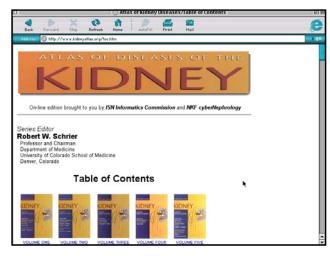








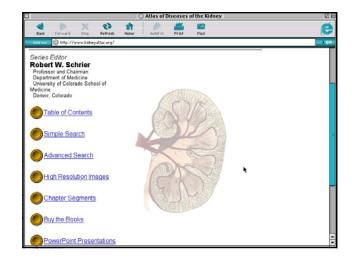


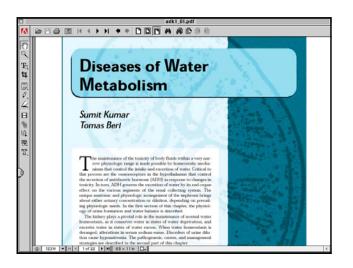


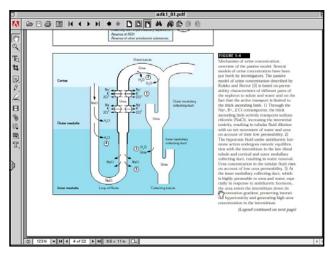
SCHRIER ATLAS OF DISEASES OF THE KIDNEY

•66 chapters covering all areas of kidney medicine, completely searchable, with outstanding graphics, preformed Powerpoint files for each chapter are an excellent resource for teaching! http://www.kidneyatlas.org

Accessed by more people per month than the total number of US nephrologists!







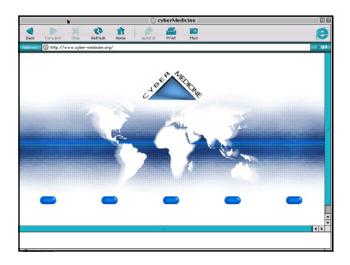




EXTENDING INTERNET KNOWLEDGE FROM NEPHROLOGY TO MEDICINE IN GENERAL!

- o cyberMedicine New Medicine http://www.cybermedicine.org
- o Discipline upgrade from other areas which can learn from nephrology - Critical Care Medicine
- o cyberMedicine as part of the technology future search strategies - efficient information retrieval, future of technology and the human spirit.





VIRTUAL PATHOLOGY SLIDE

- http://www.telepathology.dcu.ie/vps02.php 3 VPS Breast Needle Core Study (JMIR 2003)
- o http://www.medicine.uiowa.edu/pathology/ yuarep_histopathology/ Virtual slidebox
- yluarep histopathology/ Virtual slidebox of histopathology http://alf3.urz.unibas.ch/patho/pub/2002-11.htm Human Pathology -- Volume 34, No. 10 (October 2003) -- pages 968-974 Katharina Glatz-Krieger, Dieter Glatz , Michael J. Minatsch Virtual Slide: high quality demand, physical limitations and affordability.

http://vmic.unibas.ch



TECHNOLOGY EVOLUTION **NEED NOT BE COMPLEX!**

Machines should serve human beings, making our lives easier.

"Low high" technology in cell phones, the windup charger.



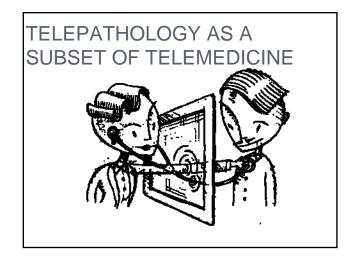
TECHNOLOGY EVOLUTION NEED NOT BE COMPLEX!

Machines should serve human beings, making our lives easier.

Virtual full size keyboards for cell phones and PDAs which project on any surface.



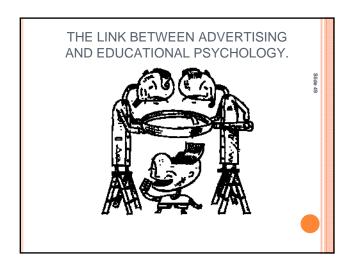


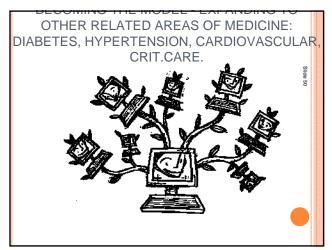


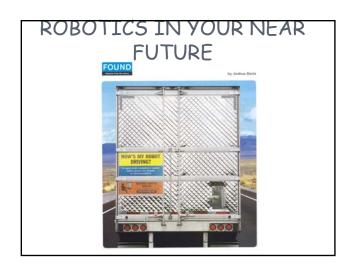
CONVERGENCE OF MARKETING, ADVERTISEMENT, AND ENTERTAINMENT CONCEPTS AND EDUCATION.

CHANGING HUMAN BEHAVIOR THROUGH MARKETING, PUBLIC RELATIONS TO PROMOTE HEALTH. OUR CORPORATE PARTNERS CAN BE OF TREMENDOUS ASSISTANCE IN THIS. CONCEPTS OF MARKETING MAPS, SOCIAL MARKETING.

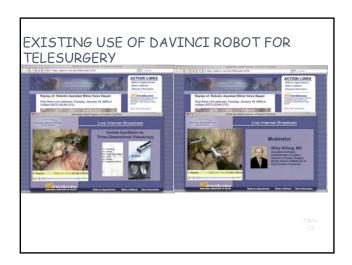
PROMOTE HEALTH THROUGH HIGH IMPACT EDUCATION. CHANGING PHYSICIAN AND PATIENT BEHAVIOR.

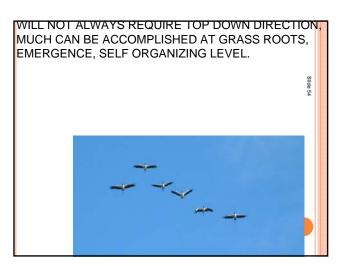


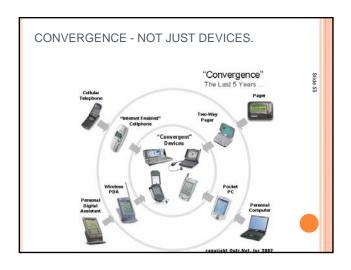












NKF CYBERNEPHROLOGY PROVIDES:

Professional and patient education and peer support over the Internet using Email and web resources, medical textbooks online, hands on workshops, symposia, videoconferencing, and technology vision for the future.

NKF cyberNephrology is the embodiment of kidney medicine's embrace of technology.

A wealth of offerings for physicians, other nephrology professionals, and patients and families at:

www.cybernephrology.org

WITH:

- Creation of web, email, and chat resources (AIM and MSN messenger like, or IRC). Online research databases.
- Recommending links for nephrology resources.

http://www.cybernephrology.org/education/eduPhysicians.htm

- Recommending searching resources on your site.
- Promotion of the resources you create.

www.cybernephrology.org

EVIDENCE-BASED MEDICINE

Sir Austin Bradford Hill, British Researcher: "All scientific work is incomplete- whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. This does not confer upon a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time. Who knows, asked Robert Browning, but that the world may end tonight? True, but on available evidence most of us make ready to commute on the 8:30 next day."

SIMPLY...

The use of computers and the Internet should be enjoyable, practical, and productive. Web, email, chat resources should be easy to create.

If you need help we are there to provide assistance. You can send us questions at the "contact us" link on www.cybernephrology.org or at the following Email addresses:

Tori Sheldon <u>vsheldon@UAlberta.CA</u> Kim Solez, M.D. <u>Vsheldon@UAlberta.CA</u> <u>Kim.Solez@UAlberta.CA</u>

We can help you create Internet resources specific to the local language and culture of your own region.

OUT IN FRONT! REMARKABLE CONSIDERING NEPHROLOGY'S SIZE VS. ALL OF MEDICINE

 There are more than 800,000 physicians in the US and only about 5,000 are practicing renal medicine, so nephrologists represents only about 0.6% of total US physicians.

UNIQUE RESOURCES FOR PATIENTS NOT FOUND IN OTHER SPECIALTIES

- NEPHKIDS For parents of children with renal disease, moderated by pediatric nephrologist.
- KIDNEYDISEASE For adult patients with kidney disease, moderated by 10 nephrologists all over the world!
- 18 Email discussion groups in all connecting more than 8000 health professionals and patients.

Mixing and Matching Medicine and Culture

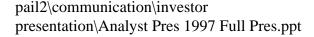
- Starts with the Banff Classification of Kidney Transplant Pathology.
- In 2002 in preparation for the 2003 Banff meeting in Scotland I suddenly ventured into the realm of Leonard Cohen events.
- Mexperience with organizing medical meetings shaped Leonard Cohen events, which in turn influenced medical initiatives.
- July 23-28, 2008 Edmonton International Leonard Cohen Event.

Lessons from the Arts brought to Medicine
Critical Path for Event Planning/Philosophy/Writing

- ARTS: Keeping track of activities via hand held devices. Security considerations.
- MEDICINE: Hand held devices ideal for securely keeping track of progress of kidney biopsy light microscopy, immunofluorescence, electron microscopy.
- o ARTS: Philosophical influences on culture.
- MEDICINE: Philosophical influences on medicine understudied except for bioethics. Gene chip vs. conventional pathology.
- ARTS: Pride in writing as writing.
- o MEDICINE: Pride in writing as writing.

Promotion/Capturing the Imagination of the Public

- ARTS: Promotion. Media attention. Capturing the imagination of the public is important.
- MEDICINE: Promotion. Media attention. Capturing the imagination of the public is important.



Lessons from Medicine brought to the Arts
Leonard Cohen remarks

o "Living life with microscopic precision"

BOOK OF MERCY

for Kim

freat artist of the surreal
thanks for all your help

Moutreal November 2005 Meetings - A Waste of Time?

- "Medical meetings are just social events. Nothing important happens at them. They are a waste of time. You should avoid organizing medical meetings." - Robert H. Heptinstall, M.D.
- I did not follow this advice. Doctors need to be socialized, humanized.
 Organized my first Acute Renal Failure Symposium in 1982, published as a book in 1984 <u>Acute Renal Failure: Correlations Between Morphology and Function</u>. Many others since then.
- My work on acute renal failure in the native kidney since 1972 gradually led to an interest in acute renal failure in the transplanted kidney.

Background – The Banff Classification

- Acute renal failure in the transplanted kidney is a high stakes situation
- Many different entities have the same clinical presentation:
 - ATN, acute rejection, CsA, FK506 toxicity
 - misdiagnosis can rapidly lead to loss of the graft or sometimes the patient

Background - The Banff Classification

- In 1990 all standard textbooks were inaccurate in interpretation of kidney transplant biopsies
 - Suggesting, for example, that arteritis meant that the kidney was doomed and antirejection treatment should be abandoned
- It became imperative for the field to correct this and standardize interpretation



DIAGNOSTIC CATEGORIES

- o 2. Antibody-mediated rejection,
- o 3. Borderline changes: 'Suspicious' for acute cellular rejection
- o 4. T-cell-mediated rejection (may coincide with categories 2 and 5 and 6)
- o 5. Sclerosis, interstitial fibrosis, and tubular atrophy, no evidence of any specific etiology
- o 6. Other Changes not considered to be due to rejection

LESION SCORING (0-3+)

Transplant glomerulitis - g Chronic transplant glomerulopathy - cg Interstitial Inflammation - i (ti)

Interstitial fibrosis - ci

Tubulitis - t

Tubular atrophy - ct

Vasculitis, intimal arteritis - v

Fibrous intimal thickening - cv

Arteriolar hyaline thickening - ah (aah)

Mesangial matrix increase - mm

Peritubular capillary cell accumulation - ptc

FUTURE BANFF MEETINGS:

- o 2009 Banff, Alberta, Canada
- o 2011 Paris, France
- o 2013 Vail, Colorado, USA
- o 2015 Stockholm, Sweden
- o 2017, 2019 Please make a proposal!



GLOBAL CONSENSUS GENERATION WHILE MAINTAINING INTELLECTUAL FREEDOM.

LIKE THE MOSH PIT AT A GREAT ROCK CONCERT.
NO PARTNER, THE ULTIMATE IN INDIVIDUALITY,
DANGEROUS, BUT WHEN THE MUSIC IS GOOD
EVERYONE DANCES IN SYNC AND LIFE IS GOOD!



BANFF CLASSIFICATION: MILESTONES

- o 1991 First Conference
- o 1993 First Kidney International publication
- o 1995 Integration with CADI
- o 1997 Integration with CCTT classification
- 1999 Second KI paper. Clinical practice guidelines. Implantation biopsies, microwave.
- o 2001 Classification of antibody-mediated rejection
 - Regulatory agencies participating
- 2003 Genomics focus, peritubular capillary cell accumulation scoring -Aberdeen, Scotland (first meeting held elsewhere)
- 2005 Gene chip analysis. Elimination of CAN, identification of chronic antibody-mediated rejection.
- o 2007 First meeting far from a town called "Banff" La Coruna, Spain.
- o 2009 Meeting in Banff, Canada.



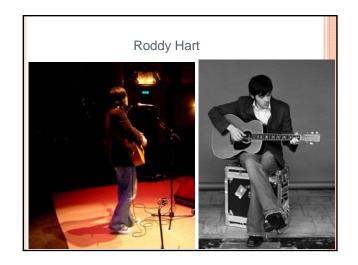


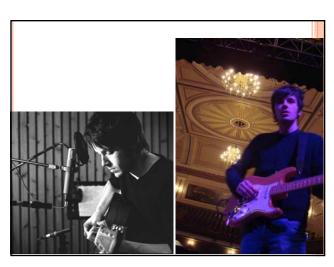


Leonard Cohen International Events 2000 - Montreal 2002 - Hydra, Greece 2004 - New York City 2006 - Berlin 2008 - Edmonton 2010 - Krakow, Poland Edmonton has had yearly Leonard Cohen Nights in September celebrating Leonard's birthday 2002-2007





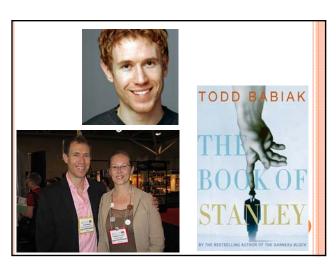


















Conclusions • Arts and culture make medicine better. • Medicine makes arts and culture better.

A FOOT IN BOTH CAMPS: APPLYING PHILOSOPHY TO GENE CHIP VERSUS TRADITIONAL PATHOLOGY INTERPRETATION KIM SOLEZ, M.D.





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DIAGNOSTIC CATEGORIES

- 1. Normal
- o 2. Antibody-mediated rejection,
- 3. Borderline changes: 'Suspicious' for acute cellular rejection
- 4. T-cell-mediated rejection (may coincide with categories 2 and 5 and 6)
- 5. Sclerosis, interstitial fibrosis, and tubular atrophy, no evidence of any specific etiology
- o 6. Other Changes not considered to be due to rejection

LESION SCORING (0-3+)

Transplant glomerulitis - g

Chronic transplant glomerulopathy - cg

Interstitial Inflammation - I

Interstitial fibrosis - ci Tubulitis - t

Tubular atrophy - ct

Vasculitis, intimal arteritis - v

Fibrous intimal thickening - cv

Arteriolar hyaline thickening - ah

Mesangial matrix increase - mm

Peritubular capillary cell accumulation - ptc (still being tested)

MY MAIN INTEREST A YEAR AGO: CONSENSUS GENERATION ONLINE...



A good example of successful use is the World Wide Web Consortium. "We reject kings, presidents, and voting. We believe in rough consensus and running code." David Clark (MIT)

"Consensus stops the majority ruling the minority and is more consistent with anarchist principles." Anarchist FAQ.

ConsensUs: Computer-moderated Structured Discourse.

FacilitatePro - Online collab. tool.

... AND THE ROLE OF PROTEST.



I actually believe if Banff meeting participants knew I researched this stuff as a science, my facilitator role would be much less effective. So shhh! Mums the word!







presentation\Analyst Pres 1997 Full Pres.ppt

GENOMICS VERSUS TRADITIONAL PATHOLOGY. A FOOT FIRMLY PLANTED IN BOTH CAMPS BUT IT SEEMED OK!

A principal investigator in Phil Halloran's 18
 Million Dollar Genome Canada transplant
 transcriptome project.
 http://www.transcriptome.ca/

Affymetrix GeneChip® probe array. Image courtesy of Affymetrix.

 The prime mover behind the Banff Conferences and Classification which mainly uses techniques of thirty to fifty years ago. http://cybernephrology.ualberta.ca/Banff/







THEN IN LATE AUGUST 2006 SOMETHING HAPPENED WHICH CHANGED EVERYTHING!

- On the same day my two best friends in science and most long standing collaborators made diametrically opposite and counterbalancing suggestions:
- 1) That we own up to all our errors of the past in traditional pathology and tie our future to the undeniable truth of genomics, rejecting from consideration the wealth of validating findings coming from the use of traditional pathology in the last 15 years.
- 2) That because it is rather difficult to decide what the relationship of genomics findings to traditional pathology is, we should leave genomics out of future transplant pathology meetings.

- These are just two examples of a general tendency to exclude one or the other modality from consideration, difficult to think of both at once. Many common entities have no known genomics signature as yet.
- There is a new search underway for genomics functional correlates, reminiscent of morphologic functional correlates of the '70s. Many patients with injury gene expression on biopsy have normal function.
- There seemed looming here some enormous gulfs that only philosophy (and creativity!) could span and make sense of. I began steeping myself in philosophy in earnest seeking the help of others who could advise me!

METHODS AND RESULTS

- Methods: We compared histological analysis of renal allograft biopsy assessed by the Banff criteria to biological evidence of T cell mediated rejection assessed by Affymetrix microarrays and clinical evidence of rejection based on retrospective chart review in 30 biopsies for cause with tubulitis. We applied various philosophers' approaches to truth and meaning to "clinical truth", the diagnosis at the time of biopsy as assessed by chart review, and to what "seeing" means when we say we "see" biopsy evidence of specific disease processes
- Results: Questions of diagnosis when biopsy histopathology, gene chip analysis, and clinical data appear in conflict give rise to circular arguments, which are clarified and made easier to accept when philosophical concepts such as Socratic dialogue, tacit knowing, the epistemic gap, and 'thing knowledge' are applied. 30% of biopsy cases (9 of 30) had data in conflict and benefited from applying philosophy.

EXAMPLE OF DATA IN CONFLICT, NOT SO MUCH A CONFLICT AS A DIFFERENT WAY OF LOOKING!

• Biopsy #1 on patient:

Traditional Pathology: Acute Cellular Rejection (tubulointerstitial) Rule out anti-tubular basement membrane antibody nephritis, glomerular features consistent with chronic transplant glomerulopathy, moderate hyaline arteriolar thickening suggesting calcineurin inhibitor toxicity

Gene Chip: Acute Cellular Rejection

• Biopsy #2 on same patient three weeks later:

Traditional Pathology: Probable calcineurin inhibitor toxicity, previous tubulointerstitial rejection appears to have resolved although anti-tubular basement membrane antibody is still evident by immunofluorescence.

Gene Chip: Acute Cellular Rejection

PHILOSOPHY - PLATO HOW TO EXAMINE LIFE?



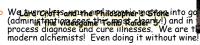
"The unexamined life is not worth living" - Plato

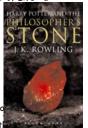
PHILOSOPHY - PATHOLOGY WE ARE ACTUALLY FULFILLING THE EXPECTATIONS OF THE PHILOSOPHER'S STONE!

 The Philosopher's Stone. This mythical, magical article was said to possess the ability to change base metals into gold and could also, if mixed judiciously with wine, produce the Elixir of Life - a comprehensive cure-all for most illnesses.









Harry Potter Philosopher's Sto

ENGRAVING FROM PETER BRUEGEL THE ELDER

- Interesting to compare our labs today to the alchemist's lab of 1559!
- of 1959!

 Bruegel
 considered his
 fellow humans to
 be at the mercy
 of folly: to be
 eccentric as a
 species, apart
 from nature yet
 exhibiting a
 distinct human
 nature.
- nature.

 Bruegel depicted many crowd scenes showing with wit a range of human behaviors in encyclopedic detail.



PHILOSOPHY - PATHOLOGY 1559 TWO SIDES THEME: BREUGEL'S THE FIGHT BETWEEN CARNIVAL AND LENT.

- Breuge's The Fight Between Carnival and Lent depicts the contrast between two sides of contemporary life, as can be seen by the appearance of the inn on the left side for enjoyment, and the church on the right side for religious
- You can imagine genomics on one side and traditional path on other!



PHILOSOPHY - QUESTION EVERYTHING. TRUST NO ONE? "THE WISDOM OF CROWDS"





Studying philosophy immediately calls into question the wisdom of experts. James Surowiecki's "The Wisdom of Crowds" suggests that groups rather than individuals will often be better at arriving at the correct answer. It is obviously desirable to be "right" when making diagnoses that are acted on clinically, but in the central slide review I do for many international clinical trials it is more desirable to be "consistent" than "right". So maybe an individual is still better there. It is a philosophical point!

OF MODERN PHILOSOPHY ("I THINK, THEREFORE I AM") DID NOT TRUST CROWDS, TRUSTED ONLY HIMSELF!



Argued for individual autonomy.

"A majority vote is worthless as a proof of truths that are at all difficult to discover, for a single man is much more likely to hit upon them than a group of people. I was, then, unable to choose anyone whose opinions struck me as preferable to those of others, and I found myself as it were forced to become my own guide"

p.28 "Discourse on the N from <u>Descartes: Selected</u> Philosophical Writings

MORE DESCARTES - HE HAD NICE THINGS SAY ABOUT THE FUTURE OF MEDICINE IN 1637!

... health, which is undoubtedly the chief good and the foundation of all the other goods in this life. For even the mind depends so much on the temperament and disposition of the bodily organs that if it is possible to find some means of making men in general wiser and more skilful than they have been up till now, I believe we must look for it in medicine. I am sure there is no one, even among its practitioners, who would not admit that all we know in medicine is almost nothing in comparison with what remains to be known, and that we might free ourselves from innumerable diseases, both of the body and of the mind, and perhaps even from the infirmity of old age, if we had sufficient knowledge of their causes and of all the remedies that nature has provided. Descartes, Discourse on the Method, 1637, Selected philosophical writings. Cambridge (Cambridge University Press), 1988, p.47.

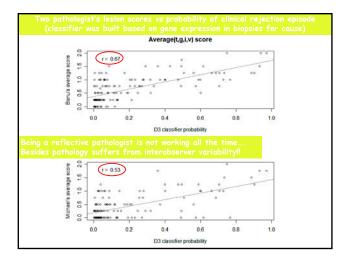
PHILOSOPHY - SCIENCE AND PHILOSOPHY The concept of cells existed in philosophy long before the invention of the microscope and confirmation of their existence in science.

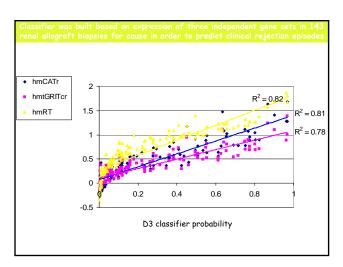
Philosophy – Armchair-reflective pathology vs. Blink-instinctive, shoot-from-the-hip.

Both have their place.

"I can always figure a case out if I just spend enough time with it!"

I thought I had a way to tell reflective pathologists – they use mechanical stage – commonly used for renal pathology, but just an irritant for general surgical pathologist ("sprong" vs. "thwak" sound) who want to pass the glass across the stage as quickly as possible. But then I discovered that Bob Colvin, Chair at MGH, does not use mechanical stage!

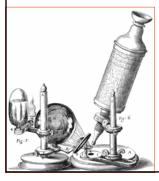


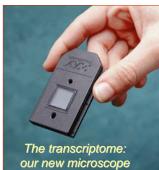


Gene expression analysis should emerge as a complementary dimension to pathology, not a competitor.

- The emergence of microarrays for genome-wide transcriptome analysis offers potential for objective and quantitative diagnosis as well as insights into pathogenesis.
- A major advantage of gene expression measurements in diagnosis is reduction of the sources of variability compared to histology.
- ${\color{blue} \circ}$ Microarray analysis should be complementary to histology, not a competitor.
- Both gene expression and pathology are empirical data to distinguish diseased from normal tissue, but do not forget: both are footprints of the truth, except that pathology includes much more nonspecificity than gene expression, whereas we do not know the genomics signature of many conditions yet.

Microarray analysis of gene expression extends a bridge between pathology and the truth, helps us to determine disease phenotypes more accurately, uncovers mechanism(s) of rejection and other diseases, and <u>finally teaches us how to use microscope</u> - more than 400 years after its invention!





PHILOSOPHY - TRUTH PHILOSOPHY OF SCIENCE - KARL POPPER



Sir Karl Popper (1902-1994) Professor of Logic and Scientific Method at the London School of Economics for 23



Popper concluded that all we know is but "a woven web of guesses."

that while empirical generalizations may not be verifiable, they are, at least, falsifable.

UNCERTAINTY ABOUT TRUTH COMES FROM BOTH CLASSICAL PHILOSOPHY AND QUANTUM PHYSICS

- Problem of Induction David Hume (1711-1776) Contended that until we know the Necessary Connection /cause of things then all human knowledge is uncertain, merely a habi of thinking based upon repeated observation (induction), an which depends upon the future being like the past.
- Heisenberg Uncertainty Principle Werner Heisenberg
 (1901-1976) Applies to the position and momentum of a
 single particle, and implies that if we continue increasing the
 accuracy with which one of these is measured, there will
 come a point at which the other must be measured with less
 accuracy. Can be extrapolated to general uncertainty about
 physical state of the world.



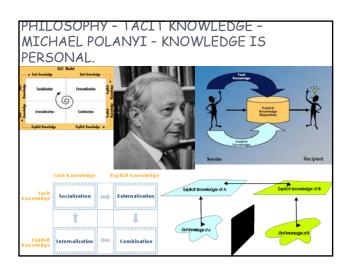
HILOSOPHyTruth is a property of gertain ideas. These rder 15 PRAGMATT 15 PRAGMATTIC 15 PRAGMATTIC 15 PRAGMATTIC 15 PRAGMATTIC 15 PRAGMATTIC 16 PRAGMATTIC 16 PRAGMATTIC 17 PRAGMATTIC

functional in

truth is whatever idea starts the verification Truth is grounded in purpose. The intent of verification process is to see if the idea is experience, thus useful. If one experience

leads us to

other moments that are worthwhile, then they have truth because they have been purposeful. The truths in these experiences are not important at all times, thus we have 'extra truths'. When the extra truth becomes practically relevant towards leading us to other worthwhile moments, it is used. For example, we assume Japan to exist without ever having



RECOGNIZING TACIT KNOWLEDGE IN MEDICAL EPISTEMOLOGY

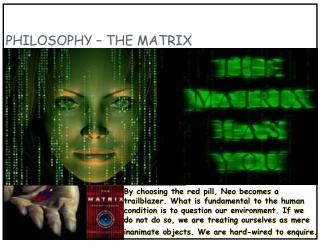
- Theor Med Bioeth. 2006;27(3):187-213.
- Recognizing tacit knowledge in medical epistemology.
- Center for Biomedical Ethics and Society, Vanderbilt University Medical Center, 319 Oxford House, Nashville, TN 37232-4350, USA. shenry@alumni.vanderbilt.edu
- Oxford House, Nashville, TN 37232-4350, USA. shenry@alumni.vanderbilt.edu

 The evidence-based medicine movement advocates basing all medical decisions on certain types of quantitative research data and has stimulated protracted controversy and debate since its inception. Evidence-based medicine presupposes an inaccurate and deficient view of medical knowledge. Michael Polanyi is theory of facit knowledge both explains this deficiency and suggests remedies for it. Polanyi shows how all explicit human knowledge depends on a wealth of tacit knowledge which accrues from experience and is essential for problem solving. Edmund Pellegrino's classic treatment of clinical judgment is examined, and a Polanyian critique of this position demonstrates that facit knowledge is necessary for understanding how clinical judgment and medical decisions involve persons. An adequate medical epistemology requires much more qualitative research relevant to the clinical epistemology requires much more qualitative research relevant to the clinical epistemology reventing an uncritical application of evidence-based medicine by health care managers that erodes good clinical practice. Polanyi's epistemology shows the need for this work and provides the structural core for building an adequate and robust medical epistemology that moves beyond evidence-based medicine.

PHILOSOPHY - ZOMBIES - EPISTEMIC GAP -PERCEPTUAL BIAS



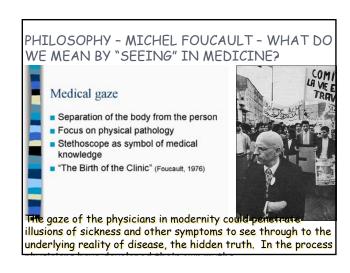
Perception versus reality. A zombie is a hypothetical creature that is physically identical to a conscious being but is not conscious at all. Many people hold that zombies are conceivable in principle, and hold further that in





PHILOSOPHY - ITALO CALVINO

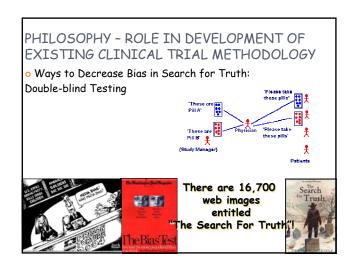
- Argued for the dismantling of interdisciplinary barriers, getting rid of departments of philosophy: "We will not have a culture equal to the challenge until we compare against one another the basic problematics of science, philosophy, and literature, in order to call them all into question."
- One might imagine a day when people would argue for getting rid of departments of pathology!



PHILOSOPHY - THING KNOWLEDGE

 Objects themselves, specifically scientific instruments, can express knowledge. Not all knowledge comes from testing theories.







BBC CREATIVITY PROJECT

"the most creative organisation in the world"?

BRAINSTORMING

- Appoint a facilitator and capture all ideas
- o Go for quantity: the more ideas, the better
- Work together: combine, build, extend
- Be playful: wild ideas are welcome.
- o Defer judgement

And remember...

it's easier to make the interesting feasible than to make the feasible interesting

SOME LITERATURE ON CREATIVITY!

- Creativity Games for Trainers: A Handbook of Group Activities for Jumpstarting Workplace Creativity (McGraw-Hill Training Series) (Paperback) by Robert Epstein
- Thinkertoys (A Handbook of Business Creativity) (Paperback)
 by Michael Michalko
- Six Thinking Hats (Paperback) by Edward De Bono

BBC CREATIVITY

"connecting with audiences"

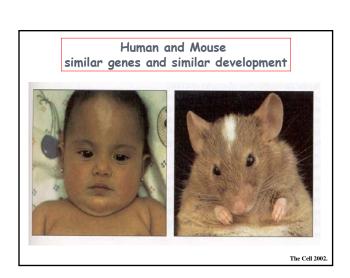
WE NEED TO CONNECT WITH AUDIENCES TOO! IF WE DO IT RIGHT WE WILL BE CHANGING THE FACE OF MEDICINE!



GLOBAL CONSENSUS GENERATION WHILE MAINTAINING INTELLECTUAL FREEDOM. LIKE THE MOSH PIT AT A
GREAT ROCK CONCERT. NO
PARTNER, THE ULTIMATE IN
INDIVIDUALITY,
DANGEROUS, BUT
THE MUSIC
IS GOOD EVERYOL
DANCES IN SYNC
LIFE IS GOOD!

CURRENT RESEARCH

- Microarray analysis of both human & mouse kidney transplants with rejection and other complications
- Correlate with Clinical data & Banff lesions.
 Common entities like glomerulonephritis,
 bacterial infection, and calcineurin inhibitor
 toxicity have no genomics signature at present.



ANOTHER GOLD STANDARD, CHANGING A PRIORI ASSUMPTIONS FOR POSITIVE AND NEGATIVE PREDICTIVE VALUE?



FUTURE BANFF MEETINGS:

- o 2007 La Coruna, Spain (June 23-29)
- o 2009 Whistler, British Columbia, Canada
- o 2011 Paris, France
- o 2013 Banff, Alberta, Canada
- o 2015 Stockholm, Sweden
- o 2017 Please make a proposal!

CONCLUSIONS: GENOMICS VS. TRADITIONAL PATHOLOGY.

- Genomics and traditional pathology are difficult to compare because they do not measure the same things and have a very different knowledge structure. Philosophy, creativity, and good humor are needed to consider them both in the mind at once
- As easy as it would be to just deal with one and exclude the other, we really need them both, as working in combination they are the future of diagnostic medicine!

CONCLUSIONS: FLUFF VS. SUBSTANCE

- In a short time the tremendous resources and intellectual effort being devoted to transplant genomics and diagnostics locally in the Genome Canada project will bring great advances. Perhaps the most important will be changes in the way we interpret and score light microscopic changes (e.g. requiring i2 for v1 to equal rejection etc.), so the new knowledge will enhance not replace traditional pathology.
- Despite this wonderful intellectual ferment, questions will remain. The philosophical approaches touched on in this presentation could provide a basis for dealing with many of them.

Acknowledgements

Genome Canada/Genome Alberta

Genome Canada/Genome Alberta
University Hospital Foundation
Alberta Innovation and Science
Roche Molecular Systems Roche Canada
Roche Organ Transplant Research Foundation (ROTRF)
Canadian Institutes of Health Research
Kidney Foundation of Canada
Alberta Heritage Foundation for Medical Research
Astellas Canada
Muttart Chair in Clinical Immunology, Canada Research Chair in Life
Sciences

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http://www.cybernephrology.ualberta.ca/misc/Solez/L