EXPERIMENT PERILOUS

HUMAN EXPERIMENTATION

DISCLOSURE: F.FITZGERALD M.D.

I HAVE NOT BEEN BRIBED

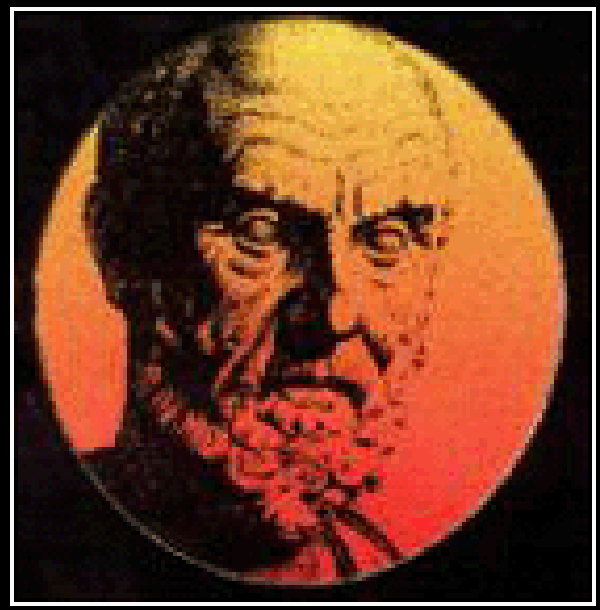
I HAVE NOT BEEN CORRUPTED

I HAVE NO HIDDEN ALLIANCES WITH RICH PEOPLE

MY MOTIVES ARE PURE

HIPPOCRATES: LIFE IS SHORT, AND…….

- THE ART IS LONG
- OCCASION FLEETING
- EXPERIENCE FALLACIOUS
- JUDGMENT DIFFICULT
- **EXPERIMENT PERILOUS……**



NEBUCHADNEZZER II 605-562BCE

- FIRST RECORDED CLINICAL TRIAL:

  STRICT DIET MEAT+WINE x 3 YEARS

(ALMOST IMMEDIATE PROTOCOAL BREAK BY 4 CHILDREN WHO PREFERRED BREAD AND WATER)

JAMES LIND,ROYAL NAVY, 1747

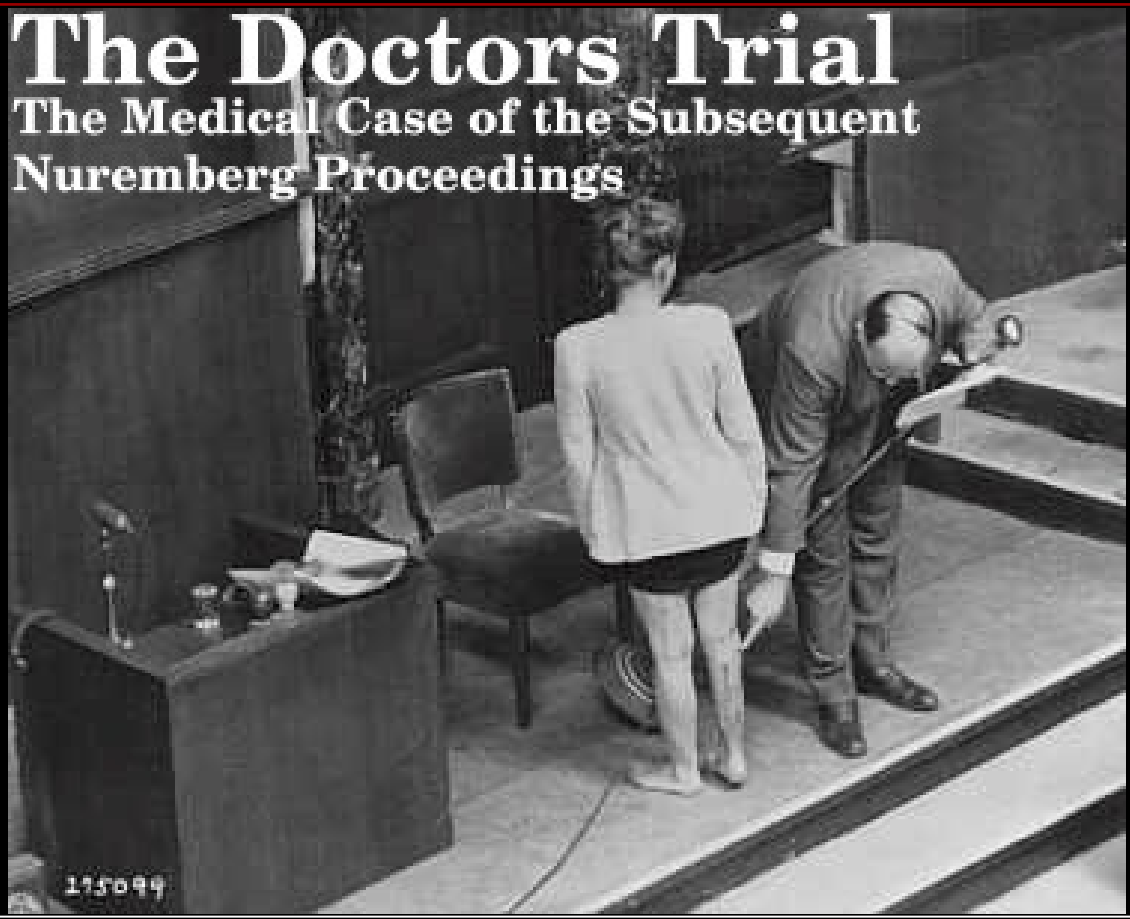
BURKE, HARE AND DR KNOX

~1800

A HARBINGER OF THINGS TO COME

NUREMBERG AND AFTER

1947


The Doctors Trial
The Medical Case of the Subsequent
Nuremberg Proceedings
115099

NAZI EXPERIMENTS

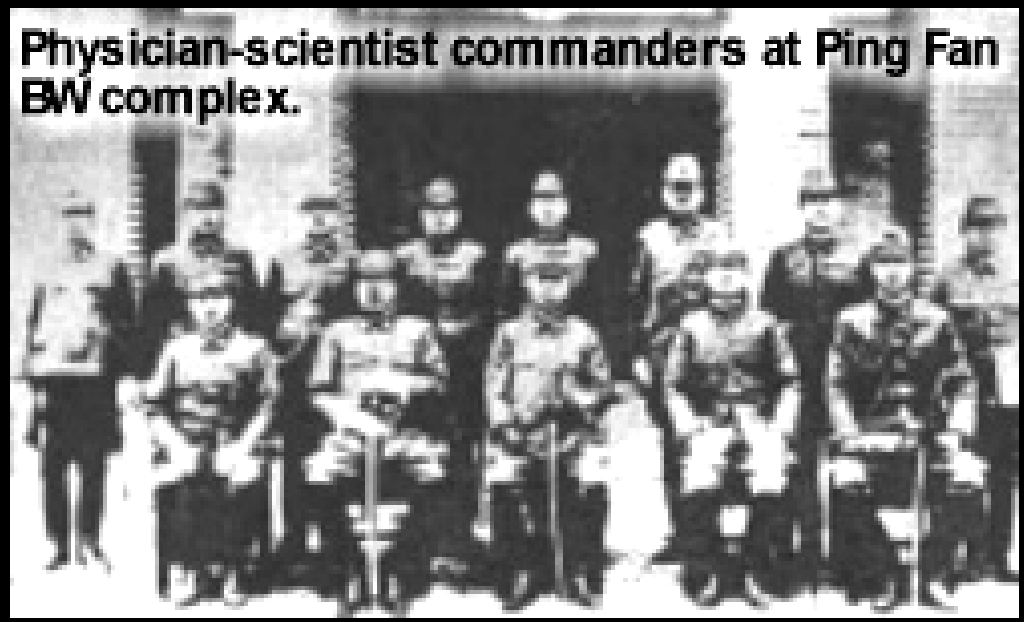
THE ‘DOCTORS’ OF THE THIRD REICH

BRANDT

MENGELE

AND THE PATIENTS

UNIT 731- MANCHURIA



UNIT 731

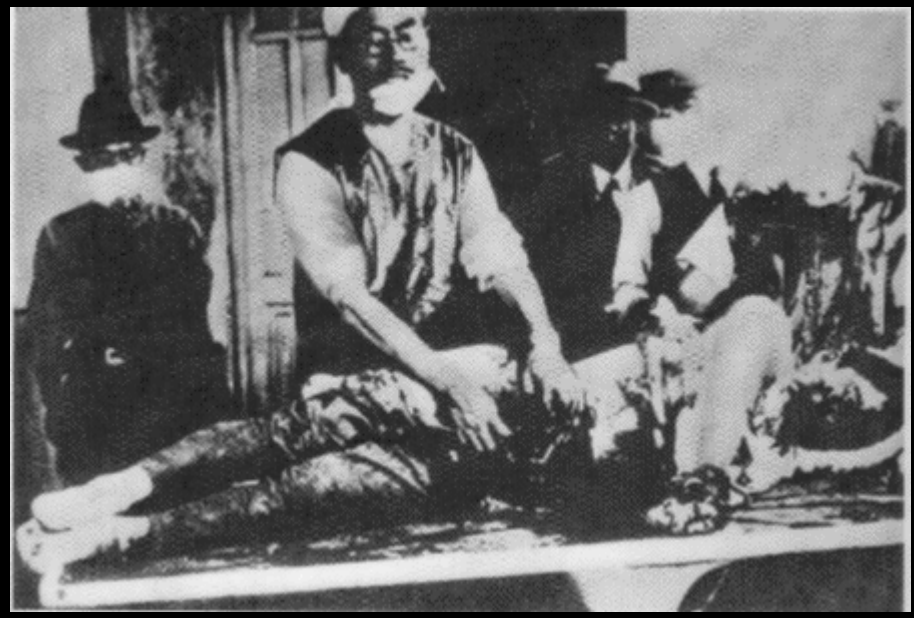
BIOLOGIC WARFARE

UNIT 731

VIVISECTION

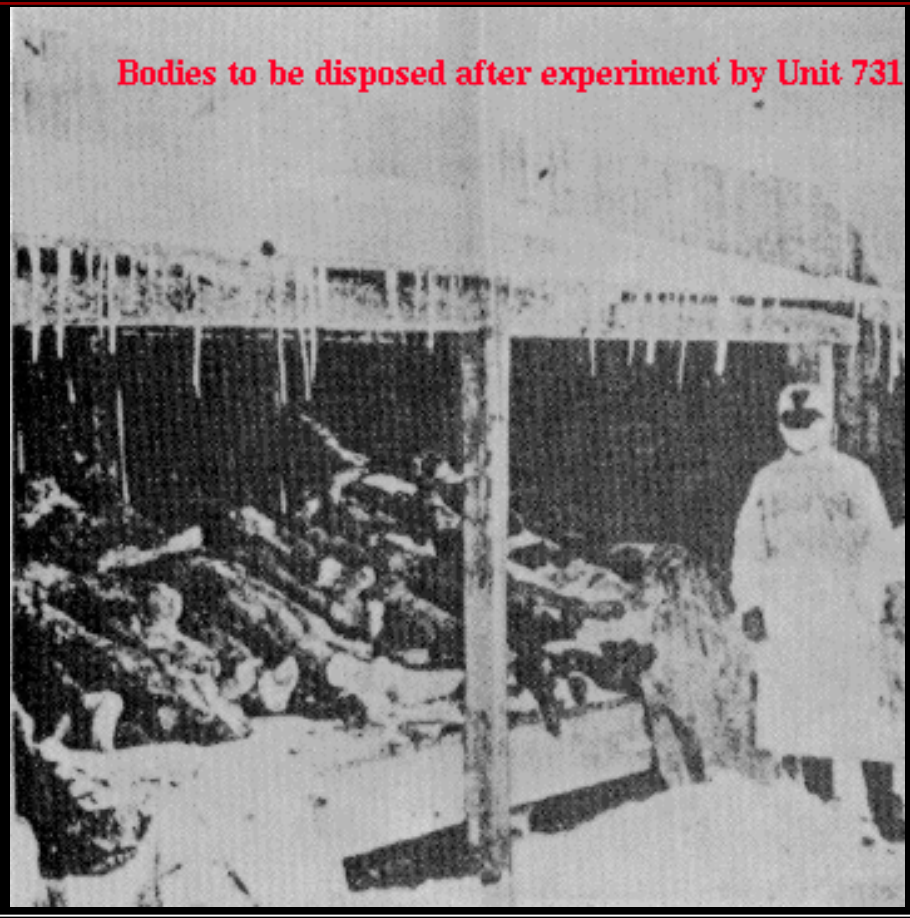
UNIT 731

‘TRAINING’ YOUNG SURGEONS



THE ‘DOCTOR’ OF UNIT 731

AND THE PATIENTS



THE NUREMBERG CODE-1948

- 1.The **voluntary consent** of the human subject is absolutely essential

  .. legal capacity to give consent

  .. free power of choice, without constraint or coercion

THE NUREMBERG CODE-1948

.. knowledge and comprehension of hazards,effects,duration,method,purpose of experiment.

….investigator (no other) must obtain consent

THE NUREMBERG CODE

- 2. The experiment should be such as to **yield fruitful results** for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

THE NUREMBERG CODE

- 3. The experiment should be so designed and **based on the results of animal experimentation** and a knowledge of the natural history of the disease or other problem under study that the anticipated **results will justify** the performance of the experiment.

THE NUREMBERG CODE

- 4. The experiment should be so conducted as to **avoid all unnecessary physical and mental suffering and injury.**

THE NUREMBERG CODE

- 5. No experiment should be conducted where there is an a priori reason to believe that **death or disabling injury** will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

THE NUREMBERG CODE

- 6. The **degree of risk** to be taken should never exceed that determined by the humanitarian **importance of the problem** to be solved by the experiment.

THE NUREMBERG CODE

7. Proper preparations should be made and adequate facilities provided to **protect the experimental subject** against even remote possibilities of injury, disability, or death.

THE NUREMBERG CODE

- 8. The experiment should be conducted only by **scientifically qualified persons**. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

THE NUREMBERG CODE

- 9. During the course of the experiment the human **subject** should be at liberty to **bring the experiment to an end** if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

THE NUREMBERG CODE

- 10. During the course of the experiment the **scientist** in charge must be prepared to **terminate the experiment** at any stage, if he has probably cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is **likely to result in injury, disability, or death** to the experimental subject.

16 YEARS WENT BY….

HELSINSKI DECLARATION(S)

- WORLD MEDICAL ASSOCIATION

1964-HELSINKI

1975-VENICE
1983-HONG KONG
1989-S.AFRICA
2000-EDINBOROUGH
2002-WASHINGTON D.C.
2004-TOKYO

WHY SO MANY REVISIONS?

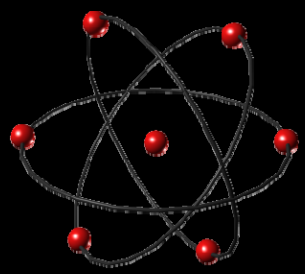
TUSKEEGE: 1932-1973

AFRICAN-AMERICANS FOLLOWED FOR NATURAL COURSE OF SYPHILIS; WHEN PENICILLIN INTRODUCED, THEY WERE DELIBERATELY NOT TREATED.*

*"NOT ONLY MUST THE LAW BE FAIR, IT MUST *APPEAR* TO BE FAIR".

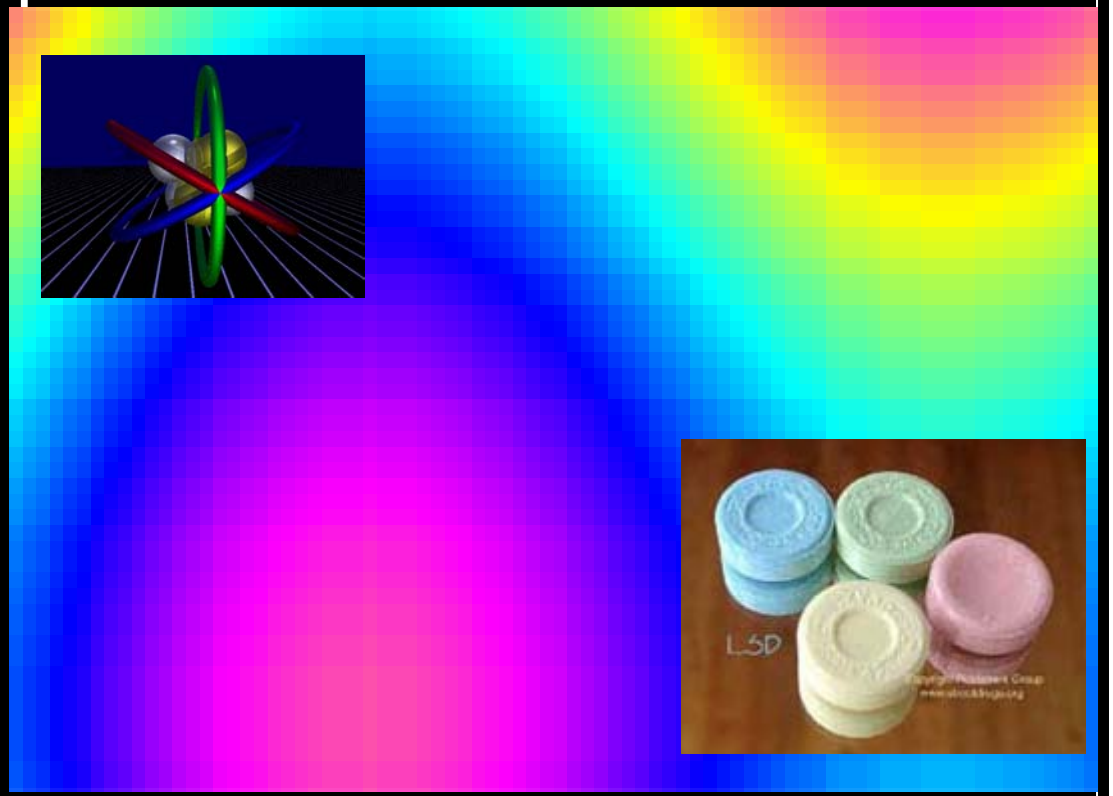
RADIOACTIVE STUDIES-1940s AND 50's.

- MANY, AMONG WHICH WAS FEEDING RADIOACTIVE CEREAL TO MENTALLY RETARDED CHILDREN IN FERNALD SCHOOL IN MASSACHUSSETS.



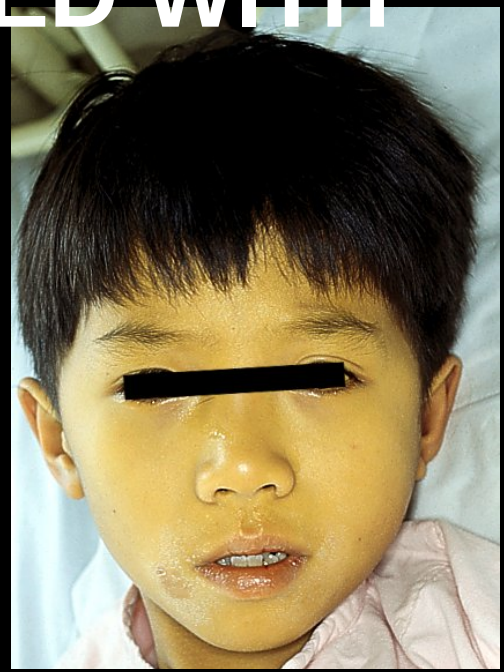
STUDIES ON SOLDIERS

- HALLUCINATORY DRUGS
- RADIATION



WOLLOWBROOK-1960's

MENTALLY IMPAIRED CHILDREN DELIBERATELY INFECTED WITH HEPATITIS A



BIOWAR STUDIES

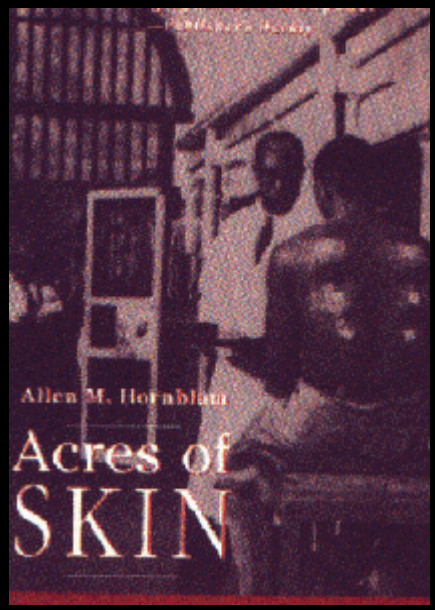
- 1950's and 60's

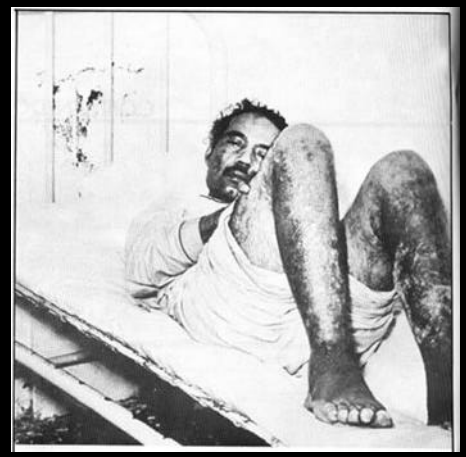
CHECKING WIND
CURRENT SPREAD
OF BACTERIA

BROOKLYN JEWISH CHRONIC DISEASE HOSPITAL - 1962

- INJECTION OF CANCER CELLS INTO ELDERLY PATIENTS WITHOUT THEIR KNOWLEDGE

PRISONER STUDIES: UNTIL 1970's





HELSINKI I-V

- CAUTIONS FOR PERSONALITY ALTERATION STUDIES
- SEPARATE RESEARCH, CLINICAL CARE
- ESTABLISH IRBs
- JOURNALS MUST REFUSE UNETHICAL STUDIES

HELSINKI I-V

- LEGAL GUARDIANS (PROXY) CONSENT
- CONTROLS MUST GET BEST CLINICAL CARE
- PATIENTS AT END OF STUDY MUST HAVE CONTINUED ACCESS IF BENEFIT
- PRIVACY MAINTAINED FOR SUBJECTS

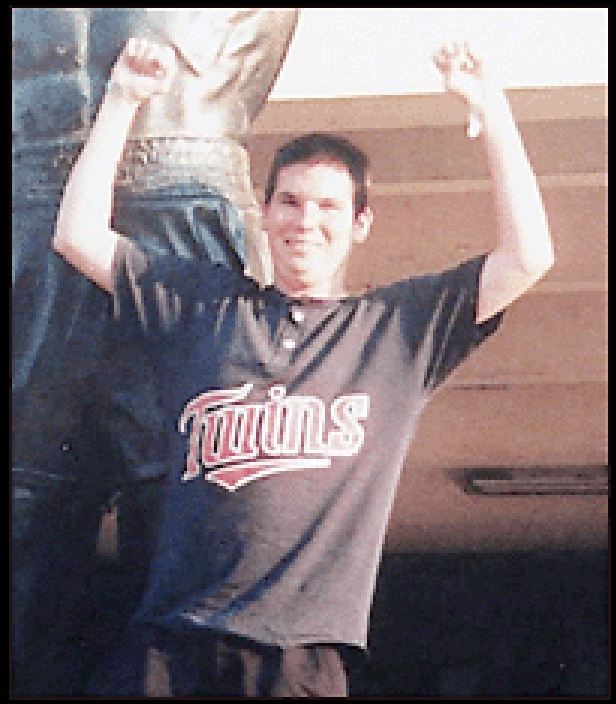
HELSINKI I-V

- UNPROVEN RX O.K. IN CONTROLS IF OFFERS HOPE TO THEM
- PLACEBO O.K. IN CONTROLS ONLY IF NO PROVEN RX OR DISEASE SO MILD THERE WILL BE NO HARM

1999- JESSE GELSINGER

UNIVERSITY OF PENNSYLVANIA.
?PROTOCOL VIOLATIONS

GENE INSERTION USING ADENOVIRAL VECTOR



2001 – ELLEN ROCHE

JOHNS HOPKINS
NORMAL VOLUNTEER

HEXAMETHONIUM

WHY DO INVESTIGATORS GO ASTRAY?

TEMPTATIONS ARE MANY…

T0 ONE'S HONOR, PRINCIPLES, INTEGRITY, VIRTUE.

CURIOSITY

MONEY APPROVAL FAME PUBLICATIONS AWARDS

FUTURE OF CLINICAL RESEARCH?

- IRB STRINGENCY → SLOWDOWN
- EXPENSES,TIME IN ACADEMIA ↑
- ↑ % $ CLINICAL TRIALS FROM INDUSTRY, RATHER THAN NIH
- MOVE FROM ACADEMIA TO PRIVATE SECTOR

  1991-80% INDUSTRY RESEARCH $$ TO ACADEMIC CENTERS AND THEN…..

CLINICAL RESEARCH: MOVING OUT OF ACADEMIC MEDICINE

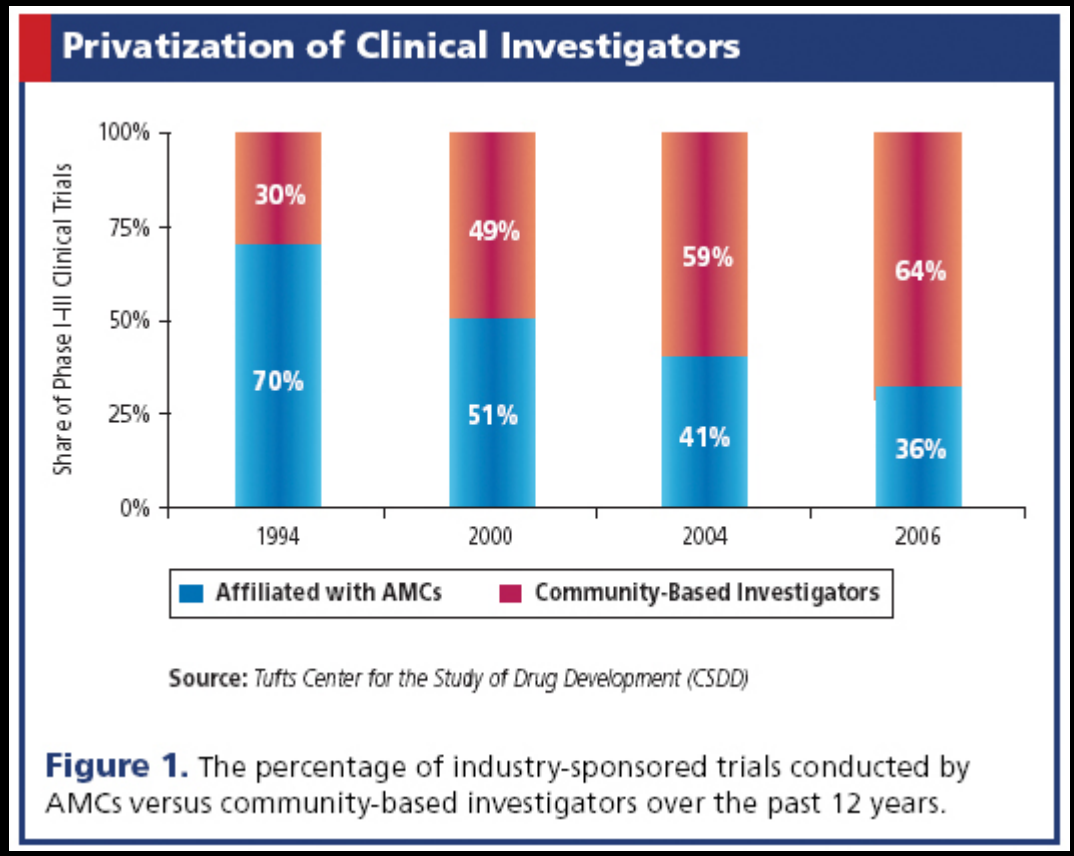


Figure 1. The percentage of industry-sponsored trials conducted by AMCs versus community-based investigators over the past 12 years.

APPLIED CLINICAL TRIALS :4/1/2007

PRACTICE CLINICAL TRIALS

?

PHYSICIANS MAY BE PAID $1000-5000
PER PATIENT ENROLLED IN TRIAL

PRACTICE CLINICAL TRIALS

- DATA MAY BE SENT DIRECTLY TO COMPANY
- DATA MAY BE ANALYZED BY THE COMPANY
- PAPER MAY BE GHOST WRITTEN BY THE COMPANY

CONTRACT RESEARCH ORGANIZATIONS

"As a contract research organization staffed by full-time professionals, GTRI brings you cutting edge technology development skills combined with practical business experience. It also draws on multidisciplinary teams from research and academic faculty … GTRI is successful because it is responsive to the needs and schedules of its customers."

AND SOMETHING NEW

- CROs. .CONTRACT RESEARCH ORGANIZATIONS ON LINE……

1747

DIRECT TO PATIENTS

(WWW. 1747.NET)

WEB RESEARCH

ISN'T THIS DEPERSONALIZING MEDICINE? (FAQ on 1747 website)

"…… participating in our studies will give you **much more timely personal attention than standard site studies**; and, we are able to accommodate individual schedules in ways that would be impossible for typical trials. **So what you miss out on is sitting in traffic, paying for parking and waiting in lobbies for a 3 minute interview with a busy nurse practitioner. We hardly think those interactions are worth preserving!"**

PARTICIPANT TESTIMONIALS

- From an online clinical trial of Kava and Valerian for symptoms of insomnia and anxiety.

  "Every time I have had a question it has been answered so that I understand. So yes the support is there…. I feel you are really interested in me and how I feel- *Treva Noon*

PARTICIPANT TESTIMONIALS

- "Your web site has great information for potential participates to review, and I have dealt with my problems via e-mail and found everyone very helpful -*Fred Gorman*
- "Bless you for your good work and the accessibility your clinical trial gives to so many...it really is groundbreaking!"

  -*Kathleen Staples*

1747.NET SEEMS TO BE OUT OF BUSINESS AS OF JULY 2006..

- **404** We're Sorry! We can't locate the page you requested. Check the spelling on the Web address (capitalization and punctuation count). Otherwise, enter a key word in the search window below.

  Поиск:

EXPORTING CLINICAL RESEARCH: ETHICAL IMPERIALISM?

PROBLEMS OF CLINICAL RESEARCH IN DEVELOPING NATIONS:

- THE NEED IS THERE
- THE CULTURE IS DIFFERENT:
  - LITERACY
  - ECONOMICS
  - ACCESS TO ALTERNATIVES
  - AUTHORITY STRUCTURE

EXPORTING CLINICAL RESEARCH

NIGERIA IS NOW
SUING A PHARMACEUTICAL
COMPANY FOR CLAIMED
DAMAGES RESULTING FROM
EXPERIMENTAL TESTING
OF A NEW ANTIBIOTIC
IN CHILDREN THERE IN 1996.

IS ACADEMIC CENTER RESEARCH "CLEANER"?

NEJM:352:2202-2210.(MAY 26,2005)

ACADEMIC MEDICAL CENTERS SURVEY(107 OF 122 RESPONDING) OF CONDITIONS OF CONTRACTS WITH INDUSTRY *

But..24% ALLOWED INDUSTRY SPONSOR TO DO STATISTICAL ANALYSIS

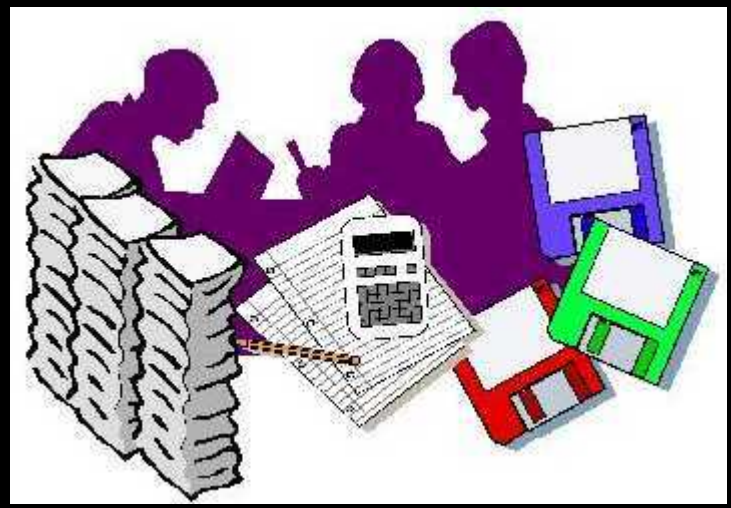
50% ALLOWED SPONSOR TO DRAFT MS.

41% AGREED WITH PROHIBITION OF DATA SHARING AFTER CLINICAL TRIAL.

*85% WILL NOT GIVE AN INDUSTRY SPONSOR AUTHORITY TO REVISE MS OR DECIDE IF IT IS TO BE PUBLISHED

ANALYSIS RESEARCH RESULTS

- EVEN THE WORLD'S FOREMOST EXPERTS IN EVIDENCE-BASED MEDICINE CANNOT ANALYZE ABSENT OR INACCURATE EVIDENCE.



“WATCHDOGS?”

THE PROBLEM IS…..

SOME COMPANIES NOW HIRE BIOETHICISTS TO REVIEW THEIR RESEARCH.

THE PRINCIPAL DUTY OF A PHYSICIAN IS TO THE WELFARE OF THE PATIENT

- 1.PROTECT THE PATIENT
- 2. PROTECT THE SCIENCE
- 3.JUSTIFY THE TRUST

PROFESSIONALISM

THE **ESSENTIAL** THING

PATIENT TRUST

- IT IS THIS SINGULAR AND REMARKABLE REALITY, THAT PATIENTS TRUST THEIR DOCTORS, THAT ALLOWS DOCTORS TO FUNCTION.

TRUST?

- WE TELL OUR PATIENTS WHAT TO EAT, WHAT THEIR BODY SHAPE SHOULD BE, WHAT PLEASURES TO AVOID, WHAT UNPLEASANT THINGS THEY MUST DO. WE ASK THEM TO TELL US THE MOST INTIMATE AND EMBARRASSING DETAILS OF THEIR PRIVATE LIVES. WE POKE INTO HIDDEN PLACES IN THEIR BODIES. WE ALTER THEM PHYSICALLY AND MAY EVEN CHEMICALLY ADJUST THEIR MOODS AND THOUGHTS.

…AND THEY SAY

- “O.K., DOCTOR.”

TRUST?

- **WE SAY TO PATIENTS:** “I KNOW WHAT’S WRONG WITH YOU AND HOW TO FIX IT. I SHALL GIVE YOU A MEDICINE. IT HAS SIDE EFFECTS, THOUGH: IT CAN WIPE OUT YOUR BONE MARROW, STOP YOUR BREATHING, COVER YOU WITH A RASH, OR EVEN KILL YOU. BUT YOU SHOULD TAKE IT.”

…AND THEY SAY

- “O.K., DOCTOR.”

TRUST?

- **WE SAY TO PATIENTS**: “I KNOW WHAT’S WRONG WITH YOU. I CAN FIX IT BY OPERATING ON YOU. THIS MEANS YOU’LL BE UNCONSCIOUS AND HELPLESS, BUT WE’LL SUPPORT YOUR BREATHING.
- WE WILL CUT OFF ONE OF YOUR PARTS. YOU COULD DIE OR HAVE MAJOR COMPLICATIONS, LIKE SHOCK, INFECTION, KIDNEY OR HEART FAILURE…BUT I THINK YOU SHOULD AGREE.”

….AND THEY SAY

- “O.K., DOCTOR”

TRUST?

- WE SAY TO THE PARENTS OF PATIENTS: “YOUR CHILD IS VERY SICK. I INTEND TO TREAT HER WITH MEDICINE AND POSSIBLY SURGERY. I KNOW THERE ARE RISKS TO BOTH, BUT I THINK I KNOW THE RIGHT THING TO DO. SHALL I GO AHEAD?”

…..AND THEY SAY

- “O.K., DOCTOR”

TRUST IN RESEARCH?

- WE SAY: WE DON'T KNOW WHETHER THIS WILL HELP YOU OR HARM YOU OR MAKE NO DIFFERENCE. IT IS NOT NECESSARILY FOR YOUR ADVANTAGE TO DO THIS, BUT IT WILL HELP US LEARN AND ***MAY*** HELP *OTHER* PATIENTS SOMEDAY.

AND PATIENTS SAY…

- “O.K., DOCTOR..”

“O.K. DOCTOR” = “I TRUST YOU, DOCTOR.”

INDIVIDUAL RESPONSIBILITY

- EACH OF US MUST CONDUCT OURSELVES IN SUCH A WAY AS TO JUSTIFY THE AWESOME HONOR OF SUCH TRUST.

ROLE RESPONSIBILITY

- **EACH OF US IS RESPONSIBLE FOR THE PROFESSIONALISM OF ALL OF US BECAUSE WE ARE EACH SWORN TO FIRST AND ALWAYS PROTECT PATIENTS FROM HARM , INCLUDING THAT HARM WHICH MIGHT BE INFLICTED BY A COLLEAGUE OR SUPERIOR .**

ROLE RESPONSIBILITY

- **EACH OF US IS RESPONSIBLE FOR THE PROFESSIONALISM OF ALL OF US, BECAUSE ANOTHER'S ACTIONS AND BEHAVIOR WILL DIRECTLY AFFECT OUR OWN REPUTATIONS , THE TRUST PATIENTS HAVE IN THEIR DOCTORS, AND THEIR WILLINGNESS TO PARTICIPATE IN RESEARCH.**

WHAT MUST A PATIENT BELIEVE TO TRUST US ?

- 1. A DOCTOR (AND STAFF) CARES ABOUT THEM AND ACTS SOLELY ON THEIR BEHALF.
- 2. A DOCTOR HAS THE KNOWLEDGE AND SKILL TO HELP THEM.
- 3. A DOCTOR WILL BE AVAILABLE WHEN NEEDED.

WHAT IS CARING?

- THE PATIENT'S GOOD IS PARAMOUNT.
- THE PATIENT IS TREATED WITH RESPECT AND KINDNESS.
- THE PATIENT IS GIVEN THE BEST OF WHICH MEDICINE IS CAPABLE.

PROFESSIONALISM

1. CONDUCTING ONESELF IN SUCH A WAY AS TO JUSTIFY PATIENT TRUST.
2. ASSURING THAT ONE'S COLLEAGUES DO LIKEWISE: TEACHING AND LEARNING FROM ONE ANOTHER.
3. ALWAYS PLACING PATIENT WELFARE ABOVE ALL OTHER CONSIDERATIONS.

HOW WILL YOU KNOW?

- ASK, ON EACH OCCASION OF ACTION OR DECISION:

  " WILL THIS BENEFIT PATIENTS?"

  "WILL THIS *HURT* THIS PATIENT?"

- **ANY ACTION THAT COULD, IF REVEALED, DIMINISH PATIENT TRUST IN YOU, IS PROBABLY UNPROFESSIONAL.**

THIS TRUST IS ESPECIALLY IMPORTANT IN CLINICAL RESEARCH…

- JUST REMEMBER HOW MANY TIMES PATIENTS HAVE ASKED : “AM I BEING USED AS A GUINEA PIG?”

NOW WHY DO YOU SUPPOSE THEY ASKED THAT?

YOU ARE ALL **GUARDIANS OF THE TRUST** THAT ALLOWS US TO GIVE CARE AND TO ADVANCE THE SCIENCE OF MEDICINE