PRACTICAL POINTERS

FOR
PRIMARY CARE

ABSTRACTED MONTHLY FROM THE JOURNALS

MAY 2003

"BUILDING" A HISTORY RATHER THAN "TAKING" ONE--A CORE CLINICAL SKILL

WHAT DO DOCTORS FIND MEANINGFUL ABOUT THEIR WORK?

USING NEW INSULIN STRATEGIES

COMBINED HRT AND ALENDRONATE FOR OSTEOPOROSIS

REPORT OF THE JOINT NATIONAL COMMITTEE ON HIGH BLOOD PRESSURE. THE JNC-VII

DIURETICS AGAIN JUDGED THE BEST INITIAL DRUG FOR UNCOMPLICATED HIGH BP

SERUM PROSTATE-SPECIFIC ANTIGEN VARIES OVER TIME. RECHECK BEFORE PROCEEDING

BENEFITS OF CHANGES IN PHYSICAL ACTIVITY AND MORTALITY AMONG OLDER WOMEN

HEART FAILURE: A REVIEW ARTICLE

DIETARY FIBER REDUCED INCIDENCE OF COLORECTAL ADENOMAS

ESTROGEN PLUS PROGESTIN DID NOT PROTECT AGAINST DEMENTIA IN OLDER WOMEN

PACEMAKER THERAPY FOR SEVERE VASOVAGAL SYNCOPE DID NOT BENEFIT

JAMA, NEJM, BMJ, LANCET

ARCHIVES INTERNAL MEDICINE

ANNALS INTERNAL MEDICINE

PUBLISHED BY PRACTICAL POINTERS, INC.

EDITED BY RICHARD T. JAMES JR. MD

400 AVINGER LANE, SUITE 203

DAVIDSON NC 28036 US

www.practicalpointers.org rjames6556@aol.com

HIGHLIGHTS MAY 2003

5-1 "BUILDING" A HISTORY RATHER THAN "TAKING" ONE

Adopting a "narrative-based medicine"**(NBM)** approach enables the sharing of information between patient and doctor. It incorporates the patient's narrative into the sharing process. This article suggests a framework of skills and attitudes that can act as a foundation to improve the medical interview.

The essence of a narrative-based approach involves the physician simultaneously attending to two narratives—one from the biomedical perspective, and one from the patient's perspective. Listen to the patient!

5-2 WHAT DO DOCTORS FIND MEANINGFUL ABOUT THEIR WORK?

Making a difference in someone else's life was the most common theme in the doctors' stories. It was not making a brilliant diagnosis or an adroit technical intervention. Most of these stories took place in the context of chronic, incurable conditions, or end-of-life care. The doctors felt awed and deeply rewarded that their mere presence could be healing and comforting to patients.

5-3 USING NEW INSULIN STRATEGIES IN THE OUTPATIENT TREATMENT OF DIABETES.

One daily injection of insulin glargine along with mealtime injections of insulin lispro significantly improves glycemic control in patients with poorly controlled type 2 DM. The combination matches each patient's needs, simplifies adjustment of dose, and improves control while causing fewer episodes of hypoglycemia. "They are easier to use than many patients and clinicians realize."

5-4 COMBINATION THERAPY WITH HORMONE REPLACEMENT AND ALENDRONATE FOR PREVENTION OF BONE LOSS IN ELDERLY WOMEN

Combination therapy with HRT + alendronate was superior to either drug alone in increasing BMD.

5-5 THE SEVENTH REPORT OF THE JOINT NATIONAL COMMITTEE ON PREVENTION, DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD PRESSURE. The JNC-VII

Provides new guidelines and key messages: Individuals with a systolic 120-139 or a diastolic 80–90 should be considered as *pre-hypertensive*. They require health-promoting lifestyle modifications to prevent CVD.

The committee recognizes that the responsible physician's judgment remains paramount.

5-6 HEALTH OUTCOMES ASSOCIATED WITH VARIOUS ANTIHYPERTENSIVE THERAPIES USED AS FIRST-LINE AGENTS

Low-dose diuretics are the treatment of first choice for patients with uncomplicated hypertension who require drug treatment. They are the most effective drugs for preventing cardiovascular disease morbidity and mortality.

5-7 VARIATION OF SERUM PROSTATE-SPECIFIC ANTIGEN

PSA may fluctuate over short periods of time. A single elevated PSA should be viewed with caution.

An isolated elevation of PSA should be confirmed several weeks later before proceeding with further testing, including biopsy.

5-8 RELATIONSHIP OF CHANGES IN PHYSICAL ACTIVITY AND MORTALITY AMONG OLDER WOMEN

Increasing and maintaining physical activity levels could lengthen life for older women.

5-9 HEART FAILURE

This review article comments on diastolic HF and presents new staging and treatment options for systolic HF.

The diagnosis of diastolic HF is usually made by a clinician who recognizes the typical signs and symptoms of HF and is not deterred by the finding of normal systolic function (ie, a normal ejection fraction) on echocardiography. Echocardiography may also be useful in detecting diastolic filling abnormalities. Diastolic HF is common.

HF is largely preventable, primarily through control of risk factors. A new approach to the classification and progression of systolic HF emphasizes four stages of HF which differ from the classical NYHA functional classification.

5-10 DIETARY FIBRE AND COLORECTAL ADENOMA IN COLORECTAL CANCER EARLY DETECTION PROGRAMME

Dietary fiber from grains, cereals and fruits was associated with decreased risk of distal colon and sigmoid adenomas.

5-11 ESTROGEN PLUS PROGESTIN AND THE INCIDENCE OF DEMENTIA AND MILD COGNITIVE IMPAIRMENT IN POSTMENOPAUSAL WOMEN

Estrogen + progestin did not reduce the risk for probable dementia in postmenopausal women age 65 and older.

5-12 PACEMAKER THERAPY FOR PREVENTION OF SYNCOPE IN PATIENTS WITH RECURRENT SEVERE VASOVAGAL SYNCOPE

Pacing therapy did not significantly reduce the risk of recurrent syncope in patients with vasovagal syncope.

The Patient's Perspective Is Often Lost. Negotiate Toward A Shared Perspective

5-1 "BUILDING" A HISTORY RATHER THAN "TAKING" ONE

A Perspective On Information Sharing During The Medical Interview

Patients and physicians enter the medical encounter with their own unique perspectives on the illness experience. These perspectives influence the way information is shared during the interview. Patients who are able to fully share their perspective often achieve better outcomes. However, patient-perspective is often lost. Adopting a "narrative-based medicine"**(NBM)** approach enables the sharing of information. NBM incorporates the patient's narrative into information sharing.

This article suggests a framework of skills and attitudes that can act as a foundation to improve the medical interview.

Both patient and physician form perspectives through which each views the medical encounter, and how information is expressed. "Information sharing", the point when patient and physician share information about the health issue at hand represents a critical juncture. It sets the tone for the entire encounter, shaping both interactants' views of their roles, and how their relationship will function.

Why is the patient's perspective important?

The patient's perspective is a critical mediator of illness behaviors. It impacts health outcomes. High quality care requires the expression of both patient and physician perspectives, along with negotiation toward a shared perspective. Greater expression of patient perspectives through active participation in the encounter favorably impacts a variety of outcomes, including better adherence to recommended treatments. Physician solicitation of patient perspectives has a positive impact on patient trust, satisfaction, and adherence. The ability for patients to share their perspectives through narrative satisfies their basic human need for expression. This may in itself have therapeutic value.

De-emphasizing the patient's narrative

History taking often (*and usually*) facilitates bio-medical communication among physicians by organizing data into a common language. The goal of this organization is to help physicians produce narratives that lead medical audiences to short lists of possible diagnoses. Yet, problems arise when this is the sole framework of information sharing. Under constraints, such as time pressure, there is tension between the relative importance of the physician's and the patient's perspectives. Both perspectives are important. The physician's perspective may exclude critical patient-oriented data necessary to achieve therapeutic effectiveness. The patient's perspective may miss critical biomedical facts needed for accurate diagnosis.

Both physician and patient might communicate and act differently if each heard and understood each other's point of view.

Building a history rather than taking it.

The essence of a narrative-based approach involves the physician simultaneously attending to two narratives—one from the biomedical perspective, and one from the patient's perspective. This includes the patient's fears and concerns. The information is told according to the patient's organization rather than the doctor's. This involves the physician engaging the patient in a mutual activity in which the two work together to "build" the complete history that includes both the biomedical and the patient-defined points of view. It provides insight into the patient's

perspectives that may influence critical treatment and planning decisions. (The authors believe this can be done efficiently, without requiring a large expenditure of time.)

The authors propose a set of key skills and attitudes that may influence history-building:

1) Start with open-ended questions and gradually increase the focus with closed-ended questions. Physicians often redirect the patient to specific biomedical information early in the interview. The focus is then on narrowly constructed yes/no questions, thus losing sight of the patient's narrative. History-building requires a conscious decision about phrasing of questions—questions that are focused, but still open-ended enough to give the patient space to discuss his narrative.

2) History-building requires the physician to listen to a narrative that is organized around the context of the patient's life while simultaneously mentally organizing the biomedical information within a diagnostic framework. If the physician frequently interrupts the discussion, the patient quickly learns that very short biomedically oriented answers are preferred and thus will leave out details. The physician's mental organization of the story is strengthened by retelling the story using the patient's organization and language, and filling in important missing biomedical pieces.

Some conversational devices other than questions are helpful in history-building:

Device	Example
Orientation statements	"Now, I would like to talk about your other medical problems".
Paraphrasing	"OK let me make sure I have this straight".
Reflection	Patient: "I'm worried." Physician: "You're worried?".
Directive	"Tell me what happened next."
Request for clarification	"Help me understand what the pain felt like."
Empathetic statements	"That sounds like it must have been difficult."
Facilitating body language	Head nods, facial expressions, hand movements
Facilitating utterances	"Uh-huh" "mm-hum" etc
Time management	"We have about 1 minute left, Is there anything else I should know?"
Silence.	

Such devices add variety to the conversation and deemphasize the interrogational nature of the interview. They help elicit information when the physician gets stuck. Silence is a particularly powerful conversational device.

The use of these devices alone will not validate the patient's narrative if the physician does not recognize that there are pieces of information just as important to the patient as biomedical information is to the physician. For example, the patient's primary concern may be getting back to work, He may wish the physician to intervene with the employer. Physicians must elicit and negotiate the role the patient might expect them to assume.

"Information sharing continues to be mostly physician-centered." The history-building approach includes and confirms the illness narrative from the patient's perspective.

Archives Internal Medicine May 26, 2003; 163: 1134-40 "Special Article", commentary, first author Paul Haidet, Veterans Affairs Medical Center, Houston TX www.archinternmed.com

Comment:

This theme has been repeated in the primary care literature. It deserves a reminder from time to time. More and more in today's culture, patients are being enabled to share responsibility for their health and negotiate directions of their own treatment.

Physicians are expert in the biomedical field. Patients are experts in their own personal histories. Patients bring worries, feelings, fears, doubts, hopes, and many questions to the interview. The accomplished primary care clinician listens and lets the patient know that indeed she is listening and understands. She shows the patient compassion and unconditional acceptance.

Other non-directive physician-comments include: "Anything else?" "Can you explain more fully?" "Tell me more." "Do you understand—can I explain more fully?" "Do you have any more questions?"

Perfecting the art of listening is a life-long quest. Few of us clinicians are expert listeners. I know that I am not, but I keep trying. Many times I think of the next step or question in the process of history-taking before allowing the patient to completely finish his comments. RTJ

==========

TWO COLLABORATING ARTISTS PRODUCE A WORK OF ART

(This editorial comments and expands on the preceding.)

"An implication of the phrase 'taking a history' is that the doctor is performing an act of extraction similar to a dentist's removing a tooth. Indeed, the process is often as brutal as it sounds, an assault of closed-ended questions punctuated briefly by faint yes or no answers from the patient, who becomes alienated, uncooperative, and dissatisfied as the process continues."

"Taking a history" implies an aggressor acting on a victim; a taker, and a taker-from. "Building a history" allows for a joint effort between doctor and patient. "Like two writers collaborating on a manuscript, physician and patients pass drafts of the narrative back and forth until both are satisfied and willing to sign the finished work." The patient brings particular and private facts of his life and illness. The physician helps him order the story so that it becomes comprehensible in both humane and medical terms.

Archives Internal Medicine May 26, 2003; 163: 1131-32 Editorial by Frederic W Platt and Constance M Platt, Denver CO. www.archinternmed.com

Comment:

On reviewing these two articles, I considered that, in abstracting them, I had spent too much time and gone into too much detail. I concluded I had not. Patient-centered interviewing is a core skill to be polished over the professional life of each physician. Of course, not all patients or illnesses require the detail outlined in the articles. Primary care clinicians have the challenge of "building a history" from patients who consult over years--trying to understand the meaning and feelings behind the patient's words. And getting to know the patient as an individual. RTJ

It's Still A Privilege To Be A Physician

5-2 WHAT DO DOCTORS FIND MEANINGFUL ABOUT THEIR WORK?

Rapid changes over the past years have questioned the meaning of medical practice. Changes in the structure and process of health care have altered doctor's roles, prerogatives, and financial compensation. Attention has increasingly been given over to the business of medicine and to bureaucratic procedures that do not contribute directly to health. Numbers of physicians are leaving practice.

The authors believe that, with a clear understanding of what nourishes and sustains physicians, physicians can attend more consciously and intentionally to enhancing that which is meaningful and attenuating that which is depleting in their practice. Although medical practice has always been difficult and the risk of burnout close at hand, most practitioners have found that the joys and satisfaction of their work have prevailed over the challenges, enabling them to sustain a lifelong commitment to service.

The authors have conducted workshops, "Meaningful Experiences in Medicine", over the past 13 years to help clinicians reflect on their own experiences in practice and discover and identify what nourishes and sustains them. Physicians were asked to write a brief account of a work-related experience they found meaningful, defined as "something that you found to be important and fulfilling or that reaffirmed your commitment to medicine". In this article they offer words from practicing physicians on themes they wrote about.

Most stories involved one of three major themes:

1) A profound event or emotional experience changed doctor's perspectives about themselves, and about human nature. The experiences included the doctor's emotional experiences with a patient, which led to sharing or reflecting on their own life experience.

> One experience concerned a doctor who home-visited a 4-year old dying of retinoblastoma. The home was ill kept. The mother was utterly isolated—abandoned by family, needed by kids. She had no resources to fall back on—no education, family, friends, spiritual framework. She watched (and smelled) her child's head rot with creeping tumor. She helped the little body stand up to pee. Why was she not crushed? Why was she was not broken? Why am I not crushed seeing her? The doctor drew two conclusions about the world: It is a capricious, horrifying place where tragedy ultimately beats us down. It is a place where, in the face of tragedy, there can be heroic, even victorious love.

This doctor went beyond his initial reaction to be inspired by the mother's courage and acts of love for her son.

Physicians often expand the boundaries of their role as scientifically detached observers. They recognize their patients as fellow human beings rather than objects of care. But, at times, doctors can be shocked by their own detachment.

2) The second theme was about connecting with patients in moments of intimacy.

> A doctor had followed a patient for several years. She had bowel obstruction due to carcinoid tumor, cord compression which failed treatment by radiation, and finally a urinary tract infection and terminal dehydration. "Nearing the end, I said "The end is coming soon . . . do you have anything more you need to say." She opened her eyes and said, "Honey, I love you." And I said "I love you too". She cried, and I cried while I held her hand and stroked her hair. She died several hours later.

Intimacy arose from the patient's emotional expression, and the doctor's willingness to respond

personally and genuinely. The language changed from technical medical jargon to personal narrative. Some doctors have been touched by a patient's concern for the doctor's well being—a role reversal. This doctor felt the role-reversal--the patients concern for the doctor as a person. Connections such as this may lead to discussions about life and what is really important to both patient and doctor.

3) The most common theme in the doctors' stories was making a difference in someone else's life. This was not making a brilliant diagnoses or an adroit technical intervention. Most of these stories took place in the context of chronic, incurable conditions, or end-of-life care. The doctors felt awed and deeply rewarded that their mere presence could be healing and comforting to patients.

> One patient told her doctor "You know, whenever I see you, I feel better. My breathing is better and I feel more relaxed. She touched the doctor and said "Thanks for all you're doing."

Doctors were often surprised to be thanked in the absence of cure or significant improvement. Some felt a shift from frustration because they could not eradicate a chronic symptom, to affirmation for continuing to care, and to do their best. Indeed, most stories took place in settings typically associated with medical failure—death and progressive illness.

DISCUSSION

The authors explored primary care clinicians' meaningful experiences through a narrative analysis of stories written during work shops. Nearly all doctors described non-technical, humanistic interactions with patients as experiences that fulfilled them, and reaffirmed their commitment to medicine. They told stories about crossing from the world of biomedicine into their patient's world. They described relationships deepened through recognizing the common ground of each person's humanity. They were deeply gratified by the intrinsic healing capacity of *simply being there*.

In the absence of cure, the doctors sought other ways to help their patients--appreciating them, maintaining their dignity and comfort, and even expressing love for them.

The participants in the study found ways to stay connected to their chronically ill patients and felt privileged to be healers.

"The essence of primary care may well be the *unwavering presence* of doctors at the sides of their patients whose suffering may be as common and benign as an itch, and as dramatic and life-threatening as metastatic cancer. The patient-physician relationship is the most consistently reported and most powerful determinant for physician satisfaction." These physicians gained a deeper appreciation of what it means to be a human being and a doctor, and how their caring actions, not just their technical ability, were so important to their patients.

Annals Int Med May 6, 2003; 138: 772-75 "Medical Writings", commentary, first author Carol R Horowitz, Mount Siani School of Medicine, New York www.annals.org

Comment:

I have been surprised by the gratitude of some patients for whom I thought I had not done a very good job. And also surprised at the apparent lack of appreciation from some for whom I thought I had done a good job. I believe I "connected" with the first, and did not "connect" very well with the second.

The primary care clinician who caringly follows patients and families for years and through multiple illnesses is the one who benefits most from meaningful relationships.

It's still a privilege to be a physician. RTJ

==========

New Insulin Analogues Make Physiologic Insulin Therapy Realistic

5-3 USING NEW INSULIN STRATEGIES IN THE OUTPATIENT TREATMENT OF DIABETES.

Meticulous glucose control decreases long-term micro-vascular complications. The American Diabetes Association recommends that patients aim for an HbA1c less than 7%. One study reported that only 29% of patients with DM have had their HbA1c measured in the previous year. Of these, 18% had HbA1c of 9.5% or higher. Only 43% had levels less than 7%.

"Most patients with type 2 diabetes **(DM)** progressively lose beta-cell function." Most patients with type 2 DM will eventually need insulin.. Newly diagnosed patients with type 2 DM have less than 25% of normal insulin secretion 6 years after diagnosis.. Almost 80% require insulin by 9 years. This explains the failure of oral agents But clinicians and patients often delay starting insulin. Insulin should be considered when HbA1c approaches 8% despite optimal oral therapy. Switching from oral drugs to insulin at times improves patient's satisfaction, general well-being, and quality of life, especially if the patient previously had poor control.

The greatest change in diabetes therapy in the last decade has been the introduction of insulin analogues. They make physiologic insulin therapy realistic. The onset and duration of action of these analogues mimic normal insulin secretion, thus simplifying dosing and increasing flexibility. This article presents strategies of use of these new analogues--long acting *insulin glargine,* and immediate-short acting *insulin lispro* to achieve more physiologic insulin replacement.

Insulin glargine is peakless with a 20 to 24 hour duration of action. It can be given once a day. Patients may perceive fewer episodes of hypoglycemia and hyperglycemia while taking insulin glargine compared with NPH. (*It can be given at any time of day, provided it is given at the same time each day. RTJ)*

Insulin lispro is given with meals. It acts within 5 to 15 minutes, peaks at 30 to 90 minutes, and remains in the body for 5 hours.

One daily injection of insulin glargine along with mealtime injections of insulin lispro significantly improves glycemic control in patients with poorly controlled type 2 DM. The combination matches each patient's needs, simplifies adjustment of dose, and improves control while causing fewer episodes of hypoglycemia. "They are easier to use than many patients and clinicians realize." The concept of basal-prandial physiologic insulin dosing helps patients improve understanding of their diabetes and increases flexibility. Patients can change meal times or skip meals. Adjustments to dose can be made as patients accumulate experience with their fasting and post-prandial capillary blood glucose levels. *(The recommended <u>plasma</u> glucose levels are 110 mg/dL or lower fasting, and 180 or lower postprandial. Comparable capillary blood levels are about 100 and 165. RTJ)*

JAMA May 7, 2003; 289: 2265-69 "Using New Insulin Strategies In The Outpatient Treatment Of Diabetes. Clinical Applications" first author Dawn E DeWitt, University of Washington, Seattle. www.jama.com

JAMA May 7, 2003; 289: 2254-64 "Outpatient Insulin Therapy In Type 1 And Type 2 Diabetes-- Scientific Review" by the same first author. www.jama.com

The authors make other clinically important points:

1) Caution in prescribing insulin. In view of the increasing numbers of insulin products available, confusion may arise in prescription-writing. The insulin name should be written in full, Use of abbreviations will be confusing. "U" for units may be confused with zero—eg, 5 U can be confused with 50 if not written clearly. Prescribe "units". Insulin glargine and insulin lispro have trade names. It may be safer to prescribe with the generic name.

2) Diabetes treatment is expensive. Oral agents, even generics, used in combination, are often more expensive than insulin products: Costs of insulins vary by drug and dose:

Insulin glargine	1000 units	$44
Insulin lispro	1000 units	$46

Add the costs of needles, capillary blood glucose monitoring, syringes and pen injectors.

Comment:

There are other successful insulin regimens and oral agents combined with insulin. Consult the original article.

The article also discusses the insulin pump.

I believe combined glargine + lispro is the simplest and safest insulin regimen. RTJ

==========

Two Drugs Better Than One

5-4 COMBINATION THERAPY WITH HORMONE REPLACEMENT AND ALENDRONATE FOR PREVENTION OF BONE LOSS IN ELDERLY WOMEN

Increase in bone mineral density **(BMD)** with anti-resorptive therapies correlates well with a reduction in rate of fracture. This study asks: Does hormone replacement therapy **(HRT)** combined with alendronate (*Fosamax*) restore BMD to a greater degree than either agent alone?

Conclusion: Combination therapy was superior to either alone.

STUDY

1. Double-blind, placebo-controlled study randomized 373 community-dwelling women over age 65 (mean 72).
2. The mean BMD in the entire cohort was in the osteopenic classification; 34% had osteoporosis.

   This reflects patients seen in usual clinical practice.

2. Randomized to:

   1) Alendronate 10 mg daily

   2) Conjugated equine estrogen 0.626 with and without medroxyprogesterone. (*About 1/3 of women had a hysterectomy and received estrogen alone. No data on this subset.)*

   3) Both combined

   4) Placebo

3. Mean baseline dietary calcium was ~ 900 mg/day; dietary vitamin D ~ 250 IU/day. All received supplemental calcium and vitamin D. (*Again reflecting the widespread deficiencies of calcium and vitamin D in the*

general USA population. RTJ)

4. Determined BMD at baseline and at 3 years.

RESULTS

1. BMD at 3 years was significantly greater at all femoral and vertebral sites in women treated with combination therapy than in those treated with either drug alone.

2. Mean *annual* percentage change in BMD	Placebo	HRT	Alendronate	Both
Total hip	-0.81	+0.48	+0.97	+1.43
Lumbar spine	-0.53	+1.30	+1.65	+2.58

3. Women treated with alendronate alone had greater increases in BMD over 3 years than those treated with HRT alone—4.2% vs 3.0%.
4. Older patients responded less often.

DISCUSSION

1. Combined therapy resulted in the greatest response at all sites.
2. Alendronate alone resulted in greater response than HRT alone.
3. The authors estimated that adding HRT to alendronate would result in an 8% reduction in fracture risk.
4. "For elderly women in whom hormone or estrogen replacement is a therapeutic alternative, combination therapy with a bisphosphonate can be considered to further improve skeletal integrity, and may be an option for women who fail to achieve an adequate response on monotherapy, or for women with more severe disease for whom monotherapy would be less desirable."

CONCLUSION

Combination therapy with HRT + alendronate was efficacious and well tolerated. The combination was superior to either drug alone in increasing BMD.

JAMA May 21, 2001;289: 2525-33 Original investigation, first author Susan L Greenspan, University of Pittsburgh Medical Center, Pittsburgh, PA www.jama.com

Comment:

Recently, attention has focused on the adverse effects of combined estrogen/progestin in postmenopausal women—increased incidence of stroke, coronary disease, breast cancer, and thromboembolic disease; and a lower incidence of colon cancer and fracture. Overall, adverse effects outweighed beneficial effects.

A study in Annals Internal Medicine 2003; 138:1-9 reported risk of type 2 diabetes in women taking HRT during a 4-year trial was considerably lower in women taking HRT vs placebo.

I believe the increased risk of stroke and coronary heart disease associated with HRT could be greatly reduced by lowering the dose of HRT and giving concomitant low-dose aspirin.

Both these beneficial factors, if confirmed, plus the added benefit of HRT combined with bisphosphonates on BMD, would tilt the balance toward overall beneficial effects. RTJ

Providing New Guidelines And Key Messages:

5-5 THE SEVENTH REPORT OF THE JOINT NATIONAL COMMITTEE ON PREVENTION, DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD PRESSURE. The JNC-VII Report

1. In persons over age 50, systolic BP over 140 mm Hg is a much more important cardiovascular disease **(CVD)** risk factor than diastolic BP.
2. The risk of CVD, begins at 115/75 and doubles with each 20/10 increment.
3. Individuals who are normotensive at age 55 will have a 90% lifetime risk of developing hypertension. **1**
4. Individuals with a systolic 120-139 or a diastolic 80–90 should be considered as *pre-hypertensive*. They require health-promoting lifestyle modifications to prevent CVD.
5. Thiazide-type diuretics should be used in drug treatment for most patients with uncomplicated hypertension, either alone or in combination with drugs from other classes. Certain high-risk conditions are compelling indications for the initial use of drug from other classes.
6. Most patients with hypertension will require 2 or more drugs to achieve goal BP (< 140/90), or < 130/80 for those with diabetes or chronic kidney disease.
7. If BP is more than 20/10 above goal BP, consideration should be given to *initiating* 2 agents, one of which usually should be a thiazide-type diuretic.
8. The best of therapy will control hypertension only if the patient is motivated.

The committee recognizes that the responsible physician's judgment remains paramount. **2**

JAMA May 21, 2003; 289: 2560-72 "Special Communication" from the National High Blood Pressure Education Program Coordinating Committee, first author Aram V Chobanian, National Institutes of Health, Bethesda MD.

Comment:

The new BP classification of "*prehypertension*" (120-139/80-89) attracted considerable lay-press attention. "Normal" BP is still < 120/80. Prehypertension usually requires only lifestyle modifications, but drugs may be given to some patients in this category if "compelling indications" exist: heart failure; post myocardial infarction; high risk of coronary heart disease; diabetes; chronic kidney disease.

1 We are a nation of people with high BP. I believe, if the guidelines are followed strictly, most would require drug therapy in addition to lifestyle changes. Thus we may become, more and more, a nation of pill-takers.

2 I believe primary care clinicians will use considerable restraint in pushing higher doses of multiple drugs in order to achieve goal BP, especially in their elderly patients. Adverse drug effects and reports of symptoms which may be due to adverse drug effects are more common as patients age. For a number of reasons many elders simply do not tolerate drugs well. The adverse effects can impair quality-of-life to a considerable degree. Go slow—go low as possible. I would settle for somewhere between 140-160 systolic in elderly patients. RTJ

==========

Low-Dose Diuretics Win Again !

5-6 HEALTH OUTCOMES ASSOCIATED WITH VARIOUS ANTIHYPERTENSIVE THERAPIES USED AS FIRST-LINE AGENTS

This meta-analysis summarizes the available clinical trials concerning safety and efficacy of various anti-hypertension therapies used as first-line agents.

Conclusion: Low-dose diuretics are the most effective.

STUDY

1. Extensive systematic review identified long-term randomized controlled trials of antihypertension therapies that assessed major cardiovascular disease end points as an outcome. The authors combined previous meta-analyses, MEDLINE search, and journal reviews.
2. Included studies with both placebo-controls, and those with actively treated controls. Active drug treatments included a variety of first-line agents: diuretics, beta-blockers, alpha blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers. Most studies used more than one drug in the treated group. Agents were usually applied in a stepped-care approach so that the first-line therapy was clearly identified.
3. Data were combined from 42 clinical trials of over 192 000 patients randomized to 7 major treatment strategies. The authors synthesized the evidence into a single meta-analysis.
5. Since high-dose diuretics (starting with 50 mg hydrochlorothiazide or chlorthalidone and titrating upward) are no longer used or recommended, the study was limited to low-dose (12.5 to 25 mg).

RESULTS

1. For all outcomes, low-dose diuretics were superior to placebo. Relative risks:

Coronary heart disease	0.79
Congestive heart failure	0.51
Stroke	0.71
Cardiovascular disease mortality	0.81
Total mortality	0.90

(Lower RR indicates a more favorable outcome from diuretics.)

2. None of the other first-line strategies (noted above) was significantly better than low-dose diuretics for any outcome.
    1) Compared with CCBs, low-dose diuretics were associated with reduced relative risk of cardiovascular disease events (RR = 0.94) and congestive heart failure (0.74);
    2) Compared with ACE inhibitors, diuretics were associated with reduced relative risk of congestive heart failure (0.88), cardiovascular disease events (0.94), and stroke (0.86)
    3) Compared with beta-blockers, diuretics were associated with a reduced relative risk of cardiovascular disease events (0.89);
    4) Compared with alpha blockers, diuretics were associated with reduced risk of congestive

heart failure (0.51) and cardiovascular disease events (0.84)

3. Blood pressure changes were similar between comparison treatments.

DISCUSSION

1. “For all outcomes, low-dose diuretics were superior to placebo.”
2. None of the other first-line treatment strategies was significantly better than low-dose diuretics for major cardiovascular disease outcome.
3. In 8 of the 30 between-drug comparisons, low-dose diuretics were significantly better than other treatments for the prevention of cardiovascular disease outcomes.
4. This provides compelling evidence that low-dose diuretics are the most effective first-line treatment for preventing the occurrence of cardiovascular disease morbidity and mortality.
5. Beta-blockers have long been identified as another preferred first-line treatment. In this analysis they were superior to placebo for prevention of stroke, congestive heart failure, cardiovascular disease events, and total mortality. They were inferior to low-dose diuretics for all outcomes, significantly so for cardiovascular disease events. For uncomplicated hypertension, they should be considered a second-line agent.
6. There are no long-term trials evaluating the optimal second-line therapy: Beta-blockers have been particularly effective for patients with coronary disease and heart failure. ACE inhibitors have proven to be robust therapy, effective in secondary prevention settings, including heart failure and coronary disease. They may be preferred in special populations such as those with diabetes.
7. “The most effective drug was also the least expensive.”

CONCLUSION

Low-dose diuretics are the treatment of first choice for patients with uncomplicated hypertension who require drug treatment. They were the most effective drug for preventing the occurrence of cardiovascular disease morbidity and mortality.

JAMA May 21, 2003; 289: 2534-44 Original investigation, first author Bruce M Psaty, University of Washington, Seattle.

Comment:

This study complements “The Antihypertensive and Lipid-lowering Treatment to Prevent Heart Attack Trial” (ALLHAT) JAMA December 18, 2002; 288: 2981-97. The trial reported that diuretics were unsurpassed in reducing clinical events in a large group of patients at high risk of coronary heart disease.

The preceding study was more generalized. RTJ

==========

May Vary Within A Few Weeks. A Single Test May Be Unreliable. Recheck Before Biopsy

5-7 VARIATION OF SERUM PROSTATE-SPECIFIC ANTIGEN

PSA testing has increased the number of men diagnosed as having prostate cancer **(PC).** Its routine use, however, has been questioned because of lack of specificity (too many false positives). Increasing numbers of men are undergoing radical prostatectomy for small cancers that may be clinically insignificant.

Seventy five % of men with PSA at a level of 4 to10 ng/mL have negative biopsy results.

This study hypothesized that there may be year-to-year natural fluctuations in PSA which may render a single PSA test unreliable. Natural variations in the PSA may occur in the short-term.

The degree of biological variation differs among patients. Some investigators concluded that a number of consecutive PSA measurements would be needed to achieve an estimate near the true mean concentration.

The present study was based on a population of healthy males who had blood drawn for a colon-polyp investigation during which blood was drawn yearly for 4 years. The investigators used the blood samples to perform PSA testing.

Conclusion: An isolated elevation of PSA should be confirmed several weeks later before proceeding with further tests, including biopsy.

STUDY

1. Retrospective analysis of an unscreened population of 972 men (median age = 62.) Obtained 5 blood samples over a 4-year period.
2. Determined total and free PSA levels and other markers.
3. Main outcome = abnormal PSA on repeat testing in groups with PSA higher than 4.0; higher than 2.5; higher than the age-specific cutoff; free to total PSA ratio less than 0.25; and a velocity higher than 0.75 ng/mL per year.

:

RESULTS

1. Of the entire cohort of men many met standard criteria for prostate biopsy on at least one PSA determination:

> 4.0	21%
>2.5	37%
Above age-specific PSA	18%
Free PSA ratio	20%
PSA velocity	15%
Any criterion	37%

(Note the high numbers of presumably healthy men who were considered to have abnormal PSA. RTJ)

2. On repeat examination many with an initial abnormal PSA returned to normal:

Number of participants with normal *second* time PSA after initial abnormal PSA:

> 4.0	30% returned to normal
>2.5	26%
Age-specific PSA	37%

Free PSA ratio 35%

3. A high percentage returned to normal at *any* subsequent visit-- between 65% and 83% of participants.
4. Between 65% and 83% with a previously abnormal test had normal levels on 2 consecutive repeat tests.

DISCUSSION

1. Screening for PC by PSA is widespread. This has led to a rapid increase in prostate cancer incidence, but the impact on PC mortality is not clear. PSA screening is not recommended as a screening tool by the US Preventive Services Task Force. The National Cancer Institute defines PSA testing as a strategy that is still under investigation.
2. About 10% to 15% of men will have a PSA greater than 4 ng/mL and will be recommended to undergo biopsy. (In the present study, 21% of men had a PSA over 4.0 during a 4-year period. Nearly half of these subsequently were found to have a normal PSA.
3. PSA fluctuations may result in many false positive elevations. A single elevated PSA should be viewed with caution.
4. A newly elevated PSA should be confirmed before proceeding with invasive tests.
5. Currently there is no standardized policy for the examination of an elevated PSA. Actual practice includes 3 likely scenarios:
   1) Immediate referral for biopsy. (Discounting any random fluctuations or laboratory error.)
   2) Immediate repeat of PSA. (Assumes a potential laboratory error.) If the second PSA is elevated a biopsy is recommended. If the second PSA is normal, the patient is not referred--the PSA is repeated semi-annually or annually.
   3) Wait 4 to 6 weeks before repeating the test, usually advising the patient to take antibiotics with or without an anti-inflammatory agent. (Assumes inflammation as a cause of the elevation.)
6. The present study repeated PSA once a year. There is no data on the time required for a newly elevated PSA to return to normal if it is to do so.
7. A policy of repeating PSA in 4 to 6 weeks may reduce a number of unnecessary procedures. It is not likely to alter prognosis of efficacy of treatment if cancer is present.

CONCLUSION

An isolated elevation of PSA should be confirmed several weeks later before proceeding with further testing, including biopsy.

JAMA May 28, 2003; 2695-2700 Original investigation, first author James A Eastham Memorial Sloan-Kettering Cancer Center, New York. www.jama.com

Comment:

I agree with the authors. This is a clinically important point. RTJ

==========

5-8 RELATIONSHIP OF CHANGES IN PHYSICAL ACTIVITY AND MORTALITY AMONG OLDER WOMEN

Previous studies have shown that persons who increase their physical activity or fitness over time reduce their risk of cardiovascular and all-cause mortality. This study asks—Do *older* women benefit from increasing their physical activity? It is not clear whether adoption of a physically active lifestyle by previously inactive older women—particularly those with chronic conditions—leads to benefits.

Conclusion: Increasing physical activity levels could lengthen life for older women.

STUDY

1. Prospective cohort study followed over 7500 community-dwelling white women age 65 and older.
2. Assessed walking and other physical activities at baseline.
3. Reassessed physical activity levels 6 years later to determine any change in physical activity over the past 6 years.
4. Determined any change in physical activity during this observation period divided into 4 groups:
    1) Those sedentary both at baseline and on follow-up.
    2) Those physically active at baseline and sedentary at follow-up
    3) Those sedentary at baseline and active at follow-up.
    4) Those physically active at both times
5. Followed for another 6 years to determine mortality
6. Compared rate and cause of death between groups.

RESULTS

1. Median walking distance at follow-up was 1.2 miles/week for those who reported being sedentary at both follow-up visits; 8.2 miles per week among those who became active after being sedentary; and 9.3 miles per week among those who were active throughout.
2. Compared with continually sedentary women, those who increased physical activity levels (group 3) had lower mortality from all cause (hazard ratio = 0.52); lower mortality from cardiovascular diseases (HR = 0.64); and lower mortality from cancer (HR = 0.49) **1**
3. The differences were independent of age, smoking, body mass index, comorbid conditions, and baseline physical activity.
4. Women who were physically active over the 12 years also had lower mortality rates than sedentary women.
5. Hazard rate ratios were lowest for women in the highest quintile for total physical activity.
6. Women who were active at baseline and became sedentary had the same mortality rates as women who remained sedentary over the entire period.

DISCUSSION

1. In this large cohort of white women over age 65 at baseline, remaining physically active and becoming active after baseline, were associated with substantially lower mortality rates. Conversely, women who remained inactive over 12 years and those who became inactive after being active did not benefit.
2. The increase in activity of those in group 3 amounted to only about 1 mile of walking per day.
3. Previously sedentary women who became active had a similar mortality rate as those who were already active.
4. Women who became sedentary after being active had the same mortality risk as those who were sedentary all along.
5. Benefits of activity were evident in those with comorbid conditions such as hypertension, diabetes, cardiovascular disease, and functional difficulties.
6. However, the benefits were less among women over age 75 and in those with poor health status.
7. The authors do remind us that observational studies such as this may mislead because of bias or confounding.

CONCLSUSION

Increasing and maintaining physical activity levels could lengthen life for older women.

JAMA May 14, 2003; 289: 2379-86 Original investigation, first author Edward W Gregg, Centers for Disease Control and Prevention, Atlanta, GA www.jama.com

Comment:

1 I was unable to calculate absolute differences and the numbers needed to treat from their data.

The encouraging message for women is that it may *never be too late* to begin to increase physical activity.

This study was part of the "Study of Osteoporotic Fractures Research Group". I presume one intervention of the study was to encourage older women to become more active in order to slow progression of osteoporosis and prevent osteoporotic fractures.

This study reemphasizes other observations that smokers, patients with cardiovascular disease, and diabetes benefit from becoming more fit regardless of any other change in risk factors. (Eg, risk is reduced by increasing fitness in smokers even if they can't or won't quit.) RTJ

==========

New Concepts: Diastolic Heart Failure And Treatment-Based Stages For Systolic Heart Failure

5-9 HEART FAILURE

(This review article is too long to abstract fully. Primary care clinicians, care for the majority of patients with HF. They may wish to read the entire article. I abstracted two sections of the article which were of particular interest to me

1) Diastolic heart failure. This has remained puzzlement. The author provides some clarification.

2) Stages of heart failure and treatment options for systolic heart failure. This complements the functional NYHA classification (stages I, II, II, and IV). RTJ

DIASTOLIC HEART FAILURE

An estimated 20% to 50% of patients with HF have preserved systolic function (a normal left ventricular ejection fraction.) Although such hearts contract normally, relaxation (ventricular diastole) is abnormal. Cardiac output, especially during exercise, is limited by the abnormal filling characteristics of the ventricles. For a given ventricular volume, ventricular pressures are elevated, leading to pulmonary congestion, dyspnea, and edema identical to that seen in patients with a dilated, poorly contracting heart.

Some characteristics of diastolic HF distinguish it from systolic HF:

- Frequently elderly as opposed to all ages in systolic HF (typically 50-70).
- Frequently female
- Left ventricular ejection fraction preserved, approximately 40% or higher
- Left ventricular cavity size usually normal with concentric left ventricular hypertrophy
- Left ventricular hypertrophy of ECG
- Chest X-ray: congestion without cardiomegaly
- Fourth sound gallop. (Atrial contraction sound.)
- Coexisting conditions: hypertension, diabetes, obesity are especially frequent.
- Atrial fibrillation frequently paroxysmal (opposed to persistent).

Mortality among these patients may be as high as those with systolic HF; rates of hospitalizations are equal.

The diagnosis of diastolic HF is usually made by a clinician who recognizes the typical signs and symptoms of HF and is not deterred by the finding of normal systolic function (ie, a normal ejection fraction) on echocardiography. (Echocardiography may also be useful in detecting diastolic filling abnormalities.)

Diastolic HF has been studied in few trials, so there is little evidence to guide care. The optimal treatment for patients with diastolic HF is not yet established.

Physiological principles used in the treatment include control of BP, myocardial ischemia, and blood volume.

STAGES OF HF AND TREATMENT OPTIONS FOR SYSTOLIC HF

HF is largely preventable, primarily through control of BP and other risk factors. Until recently the factors that rendered a patient at highest risk for HF had not been clearly defined and publicized. A new approach to the classification and progression of HF emphasizes four stages of HF:

Stage A

Patients are at high risk for developing HF, but have no apparent structural abnormality of the heart.

Stage B

Patients have structural abnormalities, but have never had symptoms of HF.

Stage C

Patients with HF have a structural abnormality of the heart, and current or previous symptoms of HF.

Stage D

Patients have end stage symptoms of HF that are refractory to standard treatment.

HF may progress from stage A to stage D in a given patient, but cannot follow the path in reverse. In contrast, a patient with NYHA class IV might have quick improvement to class III with diuretic therapy alone. This staged classification promotes a way of thinking that is similar to our way of thinking about cancer—that is, the identification and screening of patients who are at risk; patients with in situ disease; and patients with established or widespread disease.

Treatment options follow the stages:

Stage A: Risk factor reduction, patient and family education. Treat hypertension, diabetes, dyslipidemia,. Prescribe ACE inhibitors or angiotensin II receptor blockers (ARB) in some patients.

Stage B: ACE inhibitors or ARB in all patients; beta-blockers in select patients.

Stage C: ACE inhibitors and beta-blockers is all patients. Progress to dietary sodium restriction, diuretics, and digoxin. Cardiac resynchronization if bundle branch block present. Revascularization; mitral valve surgery. aldosterone antagonist (spirinolactone) ; natriuretic peptide.

Stage D: Inotropes, ventricular assist device, transplantation, hospice.

NEJM May 15, 2003; 348: 2007-18 Review Article, first author Mariell Jessup, University of Pennsylvania, Philadelphia, PA.

Comment:

The author cautioned against use of NSAIDs. They are associated with increased incidence of new HF, decompensated chronic HF, and hospitalizations for HF. I did not find any reference to low-dose aspirin. RTJ

==========

Burkitt May Have Been Right!

5-10 DIETARY FIBRE AND COLORECTAL ADENOMA IN COLORECTAL CANCER EARLY DETECTION PROGRAMME

More than 30 years ago, Burkitt noted the association of high dietary fiber intake with a low incidence of large bowel cancer in Africa. Still, the association remains controversial.

Adenomas are precursor lesions of colorectal cancer **(CRC).** If increased fiber intake is related to a lower incidence of adenomas, fiber might reduce incidence of CRC.

This study assessed the relation between fiber intake and the risk of colon adenomas.

Conclusion: Dietary fiber was associated with *decreased* risk of distal colon adenomas.

STUDY

1. The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial compared fiber intake of over 33 000 participants (mean age 62) who were simoidoscopically negative for adenomas, with over 3500 patients with at least one histologically verified adenoma of the distal large bowel. (descending colon, sigmoid, and rectum) determined by screening.
2. Determined fiber intake by a 137-item food frequency questionnaire. Determined amount of fiber intake

from grain and cereal, vegetables, legumes, and fruit.

3. Fiber intake ranged from 13 g/d to 36 g/d. (The average USA intake is 16 g/d. Intake of 30-35 g/d is recommended by current guidelines.)
4. Determined differences in incidence of adenomas related to fiber intake.

RESULTS

1. High intakes of fiber were associated with a lower risk of colorectal adenomas. Participants in the highest quintile of dietary fiber intake had a 27% lower risk of adenomas than those in the lowest quintile. (*By my calculation from table 2 p 1493, the NNT over 7 years is about 4000 to prevent one adenoma. This could have an important effect on a population basis* . RTJ)
2. The inverse association was strongest for fiber from grains, cereals and fruits. Fiber from legumes and vegetables provided no statistical benefit.
3. Risks were similar for advanced and non-advanced adenomas.
4. Risk of rectal adenomas was not associated with fiber intake.

DISCUSSION

1. Risk of adenomas in the distal colon and sigmoid was lower in subjects who consumed the greatest quantity of grain, cereal, and fruit fiber.
2. Few participants reported a fiber intake at the level reported from Africa (> 50 g/d).
3. The authors admit that confounding cannot be ruled out in observational studies such as this. (*We have been seriously led astray before by observational studies. RTJ*)

CONCLUSION

Dietary fiber from grains, cereals and fruits was associated with decreased risk of distal colon and sigmoid adenomas.

Lancet May3, 2003; 1491-95 Original investigation, first author Ulrike Peters, US National Institutes of Health, Rockville MD. www.thelancet.com

An editorial in this issue (first author Lynnette R Ferguson, University of Auckland, New Zealand pp 1487-88) comments: Plant cell-walls vary enormously in structure and composition. Different properties are likely to have diverse effects on cancer. This, and differences in amount of fiber consumed, may be a reason for the differing conclusions of studies of the possible benefits of fiber on neoplasms of the colon. Dietary fiber needs to be increased to about 30 g daily before protection can be demonstrated. Fiber itself may not be the protective factor. It may be acting only as a marker for the intake of plant foods which contain a range of components which could be protective against cancer. But, whatever the reason, “Eating a diet rich in plant foods, in the form of fruits, vegetables, and whole-grain cereals probably remains the best option for reducing the risk of colon cancer and for more general health protection.”

Comment:

See also a companion study in this issue pp 1496-1501 "Dietary Fiber In Food And Protection Against Colorectal Cancer In The European Prospective Investigation Into Cancer And Nutrition (EPIC) " "In populations with low average intake of dietary fiber, an approximate doubling of total fiber intake from foods could reduce the risk of CRC by 40%."

No doubt fiber is an important component of the healthy diet. Previous studies have reported cereal fiber reduces risk of cardiovascular disease. RTJ

==========

HRT Increased Risk Of Dementia

5-11 ESTROGEN PLUS PROGESTIN AND THE INCIDENCE OF DEMENTIA AND MILD COGNITIVE IMPAIRMENT IN POSTMENOPAUSAL WOMEN

Postmenopausal women have a greater risk than men of developing Alzheimer's disease. Some authorities have hypothesized that the lower estrogen levels accompanying menopause may remove some putative protective effects of estrogen in delaying onset of Alzheimer's. (Ie, will hormone replacement therapy **(HRT)** lower risk of dementia?)

This study evaluated the effect of estrogen + progestin on incidence of dementia and mild cognitive impairment as compared with placebo.

Conclusion: Estrogen + progestin actually *increased* risk of dementia, and did not prevent mild cognitive impairment.

STUDY

1. Randomized, double-blind, placebo-controlled clinical trial followed over 4500 postmenopausal women, all over age 65 at entry. *(By my calculation, a median age of ~ 72. RTJ*) All were free of probable dementia at baseline.
2. Randomized to:
   1) Conjugated equine estrogen 0.625 mg + medroxyprogesterone 2.5 mg daily, or
   2) Placebo
3. Structured clinical assessment (including the Mini-Mental State Examination) identified incidence of probable dementia and mild cognitive impairment.
4. Mean follow-up = 4 years

RESULTS

1. Outcome over 4 years	Estrogen + progestin (n = 2229)	Placebo (n = 2303)
Probable dementia	40	21
Mild cognitive impairment	56	55

2, Twice as many women in the estrogen group developed probable dementia as in the placebo group:

45 per 10 000 person-years vs 22. *(By my calculation, absolute difference = 0.23 persons per year.. [NNT(to harm one person over 1 year) = 434.] Can this be considered a clinically important adverse effect? RTJ)*

3. Of the probable dementia cases, Alzheimer's disease was diagnosed in 20 of the hormone group vs 12 in the placebo.
4. Treatment effects on mild cognitive impairment did not differ between groups.

DISCUSSION

1. Although participants assigned to active therapy were at about twice the risk for dementia, the absolute risk is low.
2. Some studies suggest that, for hormones to prevent probable dementia, women must initiate its use around the time of menopause. The study could not address that hypothesis. Women in this trial were over age 65.
3. The authors postulate that estrogen + progesterone increases progression of dementia possibly by increasing risk of stroke and undetected microinfarcts of the brain.
4. Estrogen-progestin should not be prescribed with the expectation that it will enhance cognitive performance.

CONCLUSION

Estrogen + progestin *increased* the risk for probable dementia in postmenopausal women age 65 and older.

JAMA May28, 2003; 289: 2651-62 "The Women's Health Initiative Memory Study", original investigation, first author Sally A Shumaker, Wake Forest University Health Sciences, Winston-Salem , NC

Comment:

The estrogen-alone trial continues. It will make an interesting comparison. But previous studies have also confirmed the futility of using estrogen in the elderly or in those with dementia in order to prevent or treat dementia. One of the remaining questions is whether estrogen at the time of menopause, as noted above, makes a difference. CDC

==========

Putting in a pacemaker helped. Turning it on didn't!

5-12 PACEMAKER THERAPY FOR PREVENTION OF SYNCOPE IN PATIENTS WITH RECURRENT SEVERE VASOVAGAL SYNCOPE

Bradycardia often occurs at the time of vasovagal syncope. Prevention of bradycardia by a pacemaker might be a reasonable intervention for prevention. However, some patients have a drop in BP first and develop bradycardia later. If profound hypotension has already occurred, pacing will not help patients even if bradycardia is demonstrated at the time of syncope.

Three previous studies of pacemaker therapy for vasovagal syncope showed a significant benefit and were terminated early. The studies, however, were not double blind. Bias may have been present. The present study attempted to address whether a pacemaker may have affected the incidence of syncope through psychological or emotional mechanisms.

Conclusion: Pacing therapy did not significantly reduce the risk of recurrent syncope in patients with vasovagal syncope.

STUDY:

1. Randomized trial entered 100 patients (mean age = 50). All had at least 3 syncopal episodes in past 2 years or 6 in lifetime. (Mean total events = 18; mean events in past year = 4.) All had a positive tilt table test.
2. Patients excluded for heart disease, EKG anomaly, any major noncardiovascular disease, or any other cause of syncope.
3. All received implantation of a dual chamber pacemaker. After implantation patients were randomized to 1) dual-chamber pacing (DDD) or 2) sensing without pacing (ODO). Both patients and their physicians remained blinded.
4. Pacemakers in patients randomized to DDD was programmed to pace if the patient's pulse dropped 20 beats per minute, or if pulse fell below 70. The intervention rate was 100 beats per minute for 2 minutes.
5. Primary outcome was transient loss of consciousness with prompt spontaneous recovery.
6. Patients kept diaries and recorded symptoms of impending loss of consciousness that did not progress to syncope (defined as presyncope).
7. Follow-up = 6 months

RESULTS:

1. Outcome

	Pacer active (n = 48)	Pacer turned off (n = 51)
Syncope in 6 mo	16 (33%)	22 (42%) [Not significant]
Pre syncope	46	49
Major complications*	1	1
Minor complications **	9	8

(* Pericardial tamponade and infection requiring reimplantation.)

(** Lead dislodgement, infection requiring antibiotics, vein thrombosis, wound hematoma, pain.)

2. Cumulative risk of syncope at 6 months was 31% for the DDD group and 40% for the ODO group (not significant).

DISCUSSION:

1. Syncope as an outcome can have a major subjective component and is difficult to verify objectively.
2. The main finding in this trial was that a statistically significant benefit was *not* found for pacemaker therapy in patients with vasovagal syncope.
3. This study was designed to detect a relative risk reduction with pacing of 50%. The observed relative risk reduction was 30% with a wide 95% confidence interval. A relative risk reduction of 50% with pacing is unlikely, but still plausible. However, the large relative risk reductions in previous unblinded studies (~ 80%) are unlikely.
4. The authors believe that a relative risk reduction of 50% would be the minimum effect size to justify the cost and complications of invasive pacemaker therapy.

CONCLUSION:

The complications of pacemaker therapy and the frequency of syncope recurrence do not recommend it as first-line therapy.

JAMA May 7, 2003; 289: 2224-2229**.** Second vasovagal pacemaker study (VPSII): A Randomized Trial

First author Stuart J. Connolly, MD, McMaster University, Hamilton, Ontario. www.jama.com

Comment:

I thought this was interesting in several aspects. The ability to double blind a surgical procedure is difficult due to the ethical concerns. Since the previous studies showed benefit and the pacemaker of the ODO patients could be turned on after the study, the ethical questions seemed addressed. The powerful placebo effect of surgery has been demonstrated before and appears to be present here

There is an editorial in this same issue on diagnosis and treatment of vasovagal syncope. In brief, volume expansion with salt, fluid intake, and support hose are standard care, but there are no controlled trials. B-blocker therapy and vasocontrictive agents were not found effective in controlled trials, although midodrine (*ProAmatine*), an alpha-1 agonist, was effective in a small trial of patients with severe vasovagal syncope. It has venoconstrictive as well as arterioconstrictive effects. Paroxetine (*Paxil*) also was beneficial in a small study. Serotonergic mechanisms have a major role in vasovagal syncope. CDC

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

:

: