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HIGHLIGHTS MAY 2000

5-1 BENEFICIAL EFFECTS OF HIGH DIETARY FIBER INTAKE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

A high intake of dietary fiber (25 g soluble, 25 g insoluble — about 3 times the usual US intake) derived from natural foods without fortification by fiber preparations and supplements, improved glycemic control, decreased hyperinsulinemia, and lowered lipids in patients with type 2 diabetes. The diet was palatable and accepted.

5-2 DIETARY TREATMENT OF DIABETES MELLLITUS

Dietary manipulation produces dividends in patients with diabetes. Combining foods with high fiber content and a low glycemic index lowers blood glucose synergistically.

The key element in dietary change is the acceptability of the food choices. If dietary modifications are attractive to patients, they will be successful.

The key to dietary change is the repetition of dietary education by the primary care physician at each visit.

5-3 LONG-TERM ACE-INHIBITOR THERAPY IN PATIENTS WITH HEART FAILURE OR LEFT-VENTRICULAR DYSFUNCTION: A Systemic Overview Of Data From Individual Patients

A variety of ACE inhibitors reduce mortality, myocardial infarction, and hospital admission for heart failure in patients with left-ventricular dysfunction or heart failure, with or without a recent myocardial infarction. Benefits began within a week and continued for 3 years. Those with the greatest impairment in left ventricular function benefited the most. Use of ACE inhibitors should be a part of routine practice in these patients.

5-4 EFFECT OF LOSARTAN COMPARED WITH CAPTOPRIL ON MORTALITY IN PATIENTS WITH SYMPTOMATIC HEART FAILURE: RANDOMISED TRIAL — The Losartan Heart Failure Survival Study ELITE II

The angiotensin II blocker losartan was not superior to the ACE inhibitor captopril in improving survival of elderly heart failure patients. ACE inhibitors should be the initial treatment. Angiotensin II blockers may be useful if ACE inhibitors cannot be tolerated.

5-5 HOW TO IMPROVE COMMUNICATION BETWEEN DOCTORS AND PATIENTS

There are 3 distinct approaches to treatment decision-making that doctors can make. Each has different implications for the roles of doctors and patients in communicating information, and the type, amount, and flow of information between the two: 1) the paternalistic approach, 2) the informed approach, and 3) the shared approach. In the 3rd approach, doctors commit themselves to an interactive relationship with patients in developing a treatment recommendation that is consistent with patient values and preferences.

5-6 INSULIN GLARGINE

This new long-acting insulin analogue (now approved by the FDA) supplies basal insulin requirements throughout 24 hours. By mimicking nature, use of an insulin with a peakless action profile should improve blood glucose control. Combining insulin glargine with short-acting insulins at mealtime should optimize control.

5-7 PANIC DISORDER —IT'S REAL AND IT'S TREATABLE

Treatment with the tricyclic antidepressant imipramine, combined with psychotherapy was superior to placebo. Drug treatment works best in the context of a therapeutic patient-physician relationship. "It is essential that primary care physicians recognize PD, make the diagnosis after appropriate evaluation, inform patients that they have a very real disorder that can be treated effectively, and assist them in obtaining appropriate treatment."

5-8 THE GLOBAL PROBLEM OF MULTI-DRUG RESISTANT TUBERCULOSIS.

Directly observed therapy short-course therapy (DOTS) even if well done, will not control MDRTB in countries in which substantial numbers of these organisms are now circulating. A poorly implemented DOTS rapidly generates more MDRTB cases. A new program has been proposed — the DOTS-Plus.

5-9 IN SEARCH OF A GOOD DEATH

A focus group observational study describes 6 attributes of a good death. The culture of death has changed dramatically. Death is considered a natural part of life, not a failure of technology. Psychosocial and spiritual issues are as important as physiologic concerns. The quality of dying is related to acknowledgement of the lifetime context.

Helping persons to achieve a good death is a skill that is rarely natural — it must be learned.

5-10 REGULAR INHALED SALBUTAMOL AND ASTHMA CONTROL: The Trust Randomised Trial

There was no evidence that 4-times daily regular use of the short acting inhaled beta-agonist salbutamol for a year increased the exacerbation rate of asthma.

5-11 META-ANALYSIS OF INCREASED DOSE OF INHALED STEROID OR ADDITION OF SALMETEROL IN SYMPTOMATIC ASTHMA. (MIASMA)

A clinically important point. Addition of the long-acting beta-agonist, salmeterol, to inhaled steroids in patients with symptomatic asthma improved lung function, increased the number of days and nights without symptoms, and reduced the need for rescue medication with no increase in exacerbations. This will spare patients the possible long-term adverse effects of inhaled steroids.

5-12 CARDIOPULMONARY RESUSCITATION BY CHEST COMPRESSION ALONE OR WITH MOUTH -TO-MOUTH VENTILATION

Bystander-witnessed cardiac arrest treated by cardiac compression alone was just as beneficial as cardiac compression plus mouth-to-mouth ventilation. This will lead to greater willingness of bystanders to apply CPR

5-13 CARDIOPULMONARY RESUSCITATION -- STRENGTHENING THE LINKS IN THE CHAIN OF SURVIVAL

Bystander-initiated CPR is critical. But a survey of laypersons assumed to know basic CPR, reported that only 15% would definitely perform CPR on a stranger that would require mouth-to-mouth ventilation. In contrast 68% would perform cardiac compression alone. The majority had an aversion to mouth-to-mouth breathing, or a fear of infection.

5-14 EFFECT OF POPULATION SCREENING AND TREATMENT FOR *HELICOBACTER PYLORI* ON DYSPEPSIA AND QUALITY OF LIFE IN THE COMMUNITY: A Randomized Controlled Trial

Community screening and treatment for *H pylori* produced only a 5% reduction in dyspepsia. This small benefit had no impact on quality of life.

Should we screen for *H pylori* in patients with troublesome, persistent dyspepsia? One approach would be to first perform endoscopy for diagnosis and reassurance. Screening for the infection would be a reasonable accompaniment. If positive, many primary care physicians would treat the infection even when a peptic ulcer was not present to possibly prevent development of future ulcer or cancer. There is a slight chance this will lead to symptom improvement.

5-15 HELICOBACTER PYLORI — IS IT A NOVEL CAUSATIVE AGENT IN VITAMIN B12 DEFICIENCY?

H pylori may be a causative agent in adult B12 deficiency — possibly by causing food-cobalamin malabsorption. Eradication of the infection without B12 supplementation led to normal serum B12 levels and cure of the anemia.

5-16 LINKS BETWEEN HELICOBACTER PYLORI INFECTION, COBALAMIN DEFICIENCY, AND PERNICIOUS ANEMIA.

There are many causes of B12 deficiency, pernicious anemia and food-cobalamin malabsorption the 2 main causes. Primary care clinicians may keep in mind the possibility that H pylori may underlie B12 deficiency.

5-17 RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF FLUTICASONE PROPRIONATE IN PATIENTS WITH MODERATE TO SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE; THE ISOLDE TRIAL

The improvements in clinical outcomes support the use of long-term inhaled corticosteroids in patients with moderate to severe COPD. However, benefits are minor.

5-18 SECONDARY PREVENTION OF PERIPHERAL VASCULAR DISEASE

Peripheral arteriosclerosis is always associated with atherosclerotic disease elsewhere. It is a valid marker for coronary, renal, and carotid disease. They share the same risk factors and treatment

5-19 STEROID THERAPY FOR VISUAL LOSS IN PATIENTS WITH GIANT-CELL ARTERITIS

Giant-cell arteritis (temporal arteritis) ranks as the prime medical emergency in ophthalmology. "There is no other disease in which the prevention of blindness depends so much on prompt recognition and early treatment."

Primary care physicians should be alert to the association with the vasculitis of polymyalgia rheumatica, and obtain immediate consultation. Corticosteroid treatment saves vision.

5-20 ORAL CLONIDINE IN POSTMENOPAUSAL PATIENTS WITH BREAST CANCER EXPERIENCING TAMOXIFEN-INDUCED HOT FLASHES

An occasional patient may be relieved of very troublesome symptoms by a medication with low toxicity.

5-21 GUIDELINES FOR MANAGING ACUTE BACTERIAL MENINGITIS.

The British Infection Society has issued guidelines making recommendations for management of suspected or diagnosed acute bacterial meningitis and meningococcal disease, and for prevention of secondary cases by vaccination and prophylactic antibiotic treatment. "In patients with obvious meningococcal disease penicillin is the drug of choice."

5-22 DOUBTS RAISED ABOUT SAFETY OF THROMBOLYSIS IN ELDERLY

Doubts raised about safety of thrombolysis in patients age over 75 given for treatment of acute myocardial infarction. Lower doses of the thrombolytic agent combined with a platelet glycoprotein IIb/IIIa inhibitor may be safer.

5-23 A 52-YEAR-OLD SUICIDAL MAN

Reference article presents the Harvard Department of Psychiatry and National Depression Screening Day Scale. Depression screening has been proven to be an effective way of identifying those with undiagnosed depressive illness and a useful tool for the primary care physician attempting to ascertain the likelihood and severity of depression and the presence of suicidal thoughts.

5-24 VIOLENCE IN PUBLIC HEALTH AND PREVENTIVE MEDICINE

This issue presents 9 articles on violence**.** "We can prevent violence if, and only if, we replace the moral and legal approach to it, which is based on moral condemnation, shaming, and punishment. This is a matter of vital importance to the future of humanity, in which the medical profession can serve as an invaluable role as educators and leaders."

REFERENCE ARTICLES

5-23 A 52-YEAR-OLD SUICIDAL MAN

http://jama.ama-assn.org/issues/v283n20/rfull/jxr00002.html

5-25 VASCULITIS

http://www.bmj.com/cgi/content/full/320/7245/1325

5-26 VARICOSE VEINS

http://www.bmj.com/egi/content/full/320/7246/1391

RECOMMENDED READING

5-5 HOW TO IMPROVE COMMUNICATION BETWEEN DOCTORS AND PATIENTS

http://www.bmj.com/cgi/content/full/320/7244/1220

5-24 VIOLENCE IN PUBLIC HEALTH AND PREVENTIVE MEDICINE

http://www.thelancet.com/newlancet/sub/issues/vol355no9217/series1802.html

5-9 IN SEARCH OF A GOOD DEATH

http://www.annals.org/issues/v132n10/full/200005160-00011.html

5-1 BENEFICIAL EFFECTS OF HIGH DIETARY FIBER INTAKE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

The American Diabetes Association recently revised dietary guidelines. The guidelines include an alternative approach — replacing saturated fat with cis-monounsaturated fat (eg, olive oil as opposed to trans-fat in hydrogenated margarines). This is similar to the Mediterranean diet. They also recommended a moderate increase in intake of dietary fiber to 20 to 35 g daily because of the cholesterol-lowering effects of soluble fiber. However, the effects of dietary fiber on glycemic control were considered inconsequential. They also considered it difficult to achieve a high dietary intake of soluble fiber without consuming foods or supplements fortified with fiber.

This study assessed the effect of increasing intake of dietary fiber on glycemic control and lipid profiles exclusively through the consumption of foods not fortified with fiber but containing more fiber than the ADA recommends.

Conclusion: The high dietary fiber diet improved glycemic control and the lipid profile.

STUDY

1. Randomized, cross-over study entered 13 patients with type 2 diabetes.
2. Randomized to: 1) diet containing moderate amounts of fiber (total 24 g — 8 g soluble, 16 g insoluble) as recommended by the ADA, or 2) a high fiber diet (total 50 g — 25 g soluble, 25 g insoluble). Diets were prepared in a research kitchen and contained the same macronutrient and energy content.
3 The high fiber diet contained unfortified foods with naturally higher fiber content: cantaloupe, grapefruit, orange, papaya, raisins, lima beans, okra, sweet potato, winter squash, zucchini, granola, oat bran and oatmeal. No fiber supplements were used.
4. Diets were consumed for 6 weeks. Subjects were then crossed-over to the other diet for another 6 weeks.

RESULTS

1. Mean outcomes at 6 weeks— high fiber diet vs the ADA diet:

Total cholesterol	-14%
Triglycerides	-21%
VLDL cholesterol	-5%
LDL- cholesterol	-9%
HDL-cholesterol	-1%

DISCUSSION

1. The intake of fiber in the Western populations is low, averaging 17 g in the U.S. It is feasible to increase a high intake of soluble fiber by consuming unfortified foods. Subjects accepted the diet well. It had few side effects. The investigators believe that such diets are more palatable than diets fortified by fiber preparations and supplements.
2. In this study, the diets were comparable in caloric and nutrient content. Only the fiber

intake differed. Results were not related to weight loss — there was none.

3. The high fiber diet improved glycemic control.
4. The mechanisms for the improvement in glycemic control remain undefined. Whether the effect is due to soluble fiber or insoluble fiber, or both, is unclear. Previous studies reported the effect on cholesterol was due to soluble fiber.
5. The fiber may increase fecal excretion of bile acids and result in lowered absorption of fat. Another possible mechanism is a delayed absorption of carbohydrates.

CONCLUSION

A high intake of dietary fiber, particularly the soluble type, above the level recommended by the ADA, improved glycemic control, decreased hyperinsulinemia, and lowered lipids in patients with type 2 diabetes.

NEJM May 11, 2000; 342: 1392-98 Original investigation, first author Manisha Chandalia, University of Texas Southwestern Medical Center, Dallas.

http://www.nejm.com/content/2000/0342/0019/1392.asp

Comment:

The fiber story as related to diabetes is over 25 years old. I am impressed by the recurring evidence of benefits of the Mediterranean-type diet. I believe that frequent small feedings during the day, combined with the high fiber diet will result in additional lowering of glucose load and insulin response.

Success and use of this type of diet will depend on palatability. No diet will be used long-term by the general public unless it is palatable.

I believe primary care physicians should, with the help of their dietician colleagues, encourage diets high in fiber and educate the general population about the benefits. This will lead to improvement in lipid profiles as well as improved glycemic control. This will lead to benefits in primary as well as secondary prevention of cardiovascular disease and complications of diabetes. RTJ

5-2 DIETARY TREATMENT OF DIABETES MELLLITUS

(*This editorial comments and expands on the preceding study and adds comments on the glycemic index*)

In the preceding study, a high natural fiber diet was associated with a 10% lower 24-hour plasma glucose concentration (ie, the area under the curve), and a 12% lower plasma insulin concentration, compared with the ADA diet. "The overall decrease in plasma glucose was similar to that typically achieved with an oral hypoglycemic drug."

Increasing dietary fiber as a treatment for diabetes is actually less controversial than the related concept of using foods with a low glycemic index.

The glycemic index refers to the increase in plasma glucose concentrations in the 3 hours after consumption of a test food containing 50 g of available carbohydrate. The index is calculated by comparing the elevation of

glucose with that produced by a reference food, typically white bread with equivalent carbohydrate content. The index is minimally affected by its protein and fat content.

Foods with a high fiber content typically have a low glycemic index. However, the two concepts are independent. Foods with both a high fiber and a low glycemic index raise post prandial glucose less than foods with the same fiber content and a high glycemic index. The glycemic index has been calculated for a large number of foods. Although use of this index is complicated, low gycemic index diets reduce hyperglycemia in type 2 diabetes. And, in type 1 diabetes as well, variation in postprandial glucose is affected primarily by glucose load.

In type 2 diabetes, early-phase insulin release is deficient. Although substantial insulin release can occur later, the decreased early-phase insulin leads to post prandial hyperglycemia. Carbohydrates with a high fiber content and a low glycemic index may delay absorption of glucose, thereby permitting a better match between the timing of insulin release and peak glucose concentration.

"It is clear that dietary manipulation produces dividends in patients with diabetes." Combining foods with high fiber content and a low glycemic index lowers blood glucose synergistically.

"The key element in dietary change is the acceptability of the food choices. If dietary modifications are attractive to patients, they will be successful."

"The key to dietary change is the repetition of dietary education by the primary care physician at each visit."

NEJM May 11, 2000; 342: 1440-41 Editorial by Marc Rendell, Creighton Diabetes Center, Omaha, Nebraska.
http://www.nejm.com/content/2000/0342/0019/1440.asp

5-3 LONG-TERM ACE-INHIBITOR THERAPY IN PATIENTS WITH HEART FAILURE OR LEFT-VENTRICULAR DYSFUNCTION: A Systemic Overview Of Data From Individual Patients

Many questions remain about the effect of ACE-inhibitor therapy for heart failure (**HF**). What is the size of the ACE-inhibitor treatment benefit on mortality? Is hospital admission for heart failure and recurrent myocardial infarction (**MI**) reduced? Do benefits begin soon after randomization, and how long do they persist?

This study assessed long-term effects.

Conclusion: ACE inhibitors lowered rates of mortality, myocardial infarction, and hospital admission for HF in patients with left ventricular dysfunction or HF, with or without a recent MI.

STUDY

1. Prospective systematic overview was based on data from 5 long-term randomized trials of (over 12 500 patients; mean age = 61) that assessed ACE-inhibitor therapy vs placebo in patients with left-ventricular dysfunction or HF. (ACE-inhibitors included captopril, ramipril, trandolapril and enalapril.)
2. 54% had myocardial infarction; 18% diabetes; 35% hypertension.
3. Mean ejection fraction = 29%
4. Mean time from onset of symptoms to randomization = 8 days.

5. Average follow-up = 3 years.

RESULTS

1. Three post-infarction trials:		ACE-inhibitors		Placebo	Difference
Mortality		23.4%		29.1%	5.7%
Readmission for HF		11.9%		15.5%	3.6%
Reinfarction	10.8%		13.2%	2.4%	
Composite of events		35%		41.9%	6.9%
2. For all trials:					
Mortality		23%		26.8%	3.8%
Reinfarction	8.9%		11%	2.1%	
Readmission for HF		13.7%		18.9%	5.2%
Composite of events		33.8%		41%	7.2%

3. Benefits started early after therapy and continued long-term.
4. Benefits were independent of age, sex, and use of diuretics, aspirin, or beta-blockers.

DISCUSSION

1. Overall a 7% absolute reduction in composite endpoints over 3 years in patients receiving ACE-inhibitor vs placebo. NNT(benefit one over 3-years) = 14. Or 1000 persons treated to prevent at least one event in 70.
2. There was a graded relation between the degree of left-ventricular dysfunction (measured by ejection fraction) and benefit. (Ie, the greater the impairment, the greater the benefit.)
3. However, there was a clinically important benefit among patients with relatively preserved left-ventricular function.
4. There was no effect on incidence of stroke. (Surprising, since BP was reduced in the treatment groups. However, the mean entry BP was low. Other studies have reported a reduction in stroke.)
5. There was an additive effect of an ACE-inhibitor in patients receiving a beta-blocker.
6. These data tend to justify the use of ACE-inhibitors in patients with left-ventricular dysfunction or HF regardless of the proximity of an MI.
7. “ACE inhibitors should be routinely used in all eligible high-risk patients.”

CONCLUSION

ACE inhibitors reduce mortality, myocardial infarction, and hospital admission for heart failure in patients with left-ventricular dysfunction or heart failure, with or without a recent myocardial infarction. Use of ACE inhibitors should be a part of routine practice in these patients.

Lancet May 6, 2000; 355:1575-81 original investigation, by the ACE-inhibitor Myocardial Infarction Collaborative Group, first author Marcus D Flather, Hamilton Health Sciences Corporation Research Centre, Hamilton, Ontario, Canada.

http://www.thelancet.com/newlancet/sub/issues/vol355no9215/article1575.html

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5-4 EFFECT OF LOSARTAN COMPARED WITH CAPTOPRIL ON MORTALITY IN PATIENTS WITH SYMPTOMATIC HEART FAILURE: RANDOMISED TRIAL — The Losartan Heart Failure Survival Study ELITE II

BACKGROUND

1. ACE-inhibitors (eg, captopril) block the conversion of angiotensin I to angiotensin II.
2. Angiotensin antagonists (eg, losartan) block the action of angiotensin II on the cell.
3. ACE-inhibitors have another action. They block the degradation of bradykinin. (Angiotensin blockers do not.) The increased concentrations of bradykinin cause some adverse effects, including cough and angioneurotic edema.)

The ELITE I [1] study reported a survival benefit (46% risk reduction) by treatment with the angiotensin II antagonist, losartan (*Cozaar*) compared with the ACE-inhibitor captopril (*Generic*) in elderly heart-failure (**HF**) patients.

This present study was designed to confirm whether losartan was superior to captopril in improving survival.

Conclusion: Losartan was not superior.

STUDY

1. Double-blind, randomized, controlled trial entered over 3000 patients — all over age 60. (Mean = 71)
2. All had class II, II, or IV HF and an ejection fraction < 40%.
3. Randomized to: 1) losartan 50 mg once daily, or 2) captopril titrated up to 50 mg three times daily.
4. Median follow-up = 18 months.

RESULTS

1. There were no significant differences in annual rate of all cause mortality (losartan 11.7% vs captopril 10.4%); sudden death or resuscitated arrests (9% vs 7.3%).
2. However, significantly more patients in the ACE-inhibitor groups discontinued medication because of adverse effects, including cough. (14.5% vs 9.4%)
3. In the subset of patients taking a beta-blocker at baseline, those assigned to captopril had a much lower risk of death than those assigned to losartan. (Hazard ratio losartan/captopril = 1.77)

DISCUSSION

1. Losartan was not superior to captopril.
2. Losartan was better tolerated.
3. The ELITE I study of 722 patients reported a 46% lower mortality in those assigned to losartan vs

those assigned to captopril. The investigators were surprised that Elite II, a larger study, did not confirm the smaller. They now consider the findings of ELITE I due to chance.

4. In the subset of patients taking a beta-blocker at randomization, those assigned to captopril had a lower risk of death than those assigned to losartan.
5. "We believe that clinicians should prescribe an ACE inhibitor for the initial treatment of patients with heart failure and systolic left ventricular dysfunction."
6. "ACE inhibitors should remain the treatment of choice in heart failure." In patients in whom ACE inhibitors are not tolerated, an angiotensin II antagonist might be a useful alternative agent to block the renin-angiotensin-aldosterone system.

CONCLUSION

The angiotensin II blocker losartan was not superior to the ACE inhibitor captopril in improving survival of elderly heart failure patients. ACE inhibitors should be the initial treatment. Angiotensin II blockers may be useful if ACE inhibitors cannot be tolerated.

Lancet May 6, 2000; 355: 1582-87 Original investigation by the ELITE investigators, first author Bertram Pitt, University of Michigan, Ann Arbor.

http://www.thelancet.com/newlancet/sub/issues/vol355no9215/article1582.html

1 Lancet 1997 ; 349: 747-52 "Randomized Trial of Losartan versus Captopril in Patients over 65 with Heart Failure." **http://www.thelancet.com/newlancet/sub/issues/vol349no9054/article747.html**

Comment:

Drugs inhibiting the renin-angiotensin-aldosterone cascade have been one of the major advances in therapeutics over the past 10 years.

I abstracted this article for several reasons:

1. Clinicians must remain cautious in accepting enthusiastic results of a first study, even if the study appears well conducted. Wait for confirmation and general usage before switching from a drug that has established benefits. There have been a number of articles in the major peer-reviewed journals reporting benefit which were later retracted.
2. Combining a beta-blocker with inhibition of the angiotensin-aldosterone system by an ACE-inhibitor yielded added benefits.
3. The angiotensin antagonists remain a valuable therapy when ACE inhibitors are not tolerated.

RECOMMENDED READING

5-5 HOW TO IMPROVE COMMUNICATION BETWEEN DOCTORS AND PATIENTS

At times, doctors and patients talk to each other with different voices. The voice of medicine is characterized by medical terminology, objective descriptions of symptoms, and classification of these within a reductionist

biomedical model. The voice of patients is characterized by non-technical discourse about the subjective experiences of illness within the context of social relationships and the patient's everyday world.

Typically, doctors have more power to structure the nature of the interaction. Consequently, patients may feel that their voice is overridden, silenced, or stripped of personal meaning.

To improve communications, we need to understand the nature of the decision making process taking place in the consultation. Misunderstandings associated with prescribing decisions leading to potential adverse consequences[1], are associated with a lack of patient participation in decision-making in terms of voicing expectations, preferences, and responses to doctor's actions.

A second article[2] explores the agendas that patients bring to the discussion with their doctor at a forthcoming consultation; those aspects of patient's agendas that they actually voice in the consultation; and the effects of unvoiced agendas on patients' subsequent behavior. Most patients did not voice all their agenda items. Unvoiced agenda items led to specific problems such as unwanted prescriptions and non-adherence. Doctors are urged to practice shared treatment decision-making with their patients. Unspoken patient agendas are barriers to this goal.

The editorialist comments that qualitative interviews such as those used in both studies, are longer and more open-ended than a normal consultation.

Decision-making about treatment in the medical encounter is a complex and dynamic process, the course of which is not predictable in advance. No two encounters are exactly the same.

There are 3 distinct approaches to treatment decision-making that doctors can make. Each has different implications for the roles of doctors and patients in communicating information, and the type, amount, and flow of information between the two:

1. *The paternalistic approach:* Doctors using this approach are not likely to have much interest in discussing patient concerns expressed "in the voice of the life world". They are more likely to want short descriptions of symptoms that can be transformed into diagnostic categories, then make treatment decisions they think are in the patient's best interest without having to explore patient's values and concerns.
2. *The informed approach:* Patients are accorded a more active role in both defining their problem and in determining approach to treatment . The doctor's role is limited to providing relevant research information about treatment options, benefits, and risks, so the patient can make informed decisions.
3. *The shared approach:* Doctors commit themselves to an interactive relationship with patients in developing a treatment recommendation that is consistent with patient values and preferences. The doctor creates an atmosphere in which patients can communicate all their agenda items. Information exchange helps the doctor understand the patient and ensures that the patient is informed of options and risks and benefits. And then permits patients to assess whether they feel they can build a relationship of trust with the doctor.

Most encounters combine elements of all three. The approach adopted at the beginning of an encounter may change as the doctor gains a better sense of whether the patient has understanding of available treatments.

BMJ May 6, 2000; 320: 1220-21 Editorial, first author Cathy Charles, McMaster University, Hamilton, Ontario, Canada

http://www.bmj.com/cgi/content/full/320/7244/1220

1 "Misunderstandings in General Practice Prescribing Decisions" BMJ 2000; 320: 484-88

2 "Patient's Unvoiced Agendas in General Practice Consultations" BMJ May 6, 2000; 320: 1246-50

Comment:

Given the lack of time in a single consultation, and the need to deal with a presenting complaint, physicians will not understand all of a patient's agenda. However, with repeated consultations, doctors have the opportunity ask about concerns, and to more fully understand.

One important way of improving communication in a consultation is to begin with the simple question "What are your concerns today?" Then listen without interruption.

There is great diversity of presenting problems as well as patient's ability to understand treatment decisions (he may be illiterate), to accept them (her culture may differ from the doctor's), and to pay for them long-term (he may lack insurance), and to abide by them (she may be infirm and have no family support).

As we all know, approach must be individualized. However, I believe the shared approach is gaining strength and adherence.

The approach depends a great deal on the presenting disease. For acute illnesses such as sore throat and, especially for serious illness such as meningitis and pneumonia, or severe trauma, patients will expect the doctor to adopt the paternalistic approach, offering immediate advice and treatment without entering into a discussion of patient preferences.

The shared approach pertains mainly to long-standing illness for which there may be different approaches, which entail great expense, and which are not curable.

Many years ago, I was trained in the paternalistic approach. The approach focused on the disease — diagnosis; treatment; making sure that the proper tests were done and interpreted accurately; not missing a diagnosis. I continued to practice in this mode. Now, if I had to do over again, I would more often practice the shared approach and be a much better physician. RTJ

5-6 INSULIN GLARGINE

(*I fast-tracked this brief article from August 2000 to May because of the potential clinical importance. RTJ*)

This new long-acting insulin analogue (*Lantus*) was approved by the U.S. FDA in April 2000 for use in patients with type 1 and type 2 diabetes. “The availability of an insulin preparation that would provide basal insulin requirements has long been awaited.”

What kind of long-acting analogue is insulin glargine? Is it safe? How should it best be used?

Insulin glargine is produced by recombinant DNA technology — adding 2 arginine molecules and substituting one glycine for asparagine. This makes the insulin more soluble at a slightly acidic pH, and less soluble at the physiological pH of subcutaneous tissue. In the bottle, it is a clear solution and does not need shaking for

resuspension. When injected, it forms a microprecipitate at the pH of subcutaneous tissue. Absorption thus lasts a long time and provides a fairly constant basal insulin supply much like that of the basal insulin secretion in non-diabetic persons in the post-absorptive state.

Clearly, insulin-requiring diabetic patients need a long-acting insulin. Glucose homeostasis in the interprandial and nocturnal periods is finely regulated by slow, continuous insulin secretions. Because the plasma concentration of insulin remains steady throughout the night, non-diabetic people do not experience hypoglycemia in the night or hyperglycemia at dawn. NPH insulin and Lente insulin cannot mimic the effect of basal insulin. NPH exhibits a peak action within 3 to 6 hours.

Thus, by mimicking nature, use of an insulin with a peakless action profile should improve blood glucose control in type 1 diabetic patients, especially in those with absolute failure of the pancreatic beta cells.

In type 1 diabetes, the action of a bolus dose of glargine starts about 90 minutes after subcutaneous injection and lasts 24 hours. Most importantly, the action profile mimics closely that of a continuous subcutaneous insulin infusion, the reference standard against which any new candidate “basal” insulin has to be compared.

However, no change in overall glycemic control (or in glycosylated hemoglobin) has yet been observed with substitution of glargine for NPH. Use of glargine could probably be optimized by a regimen of once daily glargine and short-acting insulin analogues at meal times.

“In the 50 years since NPH insulin was devised by Hagedorn and Lente insulin by Hallas-Moller, no improved formulations of intermediate-acting or long-acting insulin preparations have been introduced, until now.”

Ultimately, safety and benefit will be decided by widespread use in the general public.

Lancet August 5, 2000; 356: 443-44 Commentary by Geremia B Bolli , University of Perugia, Italy.
http://www.thelancet.com/newlancet/sub/issues/vol356no9228/commentary443.htm

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5-7 PANIC DISORDER —IT'S REAL AND IT'S TREATABLE

The commentator begins by describing a symptom complex in a healthy young adult for which the most likely diagnosis is panic disorder (**PD**):

> A previously healthy adult presents for urgent evaluation because of the most recent episode of recurrent, spontaneous attacks consisting of a rapid crescendo of intense anxiety accompanied by frightening physical sensations of "pounding heart", chest pain, sweating, shortness of breath, and dizziness, along with a fear of dying or losing control. The patient's medical history, physical examination and ECG (except for sinus tachycardia) are normal.

In 1980 the DSM-3 recognized PD as a syndrome with reliable diagnostic criteria, replacing a number of earlier terms such as: irritable heart, soldier's heart, and hyperventilation syndrome. These terms reflected the prominent cardiac and chest symptoms experienced by these patients. Lifetime prevalence of PD is as high as 3%. Social morbidity is high. Health care service use is high. Many patients suffer agoraphobia and fear of situations in which escape might be difficult or unavailable.

Specific substances such as sodium lactate, carbon dioxide[1] , and cholecystokinin can trigger attacks. Specific drug treatments can block the attacks.

The etiology is unknown. Suggested mechanisms include a dysfunctional brain alarm system possibly involving several neurotransmitters.

Several psychotherapeutic drugs are effective. Cognitive behavioral therapy also may benefit.

A study in this issue of JAMA[2] reported that drug treatment with the tricyclic antidepressant, imipramine (*Tofranil; Generic*) combined with psychotherapy was superior to placebo. The efficacy of imipramine for PD is well established and appears to be comparable to that of the selective serotonin reuptake inhibitors (SSRIs). Drug treatment works best in the context of a therapeutic patient-physician relationship.

Like major depression, PD is usually a chronic, relapsing disorder that requires long-term treatment. "It is essential that primary care physicians recognize PD, make the diagnosis after appropriate evaluation, inform patients that they have a very real disorder that can be treated effectively, and assist them in obtaining appropriate treatment."

JAMA May 17, 2000; 283: 2573-74 Editorial by Richard M Glass, Deputy Editor, JAMA

http://jama.ama-assn.org/issues/vol283n19/ffull/jed00031.html

Comment:

1 I do not understand the mechanism. Anyone out there have an explanation? In the past days, the standard treatment for hyperventilation was rebreathing in a paper bag. The comment that PD can be triggered by carbon dioxide seems contradictory. RTJ

2 "Cognitive-Behavioral Therapy, Imipramine, or Their Combination for Panic Disorder: A Randomized, Controlled Trial" JAMA May 17,2000; 282: 2529-36

5-8 THE GLOBAL PROBLEM OF MULTI-DRUG RESISTANT TUBERCULOSIS.

Drug resistant TB (multi-drug resistant TB— **MDRTB**) was first observed in 1948, subsequent to the first trials of streptomycin. It is recognized as the result of suboptimal treatment. Recently a multinational survey reported 13% of *Mycobacterium tuberculosis* strains were resistant to at least 1 drug, and over 2% resistant to both of the primary drugs used — isoniazid and rifampin.

"Today, most cases of TB are drug susceptible at the time of diagnosis, only to become drug resistant through suboptimal therapy."

The WHO has focused its efforts to combat MDRTB on a strategy of preventing the generation of new MDRTB cases. The program relies on a commitment of local governments to a sustained effort to use case detection by sputum microscopy, directly observed treatment with a standard therapeutic regimen, maintenance of an uninterrupted drug supply, and monitoring outcome.

Carefully supervised TB programs are effective in reducing MDRTB. "A poorly functioning program is worse than none at all; such a program actually produces multidrug resistant TB."

A directly observed therapy short-course (**DOTS**) drug regimen has been increasingly adopted throughout the world. It successfully prevents increase in cases of MDRTB in many countries in which preexisting levels of MDRTB are low.

Until now, it has been unclear whether a good DOTS program should be enough to control MDRTB in countries where it is already established. A study in this issue of JAMA[1] reported that achieving control of MDRTB through establishment of DOTS is false hope. In Peru and South Korea, excellent DOTS have been operating for several years. Despite this, the prevalence of MDRTB in these countries is still substantial among persons with newly diagnosed TB. Since these patients had not been treated, their disease could not have resulted from failed therapy. It must have been due to primary transmission of MDRTB from others in the community. "Multidrug-resistant TB has not been markedly reduced or prevented by the DOTS program and it is unlikely that the rates will decline to low levels without further intervention." "DOTs will not control MDRTB in countries in which substantial numbers of these organisms are now circulating."

What can be done? It is imperative that new treatment strategies be devised for patients with MDRTB. It is also essential that an effective DOTS program be ensured before beginning a MDRTB treatment program. A poor TB control program (ie, an ineffective DOTS) would rapidly generate more MDRTB cases.

A new program has been proposed — the DOTS Plus. This requires drug susceptibility testing, surveillance of trends in susceptibility, and treatment tailored to the results of the susceptibility tests.

If MDRTB increases in developing countries, rates in developed countries will increase as well. "This is not someone else's problem." Containing MDRTB is a public health emergency. Currently available second-line antibiotics to treat MDRTB are 4 to 10 times more likely to fail than standard initial therapy for drug-susceptible TB, and about 100 times more expensive.

Three commitments are required:

1. There must be a commitment to establish effective DOTS in every country in which TB occurs.
2. There must be a commitment to establish DOTS Plus in every country in which there is an effective DOTS and MDRTB persists.
3. There must be a commitment to intensify efforts to develop new drugs for treatment of TB.

JAMA May 17, 2000; 283: 2575-76 Editorial by C Robert Horsburgh Jr. Schools of Public Health and Medicine, Boston University, Boston, Mass.

http://jama.ama-assn.org/issues/v283n19/ffull/jed00029.html

1 "Standard Short-Course Chemotherapy for Drug-Resistant Tuberculosis" JAMA May 17, 2000; 283: 2537-45 The WHO Directly Observed Short-course Treatment of new cases of TB consists of directly observed administration of 4 drugs: isoniazid, rifampin, pyrazinamide, and either ethambutol or streptomycin for a period of 2 months. This is followed by a continuation phase with rifampin and isoniazid for 4 months.

The World Bank considers DOTS one of the most cost-effective interventions in human health. It is now adopted in 119 countries.

Multidrug resistance is defined as resistance to both rifampin and isoniazid. This is a major problem is some countries. If TB is multidrug resistant, the standard short course therapy will be inadequate treatment.

RECOMMENDED READING

5-9 IN SEARCH OF A GOOD DEATH: Observations Of Patients, Families, and Providers

The recent literature has reported a number of articles on death and dying which recognize death as an integral part of living. They define what are considered attributes of a "good death". The message is worth repeating. This is the latest I have encountered. RTJ

"The perception of the quality of death is constructed by family, friends, and health care providers." This study attempts to describe attributes of a good death as understood by patients and other participants in focus groups consisting of various disciplines. They identified 6 major components of a good death:

1. *Pain and symptom management:* Participants fear dying in pain. Portrayals of bad deaths usually mention inadequate analgesia during cure-directed therapies that are perceived as too aggressive. Assurance of adequate morphine administration eases minds.

2. *Clear decision making:* Patients feel empowered by participating in treatment decisions. When anticipatory conversations are not made, and treatment decisions are not clear or delayed until a crisis occurs, patients feel disregarded, family members feel perplexed, and providers feel out of control and fear that they are not providing good care.

3. *Preparation for death:* Patients want to know what they could expect during the course of their illness, and want to plan for the events that would follow — making sure the will is complete, giving directions about the funeral, and writing an obituary gives some a sense of completion and the feeling that burdens would not be placed on others. Bad dying is characterized by lack of opportunity to plan ahead and arrange personal affairs.

4. *Completion*: Patients confirmed the deep importance of spirituality or meaningfulness at the end of life, including issues of faith, reviewing the life story with family, resolving conflicts, spending time with family and friends, and saying goodbye. These issues are highly individualistic. Bad dying is characterized by a lack of meaningful time with family and friends to say goodbye, and inattention to religious and spiritual beliefs.

5. *Contributing to others:* Allow terminally ill persons to contribute to the welfare of others in the form of gifts, time, or knowledge.

6. *Affirmation of the whole person:* Affirm the patient as a unique and whole person. This applies to caretakers who treat the patient, not as a "disease", but understand them in the context of their lives, values, and preferences. Dying patients need an opportunity for life review. .

DISCUSSION

There were differences in perspectives of a good death by individual members of the focus groups . Social workers spoke from a case management perspective and were attuned to the family as the unit of care; chaplains discussed ethical issues; family spoke from the unique role of both patient advocate and recipient of care; physicians' discussions were uniformly more medical in nature.

The study affirmed the importance of the first four themes which are often found in the palliative care literature. The last 2, contributing to others, and affirmation of the whole person, were unexpected and add to our understanding.

Every provider group offered regret-filled stories of patients who died in pain. Concern about undertreatment of pain was consistent across groups. Patients expressed anticipatory fears about pain. Many dying patients are terrified of waking in the middle of the night with intense pain or air hunger. For them a good death includes providers who anticipate these fears.

Providers and family also identified the need for improved communication and clear decision making and feared entering a medical crisis without knowledge of patient preferences.

Participants demanded greater preparation for dying. Some avoided end-of-life discussions because they did not want to remove hope. "However, patients and families feared bad dying more than death."

The culture of death has changed dramatically. Death is considered a natural part of life, not a failure of technology. Psychosocial and spiritual issues are as important as physiologic concerns. "The quality of dying is related to acknowledgement of the lifetime context."

Helping persons to achieve a good death is a skill that is rarely natural — it must be learned.

Annals Int Med May 16, 2000; 132: 825-32 "Perspective" original observations study, first author Karen E Steinhauser, VA Medical Center, Durham, NC

http://www.annals.org/issues/v132n10/full/200005160-00011.html

Comment:

I did not find any direct reference to the need for forgiveness. Assurance of forgiveness for things done, and things not done, without reservation, must be one of the greatest comforts of the dying process. RTJ

5-10 REGULAR INHALED SALBUTAMOL AND ASTHMA CONTROL: The Trust Randomised Trial

Previous studies have reported that long-term regular use of inhaled beta-agonist bronchodilators might lead to a deterioration in asthma control.

This study assessed the effects of regular long-term use of the short-acting beta-agonist salbutamol (Albuterol in U.S.; *Proventil*; *Ventolin*. *Generic*) on the control of asthma.

Conclusion: No evidence that regular use increased exacerbation rate of asthma.

STUDY

1. Multicenter, randomized, double-blind, placebo-controlled trial entered over 950 patients with asthma. (Mean peak expiratory flow = 85% of predicted normal.)
2. All were being treated at least twice a week with a short-acting inhaled beta-agonist. Almost all (90%) also took a daily inhaled corticosteroid (2 mg or less) while continuing the beta-agonist for symptomatic relief. (Most UK patients with asthma use inhaled corticosteroids.)
3. Randomized to: 1) 400 ug salbutamol by diskhaler 4 times daily, or 2) inhaled placebo (+ inhaled beta-agonist as needed for relief).
4. Primary outcome measure = rate of exacerbations of asthma. Exacerbations defined as:

increased use of corticosteroids, and two of following — fall in peak expiratory flow to less than 80% of baseline; bronchodilator use increased by 3 or more inhalations per 24 h; symptom score increased by 2 or more over baseline

5. Follow-up = 1 year.

RESULTS

1. No difference in the annual rate, timing, or duration of exacerbations between groups.
2. Mean morning peak expiratory flow was similar in the 2 groups.
3. In the salbutamol group, mean evening peak expiratory flow was greater. And the use of rescue bronchodilator was less.

DISCUSSION

1. Control of asthma was similar in those taking inhaled corticosteroids plus salbutamol 400 ug 4 times daily over 12 months as in those taking inhaled corticosteroids plus intermittent beta-agonist bronchodilators.
2. Current national (UK) and international asthma management guidelines recommend inhaled beta-agonists should be used only for symptomatic relief, and advise inhaled corticosteroids if beta-agonists are required more than once daily.
4. "Our study provides reassurance that regularly inhaled salbutamol used over 12 months in a normal therapeutic dose, should not affect the rate of exacerbations in most asthmatic patients in th UK."
5. The need for use of increased doses of inhaled beta-agonists is an indication that asthma is not optimally controlled.

CONCLUSION

There was no evidence that 4-times daily regular use of the short acting inhaled beta-agonist salbutamol for a year increased the exacerbation rate of asthma.

Lancet May 13, 2000; 355: 1675-79 Original investigation by The Therapy Working Group of the National Asthma Task Force, first author Sarah M Dennis, St Bartholomew's and the Royal London School of Medicine and Dentistry, UK

http://www.thelancet.com/newlancet/sub/issues/vol355no9216/article1675.html

Comment:

Therapy of asthma rests on corticosteroids. Whether to add an inhaled short-acting beta-agonist, a long-acting beta-agonist, or inhaled ipratropium, or a combination is a matter of individual response and preference.

The main contribution of this study is a reassurance that daily use of modestly high doses of beta-agonists are not harmful. However, it provided little evidence that 4-times daily use was more beneficial than as needed use. Patients who take regular beta-agonists likely have more severe asthma than those who take intermittent beta-agonists.

Note that 2800 potentially eligible persons were screened, 983 were randomized, and 660 (67% of randomized; 23% of potentially eligible) completed the one year study. This indicates the difficulty in acceptance of a protocol asthma treatment by the general public. RTJ

5-11 META-ANALYSIS OF INCREASED DOSE OF INHALED STEROID OR ADDITION OF SALMETEROL IN SYMPTOMATIC ASTHMA. (MIASMA)

Some patients with asthma continue to have symptoms while taking low to moderate doses of inhaled steroids. Which then, is more beneficial — adding the long-acting beta-agonist salmeterol (*Serevent*) or doubling the dose of steroid?

Conclusion: Adding salmeterol was superior.

STUDY

1. Meta-analysis of 9 randomized, double-blind clinical trial collected over 3600 symptomatic patients with asthma. All over age 12..
2. All were taking inhaled corticosteroids (fluticasone or beclomethasone 400 to 1000 ug/d) All continued to have symptoms on their current dose of steroids
3. Randomized to: 1) increased dose of the steroid, or 2) adding salmeterol (dose not specified) to the current dose of steroid.
4. Follow-up = 12 weeks or more.

RESULTS

1.	Salmeterol + steroids vs added steroids
Peak expiratory flow	
At 3 months	Greater by 22 liters /min
At 6 months	Greater by 28 liters /min
FEV1	
At 3 months	Greater by 0.10 liters
At 6 months	Greater by 0.08 liters
Days and nights without symptoms	
At 3 months	Days greater by 12%; nights by 5%
At 6 months	Days greater by 15%; nights by 5%
Days and nights without need for rescue medication	
At 3 months	Days greater by 17%; nights by 9%
At 6 months	Days greater by 20%; nights by 8%

2. Fewer patients experienced any exacerbation of asthma while taking salmeterol. (Difference = 2.7%)
3. Fewer patients had severe exacerbations. (Difference = 2.5%)

DISCUSSION

1. Asthma is defined as a chronic inflammatory disease of the airways. Anti-inflammatory therapy is the cornerstone of treatment. Despite use of inhaled corticosteroids, many patients continue to have symptoms.

2. Adding salmeterol (vs increasing the dose of corticosteroids) led to symptomatic improvement and fewer exacerbations, and improvement in lung function.
3. There was no evidence of increased number of exacerbations. Control of the asthma was not compromised by the salmeterol.
4. The number needed to treat to prevent one exacerbation over 6 months was 40.

CONCLUSION

Addition of salmeterol to inhaled steroids in patients with symptomatic asthma improved lung function, increased the number of days and nights without symptoms, and reduced the need for rescue medication with no increase in exacerbations.

BMJ May 20, 2000; 320: 1368-73 Original investigation, first author Stephen Shrewsbury, Glaxco Wellcome, Uxbridge, UK **http://www.bmj.com/cgi/content/full/320/7246/1368**

5-12 CARDIOPULMONARY RESUSCITATION BY CHEST COMPRESSION ALONE OR WITH MOUTH -TO-MOUTH VENTILATION

In Seattle, where extensive training of citizens has taken place, bystanders do not provide CPR in almost half of witnessed cardiac arrests.

In experimental studies, chest compression alone was associated with survival rates similar to those with chest compression plus month-to-mouth ventilation.

This study compared CPR by chest compression alone with CPR combining chest compression plus mouth-to-mouth ventilation. (Instructions in chest compression plus mouth-to-mouth ventilation given by dispatchers over the telephone take 2.4 minutes.)

Conclusion: Outcomes were similar.

STUDY

1. Fire department telephone dispatchers gave bystanders witnessing a cardiac arrest instructions randomized to:
    1) month-to-mouth ventilation plus cardiac compression (n=279), or
    2) cardiac compression alone (n=241).
2. Subjects averaged age 68.

RESULTS

1. Complete instructions were given to 62% of cases in group 1) and 81% of cases in group 2).
2. Instructions in group 2) required 1.4 minutes less to complete than instructions for group 1).
3. Survival to hospital discharge was higher in the chest compression alone group (15% vs 10%). However the difference was not statistically significant.

DISCUSSION

1. The prevailing opinion in Seattle is that bystander-initiated CPR is a highly effective aid to resuscitation.
2. Seattle has a system with relatively short response time and a tightly structured dispatch protocol. It is assumed that experienced personnel will soon be on the scene. In this situation, chest compression alone was just as beneficial as chest compression + mouth-to-mouth ventilation.
3. Instructions for mouth-to-mouth ventilation are time consuming. Mouth-to-mouth is difficult to carry out. Chest compression alone is relatively simple. Simple instructions to open the upper airway may be added.
4. Cardiac arrest due to primary ventilatory failure is less common than arrest due to cardiac causes. In many cases instructions on mouth-to-mouth ventilation may be an unnecessary addition.
5. Going directly to chest compression may save valuable time.
6. Cerebral arterial oxygenation remains relatively high for a substantial time after onset of ventricular fibrillation. Thus, perfusion of the brain and heart (by chest compression) is more important in the emergency situation than ventilation.

CONCLUSION

"We believe chest compression CPR may be applicable to the more general setting of bystander-initiated CPR." Outcomes with combined mouth-to-mouth ventilation + chest compression were no better than with chest compression alone.

NEJM May 25, 2000; 342: 1546-53 Original investigation, first author Alfred Hallstrom, University of Washington, Seattle.

http://www.nejm.com/content/2000/0342/0021/1546.asp

Comment:

Another change in the fashion of medicine. I believe this may be an important step in the public's willingness to apply CPR. RTJ

The American Heart Association has also simplified CPR guidelines for lay people. "News" Lancet August 26, 2000: 741:

1. Lay people are no longer to check pulse before starting CPR. Their detection of pulse is unreliable.
2. Look for other signs indication the presence of circulation — breathing, coughing, spontaneous motion. If absent, begin chest compression.
3. Now ratio of compressions to mouth-to-mouth breathing is changed to 2 to 15, whether there are one or two rescuers.
4. No longer required to try to clear the airway of unconscious adults. Chest compression

generates enough force to clear most obstructions. Abdominal thrusts (Heimlich maneuver) are still recommended when a choking victim is conscious.

5. Automatic external defibrillators must be made available in all public places where there is a reasonable probability of one sudden death in every 5 years.

5-13 CARDIOPULMONARY RESUSCITATION -- STRENGTHENING THE LINKS IN THE CHAIN OF SURVIVAL

(This editorial comments and expands on the preceding study.)

The major determinants of survival after a witnessed cardiac arrest due to ventricular fibrillation include whether a bystander initiates CPR and how quickly defibrillation is accomplished. Classical studies report that, if CPR is initiated within 4 minutes, and if definitive therapy is delivered within 8 minutes, 43% survived to hospital discharge. Rates decline dramatically to less than 7% if CPR is not initiated within 8 minutes. No patient has survived after 16 minutes of untreated ventricular fibrillation.

Bystander-initiated CPR is critical. But a survey of laypersons assumed to know basic CPR, reported that only 15% would definitely perform CPR on a stranger that would require mouth-to-mouth ventilation. In contrast 68% would perform cardiac compression alone. The majority had an aversion to mouth-to-mouth breathing, or a fear of infection.

At the time of sudden cardiac arrest due to ventricular fibrillation in adults, the pulmonary veins, left atrium, left ventricle, and the entire arterial system are filled with oxygenated blood. “To waste time by performing assisted ventilation before initiating chest compression does not make physiologic sense. The most reasonable response is prompt, rapid, forceful chest compression.”

The chief factor in providing myocardial perfusion during basic CPR is the coronary perfusion pressure – that is, the aortic diastolic pressure (pressure during the release phase of chest compression) minus the coronary sinus or right atrial diastolic pressure. Cerebral perfusion is related to the “systolic” pressure – the pressure during the chest compression phase. If chest compression is interrupted for ventilation, it takes time to build up the coronary perfusion pressure again once the chest compression is reinitiated.

Chest compression alone is easier to learn and more readily initiated.

NEJM May 25, 2000; 342: 1599-1600 Editorial by Gordon A Ewy, University of Arizona Sarver Heart Center, Tucson.

http://www.nejm.com/content/2000/0342/0021/1599.asp

5-14 EFFECT OF POPULATION SCREENING AND TREATMENT FOR *HELICOBACTER PYLORI* ON DYSPEPSIA AND QUALITY OF LIFE IN THE COMMUNITY: A Randomised Controlled Trial

Dyspepsia is common and imposes a substantial clinical and financial burden. The causes of dyspeptic symptoms are poorly characterized. Lifestyle factors such as smoking and alcohol consumption are important, but their overall effect is likely to be small.

H pylori is a necessary, but not sufficient cause of peptic ulcer disease. *H pylori* may have a role in non-ulcer dyspepsia as well. But, studies relating *H pylori* to dyspepsia have resulted in uncertain conclusions due to bias and confounding.

This study was based on the assumption that eradication of *H pylori* in the community would reliably show the effect the infection has on population dyspeptic symptoms.

Conclusion: Community screening and treatment produced only a small reduction in dyspepsia.

STUDY

1. Randomly selected over 8000 subjects age 40-49. Tested all for *H pylori* infection by a carbon-13 labeled urea breath test.
2. Almost 2400 (27%) were positive for *H pylori*. This cohort was the subject of the trial. About 45% had dyspepsia over the past 6 months determined by a previously validated questionnaire.
3. Randomized the 2400 to: 1) active treatment with omeprazole, clarithromycin, and tinidazole for 7 days, or 2) placebos.
4. Follow-up at 2 years. 75% completed the trial.

RESULTS

1. At 2 years, *H pylori* had been eradicated in 74% of the treatment group vs 5% in the placebo group.
2. At 2 years, dyspepsia was significantly less frequent in the eradication group (relative risk = 0.84). Absolute reduction = 5%. NNT (2-years to benefit one) = 20
3.

Outcome:	Treatment group	Placebo group
Continuing dyspepsia or symptoms of reflux	28%	33%

4. No significant effect on quality of life.
5. Over the 2 years about 1% were diagnosed with peptic ulcer.

DISCUSSION

1. The clinical effect of eradication was small. The causes of dyspepsia remain uncertain.
2. Other studies report that 5% to 20% of persons with *H pylori* infection have peptic ulcer disease, although it is symptomless in many cases.
3. Cure of underlying, undiagnosed ulcer disease may be the main reason for the reduction in dyspepsia in this community trial.
4. The association between *H pylori* and reflux is controversial. This trial found a slightly lower rate of reflux symptoms in the eradicated group.

CONCLUSION

Community screening and treatment for *H pylori* produced only a 5% reduction in dyspepsia. This small benefit had no impact on quality of life.

Lancet May 13, 2000; 355: 1665-69 Original investigation by the Leeds HELP Study Group, first author Paul Moayyedi, General Infirmary at Leeds, UK **http://www.thelancet.com/newlancet/sub/issues/vol355no9216/article1665.html**

Comment:

This study was conducted in an urban population. The prevalence of *H pylori* infection is astoundingly high. The high prevalence of dyspepsia was not surprising.

Other studies reported a worsening of symptoms of reflux after eradication. This study did not confirm this. The question remains unsettled.

For an individual patient with troublesome, persistent dyspepsia, what should be done? I believe endoscopy is a reasonable approach. It will bring reassurance whether positive or negative.

1. If peptic ulcer is present, *H pylori* infection will also be present and should be treated.
2. If no ulcer, and *H pylori* is present, what then? I would inform the patient about risks of future peptic ulcer (modest association), and gastric cancer (unlikely). And the likelihood of improvement in symptoms if the infection is eradicated (about 5%). If the patient then asks my advice, I would tilt toward treatment because it effectively cures the infection, is short-term, and has a low adverse effect profile.
3. What to do about patients with troublesome dyspepsia and no *H pylori* infection?
   — reassurance, symptomatic treatment (antacids, H2 blockers, and proton pump inhibitor),and follow-up
4. In any case, correct lifestyle and NSAID use. RTJ

5-15 HELICOBACTER PYLORI — IS IT A NOVEL CAUSATIVE AGENT IN VITAMIN B12 DEFICIENCY?

A first step in absorption of B12 is the release of the B12 complexed with protein in food. Released B12 is combined with a gastric R binder (protein) which, on entering the duodenum, is digested by enzymes, releasing free B12. Food-cobalamin malabsorption is marked by the inability to release B12 from food. Therefore free B12 is not present to combine with gastric intrinsic factor for absorption in the ileum. Release of B12 from food requires acid and pepsin. Most food-cobalamin malabsorptive states can be traced to gastric defects.

H pylori infection is associated with atrophic gastritis. Is the gastritis related to food-cobalamin malabsorption? Will eradication of *H pylori* and reversing the gastritis improve B12 absorption?

This study evaluated the prevalence of *H pylori* infection in patients with B12 deficiency and assessed whether treatment of the infection would correct the malabsorption.

Conclusion: Eradication of *H pylori* infection alone, without B12 administration, was associated with normalization of serum B12 levels and cure of the anemia.

STUDY

1. Prospective cohort study of 138 patients who had B12 deficiency and macrocytic anemia.

2. All had endoscopy to assess the severity of the gastritis and to test for *H pylori* infection.
3. Seventy seven (56%) of the patients with B12 deficiency had *H pylori* infection and histologic gastritis. All 77 were treated with triple therapy.
4. Follow-up = a mean of 42 months.

RESULTS

1. In the 77 patients with *H pylori* infection, treatment of the infection successfully improved anemia and B12 levels in 31 (40%).(None had received B12 therapy.)

2. Outcomes (of 31 patients)	Baseline	42 months
Hematocrit	29	40
MCV (fL)	109	89
Ferritin (ug/L)	103	117
B12 level (pmol/L)	63	223

(Actually improvement began at 4 weeks, and full improvement occurred within 3 to 6 months.)

DISCUSSION

1. It might be that the *H pylori* gastritis, initially confined to the antrum, progresses to the body of the stomach and results in reduction of acid-pepsin production. This may lead to food-cobalamin malabsorption.
2. Other studies have reported that, after successful treatment of the infection, the gastritis improves and the gastric epithelium appears normal.
3. The investigators believe these data support a role of *H pylori* in the pathogenesis of one form of B12 deficiency.

Conclusion:

H pylori may be a causative agent in adult B12 deficiency. Eradication of the infection without B12 supplementation led to normal serum B12 levels and cure of the anemia.

Archives Int Med May 8, 2000; 160: 1349-53 Original investigation, First author Kursad Kaptan, Gulhane Military Medical Academy, Ankara, Turkey

http://archinte.ama-assn.org/issues/v160n9/rfull/ioi90448.html

Comment:

This study could not have been conducted in the US. I applaud the Turkish patients for their forbearance in not receiving B12 supplements. This interesting observation calls for replication and confirmation.

The fascinating *H pylori* story is gradually unfolding. Much remains unknown. A question — would it be easier and cheaper to supply oral B12 to these patients than to treat the infection? Would not the decision to treat the *H pylori* depend on factors other than any associated anemia?

The prevalence of *H pylori* infection is very high world-wide. If the infection is related to B12 deficiency, would not prevalence of B12 deficiency be higher than it is now?

This is not pernicious anemia. To the purist, pernicious anemia is strictly defined. It is an autoimmune disease leading to destruction of the parietal cells of the stomach and inactivity of intrinsic factor. There are many other causes of B12 deficiency anemias. RTJ

5-16 LINKS BETWEEN HELICOBACTER PYLORI INFECTION, COBALAMIN DEFICIENCY, AND PERNICIOUS ANEMIA.

(*This editorial comments and expands on the preceding study.)*

Cobalamin (vitamin B12) is obtained exclusively from the diet, mainly associated with animal proteins. Absorption of B12 is a complicated process, involving several steps of digestion before absorption: 1. Peptic digestion in an acid environment releases B12 from food proteins.

2. B12 is released from the food protein and combined with an R protein.
3. B12 bound to R protein passes into the duodenum where pancreatic proteases degrade the R protein, releasing free B12.
4. The free B12 then binds to intrinsic factor.
5. The B12/intrinsic complex transits the small bowel and is absorbed by specific intrinsic factor/B12 receptors in the terminal ileum.
6. Without intrinsic factor less than 2% of ingested B12 is absorbed; with it 70% is absorbed.

(*Note that some B12 is absorbed by mass action without the presence of intrinsic factor. This permits oral treatment of pernicious anemia by doses of B12 about 50 to 100 times daily requirements. RTJ*)

B12 deficiency is common. There are many causes. It is associated with aging and chronic gastritis. The most common causes are: 1) pernicious anemia and 2) food-cobalamin malabsorption. The preceding study reports a possible food-cobalamin B12 deficiency caused by *H pylori* gastritis.

1) Pernicious anemia is a disease of unknown etiology characterized by atrophic gastritis affecting primarily the parietal cells of the body of the stomach, decreased acid secretion, and autoimmune manifestations including high prevalence of antibodies directed against parietal cells and/or intrinsic factor.

The Schilling test demonstrates a lack of intrinsic factor. Oral free B12 made radioactive by a cobalt isotope will not be absorbed when given by itself (no intrinsic factor to bind it). When intrinsic factor is added the B12 is absorbed and detected in the urine.

2) Food-cobalamin malabsorption is characterized by the inability to release B12 from food. Release of B12 from food requires acid and pepsin. Most food-cobalamin malabsorptive states can be traced to gastric defects.

The Schilling test demonstrates that intrinsic factor is present. Radioactive free B12 given by mouth is absorbed without added intrinsic factor. (The intrinsic factor is not lacking. Adding it is not needed for absorption.)

Now *H pylori* -associated gastritis is described as a possible cause of food-cobalamin malabsorption and B12 deficiency. This is possibly due to spread of the gastritis to the body of the stomach, leading to decreased acid-pepsin production. *H pylori* eradication has also been shown to improve absorption of iron.[1]

The pathogenesis of B12 malabsorption is complex. Other small studies have suggested that bacterial overgrowth in the gastrointestinal tract (without *H pylori* infection) can result in bacterial binding of B12 and decreased absorption. Treatment with tetracycline resulted in improvement. Other studies link proton pump antagonists and H2 blockers with food-cobalamin deficiency

Archives Int Med May 8, 2000; 160: 1229-30 Editorial by Alison Stopeck, University of Arizona Health Sciences Center, Tucson **http://archinte.ama-assn.org/issues/v160n9/ffull/ied00000.html**

1 "Reversal Of Iron Deficiency Anemia After *Helicobacter Pylori* Eradication In Patients With Asymptomatic Gastritis " Annals Int Med 1999; 131: 668-72

http://www.archinte.ama-assn.org/issues/v160n9/ffull/ied00000.html

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5-17 RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF FLUTICASONE PROPRIONATE IN PATIENTS WITH MODERATE TO SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE; THE ISOLDE TRIAL

In at least 10% of patients with stable COPD, FEV1 will increase (improve) significantly after oral prednisone. Inhaled corticosteroids have been used widely on an empirical basis.

Recently, 2 studies of inhaled budesonide over 3 years reported no effect of treatment on the decline of FEV1 over time.

This study assessed the effect of long-term inhaled corticosteroid on lung function and health status in patients with moderate to severe COPD.

Conclusion: The inhaled steroid did not affect the rate of decline of FEV1. But patients had fewer exacerbations of the disease and a slower decline in health status.

STUDY

1. Double-blind, placebo-controlled multicenter trial entered 750 patients with COPD.
2. Mean FEV1 = 50% of predicted normal.
3. Randomized to: 1) inhaled fluticasone (*Flovent*) 500 ug twice daily, or 2) placebo.
4. Follow-up = 3 years.

RESULTS

1. Almost 40% of subjects continued to smoke during the trial.
2. No significant difference in rate of decline of FEV1 between groups.
3. Mean FEV1 after bronchodilator remained significantly higher in the fluticasone group.
4. Median exacerbation rate was reduced by 25% in the fluticasone group.

5. Health status, determined by a respiratory questionnaire, deteriorated in both groups, but was slower in the fluticasone group.
6. Withdrawals in the fluticasone group were fewer than in the placebo group (19% vs 25%).
7. Adverse effects of fluticasone were mainly topical. Serious co-morbid events occurred in both groups.

DISCUSSION

1. There was no improvement in either group in rate of decline of FEV1 (about 50 mL at one year)
2. There was a slight improvement in FEV1 after bronchodilator therapy in the treated group.
3. There was a decline in the incidence of exacerbations of symptoms of COPD in the treated group.
4. Fluticasone reduced the rate of decline in health status, delaying the average time for a clinically important reduction by about 6 months.

CONCLUSION

The improvements in clinical outcomes support the use of inhaled fluticasone in patients with moderate to severe COPD.

BMJ May 13, 2000; 320: 1297-303 Original investigation by the ISOLDE study investigators, first author P S Burge, Birmingham Heartlands Hospitals, UK

http://www.bmj.com/egi/content/full/320/7245/1297

Comment:

Study supported by GlaxcoWellcome.

This is discouraging. COPD is a devastating disease, resistant to treatment. The chief therapy is discontinuation of smoking, but, an astounding number of subjects continued to smoke. The authors did not mention any difference in outcomes between continuing smokers and those who quit at baseline.

Almost 1000 subjects were eligible; and about 250 were withdrawn before randomization — 750 actually entered the trial; fewer than 400 completed the trial.

Conclusions about trials based on "the intention to treat" are closer to clinical practice in the real world than those not so based. I believe conclusions based on numbers "eligible to enter" would be closer still. I would judge the benefits of inhaled corticosteroids to be borderline, although there may be some outliers who will benefit significantly after smoking cessation. RTJ

5-18 SECONDARY PREVENTION OF PERIPHERAL VASCULAR DISEASE

"Most patients with peripheral vascular disease (**PVD**) may be reassured that, with respect to their legs, the condition usually runs a benign course." However, PVD is an independent predictor of increased risk of cardiovascular death. Most patients presenting with PVD have symptoms of coronary artery disease. Most have abnormalities on ECG, coronary angiography, and ultrasound examination of the carotid arteries.

Symptomatic PVD carries a 30% risk of death within 5 years, primarily due to myocardial infarction or stroke. Even asymptomatic patients (ankle/brachial pressure index < 0.9) have a 2-fold to 5-fold risk of fatal and non-fatal cardiovascular events.

"Although modification of risk factors has not been shown to prevent progression of peripheral vascular disease or loss of limbs, detection of the disease mandates an aggressive approach to modifying the risk factors in order to reduce the risk of fatal and non-fatal myocardial infarction and stroke."

The approach to risk reduction is based on extrapolation from studies of patients with coronary artery disease.

The authors list risk factors. (They are the same as those for coronary disease.) Some specific therapeutic measures are discussed. (Also the same.)

Arterial Disease Assessment, Prevention, and Treatment (ADAPT) clinics provide a common strategy for all patients with cardiovascular disease regardless of the target organ affected. (*Figure p 1265*)

Individual specialties tend to treat arterial lesions in isolation. This approach ignores the real risk to patients from the effects of the same disease in other vascular beds. "The holistic approach to the management of cardiovascular disease is the best way to minimize the risk of disease progression and premature death in patients with peripheral vascular disease."

BMJ May 6, 2000; 320:1262-65 "ABC of Arterial and Vascular Disease", clinical review article, first author Sean Tierney, Beaumont Hospital, Dublin, Ireland. **http://www.bmj.com/cgi/content/full/320/7244/1262**

Comment:

Sometimes we forget the intimate links between atherosclerotic disease in various anatomical sites. Coronary disease, carotid disease, renal artery disease, aortic disease, and peripheral vascular disease are linked. Reducing risk of one will reduce risk of others. I believe we tend to ignore the importance of diagnosing peripheral vascular disease as a marker. The ankle/brachial pressure index is a valuable and meaningful diagnostic procedure. RTJ

5-19 STEROID THERAPY FOR VISUAL LOSS IN PATIENTS WITH GIANT-CELL ARTERITIS

Giant-cell arteritis (temporal arteritis) ranks as the prime medical emergency in ophthalmology. "There is no other disease in which the prevention of blindness depends so much on prompt recognition and early treatment."

The visual loss is due to thrombotic occlusion usually of the posterior ciliary artery, the main source of blood supply to the optic nerve head. This causes "arteritic anterior ischemic optic neuropathy (A-AION)". Occasionally occlusion occurs in the central retinal artery causing retinal infarction. The damage is permanent.

Retinal survival time after the severe ischemic damage is short. It is usually irreversible by the time the patient is seen by an ophthalmologist. There is no scientifically valid rationale for claims of visual improvement with steroid therapy

Since there is no chance for a cure of the ischemic damage, early diagnosis of the arteritis is crucial. Five diagnostic criteria are defined: age over 5, localized headache, tenderness or decreased pulse in the temporal artery, raised sedimentation rate, and histologic evidence of necrotizing arteritis of the temporal artery.

Odds of a positive temporal biopsy are greatly increased if the following are present: jaw claudication; neck pain; sed rate over 47; C-reactive protein over 2.45 mg/dL; and age over 75. However, a low sed rate does *not* rule out arteritis. C-reactive protein is more helpful.

Occasionally the patient will have no systemic symptoms (ie, occult giant cell arteritis).

Systemic corticosteroids are universally agreed to be the treatment of choice. But, the initial and maintenance dose and the rate of reduction in dose and the total duration of treatment have been highly controversial. One reason is that in some studies the arteritis was not differentiated from polymyalgia rheumatica. Patients with visual loss were not differentiated for those without loss, and studies were retrospective rather than long-term prospective.

The view of rheumatologists dealing with polymyalgia rheumatica is that stopping steroid therapy after 2 years is reasonable. However, repeat temporal artery biopsy has shown evidence of active disease even after 9 years of steroid therapy. "Ophthalmologists find that most patients require a maintenance dose indefinitely to eliminate risk of visual loss." Those with some loss require a much higher dose for longer time than those with only rheumatological manifestations. Patients may lose vision irrevocably without any clinical warning symptom. C-reactive protein is the most reliable variable in monitoring the activity of the arteritis. "Periodic individual monitoring is essential".

Lancet May 6, 2000; 355: 1572-73 Editorial by Sohan Singh Hayreh, University of Iowa, Iowa City
http://www.thelancet.com/newlancet/sub/issues/vol355no9215/commentary1572.html

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5-20 ORAL CLONIDINE IN POSTMENOPAUSAL PATIENTS WITH BREAST CANCER EXPERIENCING TAMOXIFEN-INDUCED HOT FLASHES

Hot flashes are the most common (and troublesome) adverse effect associated with the anti-estrogen, tamoxifen (Nolvadex).

Clonidine (*Catapres; Generic*) is non-hormonal — a centrally active alpha-adrenergic agonist that reduces vascular reactivity. It is currently used to treat hypertension.

This study evaluated the effectiveness of oral clonidine for control of hot flashes in post-menopausal women taking tamoxifen for breast cancer.

Conclusion; Oral clonidine was effective in alleviating the tamoxifen-induced hot flashes.

STUDY

1. Entered 194 women with breast cancer who were receiving adjuvant tamoxifen.
2. Randomized to: 1) Oral clonidine 0.1 mg daily, or 2) Placebo.
3. Subjects maintained a daily diary about number and severity of hot flashes, and their quality of life.

4. Follow-up = 12 weeks.

RESULTS

1. 76% completed the 12 weeks.

2. Outcomes	Baseline	Clonidine	Placebo
Hot flashes per day (mean)	8	-24%	-14%
Hot flash severity (scale of 1 to 4)	2.2	-15%	-6%
Hot flash duration (min)	8	-21%	-17%
Hot flash score (number X severity)	18	-28%	-16%
Quality of life score (10 point scale)		+0.3	-0.2

(*Note the placebo effect. RTJ*)

3. Clonidine had a small beneficial effect on hot flashes and quality of life especially for the first 8 weeks of therapy. Benefit seemed to be reduced thereafter.
4. Adverse effects. Clonidine patients were more likely to report difficulty sleeping (41% vs 21%).

DISCUSSSION

1. Response to both clonidine and placebo varied considerably between individual patients. Some women experienced no benefit from clonidine, and some experienced benefit from placebo — and vice versa.
2. Toxicity was low.

CONCLUSION

Oral clonidine 0.1 m daily was effective against tamoxifen-induced hot flashes in post-menopausal women with breast cancer.

Annals Int Med May 16, 2000; 132; 788-93 Original investigation, first author Kishan J Pandya, University of Rochester Cancer Center, NY

http://www.annals.org/issues/v132n10/full/200005160-00004.html

Comment:

The results are unimpressive. I abstracted the article because of the extreme discomfort some women experience when taking tamoxifen (when estrogens are contra-indicated). Clonidine therapy might be tried on a one-of-one basis to judge individual response. An occasional patient may obtain considerable relief. RTJ

5-21 GUIDELINES FOR MANAGING ACUTE BACTERIAL MENINGITIS.

"Nearly one in four adults with acute bacterial meningitis will die, and many survivors sustain neurological defects. The outcome has not changes since the early 1960s despite the introduction of potent antibiotics and specialized intensive care units."

When treatment is delayed, prognosis worsens. The outcome depends on whether the attending physician suspects acute bacterial meningitis, and whether the healthcare system is set up to make a rapid accurate diagnosis, and initiate fast and effective treatment.

The British Infection Society has issued guidelines[1] making recommendations for management of suspected or diagnosed acute bacterial meningitis and meningococcal disease, and for prevention of secondary cases by vaccination and prophylactic antibiotic treatment.

The guideline advises family doctors to give benzylpenicillin (aqueous penicillin G) immediately when meningococcemia is suspected, and then arrange immediate hospitalization. "In patients with obvious meningococcal disease penicillin is the drug of choice."

For patients suspected bacterial meningitis of other causes, it may be more reasonable to arrange rapid hospitalization followed by speedy microbiological tests and antibiotic treatment. A widely accepted empirical treatment is a third generation cephalosporin (cefotaxim *Claforan* or ceftriaxone *Rocephin*) with ampicillin if listeria meningitis cannot be ruled out.

For pneumococci resistant to penicillin, increased doses and frequency of penicillin administration may overcome the resistance, Rifampin may be useful for pneumococci truly resistant.

Supportive treatment is hotly debated. Corticosteroids reduce neurological defects in children with *H influenzae* meningitis.[2] Benefit in adults is not proven. The need for full fluid replacement and maintenance is emphasized.

BMJ May 13, 2000; 320: 1290 Editorial by Kirsten Moller and Peter Skinhoj, University Hospital, Copenhagen, Denmark.

http://www.bmj.com/egi/content/full/320/7245/1290

1 "Consensus Statement On Diagnosis, Investigation, Treatment, And Prevention Of Acute Bacterial Meningitis In Immunocompetent Adults." J Infec 1999; 39: 1-15

2 Given immediately before any antibiotic is administered.

Comment:

Recent studies report an increasingly high incidence of meningococcal carriage in students in the first weeks after returning to university. There is a good case for vaccination in this group. RTJ

5-22 DOUBTS RAISED ABOUT SAFETY OF THROMBOLYSIS IN ELDERLY

This brief "News" article comments on a study published in Circulation.[1] (David Thiemann, Johns Hopkins Hospital, Baltimore MD)

In over 2600 patients age 76-86, 30-day mortality was higher in those receiving thrombolysis for acute myocardial infarction than in those receiving aspirin and heparin. (Mortality = 18% vs 15.4%; Hazard ratio = 1.4) "The patients given thrombolysis did worse right from the start."

Conversely, in the age 65-75 patients (n = 5200) 30-day mortality was higher in the those who did not receive thrombolysis (8% vs 6.8%).

There was concern that adverse effects on the elderly may have been missed in randomized trials because patients enrolled were younger than those cardiologists normally see.

However Eric Topol, Cleveland Clinic noted that of the over 50 000 patients in trials comparing thrombolysis with placebo, about 10% were over age 75. The absolute benefit this group gained from thrombolysis was at least as great as that seen in younger patients.

Both authorities agreed that, if available and possible, primary angioplasty would be preferable in most patients over 75 with acute myocardial infarction.

In the long-term, better therapies designed specifically for the elderly are the answer — eg, lower thrombolytic doses in combination with glycoprotein IIb/IIIa inhibitors.

Lancet May 20, 2000; 355: 1794 "News" Reported by Jane Bradbury, Lancet Staff.

http://www.thelancet.com/newlancet/sub/issues/vol355no9217/news_sm1793.html

1 Circulation 2000; 101: 2239-46.

Comment:

I abstracted this brief report to point out that, as powerful as double-blind randomized trials are, they may mislead in certain groups of subjects. Clinicians may be enthusiastic in applying a reportedly beneficial therapy not understanding the entrance requirements, and not realizing the exclusion criteria. In addition, there may indeed be subsets of the subjects hidden in the study who are harmed by the reportedly highly significant beneficial treatment.

Harmful effects occur in all treatments in randomized trials. Clinicians must make a reasonable estimate about the benefit/harm ratio in each individual. It is impossible ever to be certain. Even n-of-1 trials may mislead. RTJ

REFERENCE ARTICLE

5-23 A 52-YEAR-OLD SUICIDAL MAN

This is a case report. The article discusses the extent of the problem of suicide in the U.S., and how to evaluate suicide risk.

It presents

"A Suicide Assessment Protocol" (table 1 p 2694).

"Suicide Risk Factors in Adults" (table 2 p 2694).

"The Harvard Department of Psychiatry and National Depression Screening Day Scale" —

THE HANDS (figure p 2695).

Depression screening has been proven to be an effective way of identifying those with undiagnosed depressive illness and a useful tool for the primary care physician attempting to ascertain the likelihood and severity of depression and the presence of suicidal thoughts. HANDS is designed to minimize physician time by quickly identifying patients who have a positive score or who endorse a suicidal question. The patient fills it out himself.

"The results of this screening effort are striking." Fully 22% of primary care patients had a positive score for depression; 45% of these suffered with alcohol abuse, 28% with stroke, 19% with cancer, 23% with diabetes, 23% with arthritis, and 23% with heart disease.

"These findings underscore the need for depression screening in primary care settings and the ease with which it can be incorporated."

JAMA May 24/31;283: 2000; 2693-99 "Clinical Crossroads" discussant Douglas G. Jacobs, Harvard Medical School, Boston Mass.

http://jama.ama-assn.org/issues/v283n20/rfull/jxr00002.html

Comment:

The tables and figure can be downloaded from the internet. The clinical importance is self-evident. RTJ

RECOMMENDED READING

5-24 VIOLENCE IN PUBLIC HEALTH AND PREVENTIVE MEDICINE

"A consensus on the causes and prevention of violence has been emerging over the past few decades among investigators of this subject from virtually every branch of the behavioral sciences. All specialties, independent of each other, have identified a pathogen that seems to be a necessary but not sufficient cause of violent behavior, just as specifically as exposure to the tubercle bacillus is necessary but not sufficient for the development of tuberculosis. The difference is that in the case of violence the pathogen is an emotion, not a microbe — namely, the experience of overwhelming shame and humiliation. And just as people's vulnerability to tuberculosis is influenced by the state of their body's defense mechanisms, so their vulnerability to violence is influenced by the state of their psychological defense mechanisms."

These defenses include the degree to which violent individuals have developed the capacity for an emotion that is antagonistic to shame, and inhibits the violence toward others, based on guilt and remorse, that shame stimulates. "And this is a capacity that the most violence-prone individuals and groups notably lack."

Shame has many synonyms: feeling slighted, insulted, ridiculed, rejected, disrespected, dishonored, disgraced, demeaned; feeling inferior, inadequate, incompetent, weak, ugly, worthless; suffering "loss of face", or "an inferiority complex".

"Worldwide, the most powerful predictor of the murder rate is the size of the gap in income and wealth between the risk and the poor." "And the most powerful predictor of the rate of national and collective violence — war, civil insurrection, and terrorism — is the size of the gap in income and wealth between risk and poor nations."

The likelihood of being so overwhelmed by shame as to become violent is strongly influenced by whether or not they possess internal sources of pride and self-esteem, such as education, or external sources of esteem from others, such as wealth or other sources of social status.

"We can prevent violence if, and only if, we replace the moral and legal approach to it, which is based on moral condemnation, shaming, and punishment. This is a matter of vital importance to the future of humanity, in which the medical profession can serve as an invaluable role as educators and leaders."

Lancet MAY 20, 2000; 355: 1802-04 Commentary by James Gilligan, MD, President of the International Association of Forensic Psychotherapy, West Stockbridge, MA

http://www.thelancet.com/newlancet/sub/issues/vol355no9217/series1802.html

Comment:

This issue of Lancet presents 9 articles on violence, ranging from violence and provision of community psychiatry, violence toward children (in larger part due to indifference), role of injury prevention in medicine, cultural violence toward women, Kosovo, and war. RTJ

REFERENCE ARTICLE

5-25 VASCULITIS

The clinical and pathological features of vasculitis are variable and depend on the site and the type of blood vessels affected. The main types are described in this review based on the Chapel Hill Consensus Conference. However, since etiology and pathogenesis are rarely known, definitive classification is unsatisfactory. Clinical and histologic features overlap.

Vasculitis can be a primary process or secondary to other disease such as systemic lupus erythematosus and rheumatoid arthritis.

Fever, night sweats, malaise, myalgia and arthralgia are common to all types. Active vasculitis is usually associated with an acute phase response with an increase in C reactive protein and sed rate.

The authors propose this classification and present descriptions of each:

Large vessel vasculitis

Giant cell arteritis (temporal arteritis)

Takayasu's arteritis

Medium vessel arteritis

Polyarteritis nodosa

Kawasaki disease

Small vessel vasculitis associated *with* anti-neutrophil cytoplasmic antibody

Wegener's granulomatosis

Microscopic polyarteritis

Churg-Strauss syndrome.

Small vessel vasculitis associated *without* anti-neutrophil cytoplasmic antibody

Henoch-Schonlein Purpura

Cryoglobulinaemic vasculitis

Isolated cutaneous leukocytoclastic vasculitis

Antiglomerular basement membrane antibody mediated disease

Goodpasture's disease

BMJ May 13, 2000; 320: 1325-28 "ABC of Arterial and Vascular Disease, clinical review, first author C O S Savage, University of Birmingham, UK

http://www.bmj.com/cgi/content/full/320/7245/1325

REFERENCE ARTICLE

5-26 VARICOSE VEINS

This reviews incidence and prevalence, pathophysiology, risk factors, symptoms, clinical management (history, examination and treatment), management of complications including thrombophlebitis, bleeding, and varicose eczema.

An illustration on p 1392 describes how an incompetent vein valve allows some of the blood pumped up out of the leg by the calf muscles to reflux back down the superficial veins when the calf muscles relax. The retrograde circuit can overload the calf muscle pump leading to dilatation and failure of the vein.

Varicose veins can be classified as trunk, reticular, or telangiectasia. (See illustrations)

"The use of injection sclerotherapy for trunk varices has fallen in recent years because of concern about complications such as skin staining and ulceration, and also because up to 65% of patients treated by sclerotherapy develop recurrent varicose veins within five years."

"Reticular varicosities are not connected to major trunk varices and are treated by sclerotherapy or avulsion through small stab incisions. Patients who present with capillary telangiectasia should have colour duplex scanning because roughly 25% will have clinically unapparent long or short saphenous incompetence. The telangiectasia are treated by microinjections, laser, or high intensity light. The last two are being increasingly used."

Areas of controversy remain:

Whose varicose veins should be treated with surgery?

Varicose vein relation to deep vein thrombosis, contraceptive pills, and hormone replacement therapy.

BMJ May 20, 2000; 320: 1391-94Clinical review "ABC of Arterial and Venous Disease", first author Nick J M London, University of Leicester, UK

http://www.bmj.com/egi/content/full/320/7246/1391
