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HIGHLIGHTS JANUARY 1999

1-1 SOLICITING THE PATIENT'S AGENDA

Physicians often redirect patients' initial descriptions of their concerns before the description is fully completed. Once redirected, the list of concerns are rarely completed. Soliciting the patients' complete agenda at the outset of the interview can improve interview efficiency and yield increased data. Ask — "What concerns do you have" and then "Anything else" to complete the agenda. JAMA January 20, 1999; 381: 283-87

1-2 THE ASSOCIATION BETWEEN CARDIORESPIRATORY FITNESS AND IMPAIRED FASTING GLUCOSE AND TYPE 2 DIABETES MELLITUS IN MEN

Poor cardiorespiratory fitness was associated with increased risk for developing impaired fasting glucose and type 2 diabetes. A sedentary lifestyle may contribute to progression from normal fasting glucose to impaired fasting glucose, to diabetes. Annals Int. Med. January 19, 1999; 130: 89-96

1-3 QUALITY END-OF-LIFE CARE: Patient's Perspectives

From a patient's perspective, quality end-of-life includes: receiving adequate pain and symptom management, avoiding inappropriate prolongation of dying, achieving a sense of control, relieving burden, and strengthening relationships with loved ones. JAMA January 13, 1999; 281: 163-68

1-4 PATIENT'S PRIORITIES

"A revolution is underway in health care. After decades of patriarchal provision of services, governments are now accepting that patients should have a say in what they are provided." Patients now demand information. Providing patients with accurate, high quality up-to-date information is a priority.

Patients hold remarkably similar views about what they want from primary care. Top of the list are: 1) having enough time in the consultation, 2) being able to get quick service in an emergency, and 3) having a general practitioner who listens and provides helpful information about their illnesses and treatment, and encourages them to discuss all their problems. They also want their physicians to keep up to date, and meet their need for confidentiality and advocacy. BMJ January 30, 1999; 277

1-5 BACTERIOLOGIC ANALYSIS OF INFECTED DOG AND CAT BITES

Infected dog and cat bites have a complex microbiologic mix that usually includes pasteurella species and may include many other organisms not previously recognized as bite-wound pathogens. NEJM January 14, 1999; 340: 85-92

1-6 THE MANAGEMENT OF BITE WOUNDS

Whether antibiotics prevent infection remains controversial. Five of 8 studies reported prophylactic antibiotics reduced rate of infection, but in only 1 (amoxicillin-clavulanate [Augmentin] was the difference statistically significant. A meta-analysis found the relative risk of infection after prophylactic antibiotics was 0.56. "Currently antibiotics are not given routinely, but they are almost always recommended for high-risk wounds (deep punctures, and those requiring surgical repair and those involving the hands). "

For empirical treatment of infection, in most cases a beta-lactam combined with a beta-lactamase inhibitor [eg, amoxicillin-clavulanate] should be the appropriate choice. NEJM January 14, 1999; 340: 138-40

1-7 THE CARDIAC INSUFFICIENCY BISOPROLOL STUDY II (CIBIS II)

Beta-blocker therapy with bisoprolol had benefits for survival in stable heart-failure patients. THE LANCET January 2, 1999; 353; 9-13

1-8 A TRIAL OF ETANERCEPT, A RECOMBINANT TUMOR NECROSIS FACTOR RECEPTOR:Fc FUSION PROTEIN, IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING METHOTREXATE.

In patients with persistently active RA while on a stable dose of methotrexate, addition of etanercept was safe and well tolerated, and provided significantly greater clinical benefit than methotrexate alone. NEJM January 28, 1999; 340: 253-59

1-9 ANTICYTOKINE THERAPY — A New Era in the Treatment of Rheumatoid Arthritis?

Two TNF receptor blockers are under investigation: 1) infliximab is an antibody to TNF, 2) etanercept is a TNF receptor which, when administered locally, binds TNF, and prevents its action. Infliximab combined with methotrexate also leads to substantial improvement in RA. It has recently been approved for use in Crohn's disease.

"On the basis of data currently available, it appears that patients who have suboptimal response to methotrexate are the best candidates for etanercept or infliximab." NEJM January 28, 1999; 340: 310-12

1-10 BENEFITS OF LIFESTYLE ACTIVITY VS STRUCTURED EXERCISE.

Two randomized clinical trials in the issue of JAMA 1, 2 compared the effects of lifestyle physical activity vs structured exercise on fitness, body composition, and risk factors for cardiovascular disease. The studies demonstrated that a lifestyle approach to increasing activity among previously sedentary persons can be effective and has similar effects on fitness, body composition, and blood pressure as a traditional structured exercise program. JAMA January 27, 1999, 281: 375-76

1-11 ORAL CONTRACEPTION AND HEALTH

The evidence suggests that women who do not smoke, who have their blood pressure checked, and do not have hypertension, have no increased risk of myocardial infarction and little risk of stroke when they use combined OCs. (BP should be always measured before starting OCs.) BMJ January 9, 1999; 318: 69-70

1-12 WEIGHT CONTROL AND RISK REDUCTION IN OBESE SUBJECTS TREATED FOR 2 YEARS WITH ORLISTAT

Partial inhibition of fat absorption by orlistat combined with a mildly controlled energy diet over 2 years in obese subjects promoted weight loss, lessened weight regain, and improved some obesity-related risk factors. JAMA January 20, 1999; 281: 235-42

1-13 THE PROTECTIVE EFFECT OF MODERATE ALCOHOL CONSUMPTION ON ISCHEMIC STROKE

Moderate alcohol consumption was independently associated with a decreased risk of ischemic stroke. Heavy alcohol consumption was deleterious. JAMA January 6, 1999; 281: 53-60

1-14 COX-2 INHIBITORS

1. COX-1 acts constantly (not inducible). It predominates in the stomach. It is the predominant source of the gastric mucosal prostaglandins which protect the stomach. NSAIDs tend to selectively inhibit COX-1, reducing the protective effect of the prostaglandin, leading to acid-producing gastric mucosal injury.

2. COX-2 is inducible by inflammation. Its prostaglandin is associated with pain, swelling, and stiffness.

The idea then is to inhibit the "bad guy" — COX-2 while preserving the "good guy" — COX-1. Inhibiting COX- will relieve some symptoms of inflammation. THE LANCET January 23, 1999; 353; 307-14

1-15 NARRATIVE IN MEDICAL ETHICS

Narrative ethics focuses on the patient as narrator of his of her own story, including the ethical choices that belong to their story. The doctor must work as co-author with the patient to construct a joint narrative of illness and medical care.

"Narrative practice is relational and requires the doctor to be an empathic witness to the patient's suffering. "BMJ January 23, 1999; 318: 253-56

1-16 NARRATIVE BASED MEDICINE IN AN EVIDENCE BASED WORLD

Appreciating the narrative nature of illness and the intuitive and subjective aspects of the clinical method does not require us to reject the principles of evidence-based medicine. Genuine evidence- based practice actually presupposes an interpretive paradigm in which patients experience illness in a unique and contextual way.

It is only within such an interpretive paradigm that a clinician can reach an integrated clinical judgement and meaningfully draw on all aspects of evidence — his or her own case based experience, the patient's individual and cultural perspectives, and the results of rigorous clinical research trials and observational studies. BMJ January 30, 1999; 318: 32325

1-17 THE TROUBLE WITH FAMILIES: Toward an Ethic of Accommodation

A system that saves lives or prolongs lives only to cast patients and families into the abyss of fragmented chronic care and financial and emotional ruin, while at the same time criticizing them for being "too emotional", is unjust. Many families are willing to make enormous sacrifices, but martyrdom is not a good basis for health care policies or practice.

When families are pushed beyond their limits, the patient's care is jeopardized, the caregiver's health is at risk, professionals are frustrated, and the health care system is burdened by greater costs. "Our recommendations focus on human relationships, not technology." A health care system that depends so heavily on the patient care provided by families should involve families as partners rather than define them as problems. Annals Int. Med. January 19, 1999; 130:148-52

1-18 NICOTINE NASAL SPRAY WITH NICOTINE PATCH FOR SMOKING CESSATION:

Combination nicotine spray plus patch used for 1 year was more effective than the patch used alone. Most subjects attaining cessation had stopped using the spray at 1 year. BMJ January 30, 1999; 318: 285-88

1-19 RECENT ADVANCES IN THE PHARMACOTHERAPY OF SMOKING

Physicians should remind patients that most smokers make many (often over 5) attempts to stop before they succeed.

"All currently available therapies appear to be equally efficacious, approximately doubling the quit rate compared with placebo.

"Concomitant behavioral or supportive therapy increases quit rates and should be encouraged but not required.

Combining patch with gum or patch with buproprion [Zyban] may increase the quit rate compared with any single treatment. JAMA January 6, 1999; 281: 72-76

1-20 MANAGING SMOKING CESSATION

Most time and resources should be spent on individuals who are motivated to stop. After raising the issue of smoking clinicians should assess smokers' motivation to stop and tailor any further discussion accordingly. BMJ January 16, 1998; 318: 138-39

1-21 CALCIUM SUPPLEMENTS FOR THE PREVENTION OF COLORECTAL ADENOMAS

Calcium supplementation was associated with a significant — though moderate— reduction in risk of recurrent colorectal adenomas. NEJM January 14, 1999; 340: 101-07

1-22 SEVERE MENTAL ILLMESS AND SUBSTANCE ABUSE

"Evidence suggests that half of all patients with schizophrenia also have a substance misuse disorder." In one inner district in London, 36% of psychotic patients misused drugs or alcohol. BMJ January 16, 1999; 318: 137-38

RECOMMENDED READING

1-15 NARRATIVE IN MEDICAL ETHICS
1-16 NARRATIVE BASED MEDICINE IN AN EVIDENCE BASED WORLD
1-17 THE TROUBLE WITH FAMILIES: Toward an Ethic of Accommodation

REFERENCE ARTICLES

1-14 COX-2 INHIBITORS
1-19 RECENT ADVANCES IN THE PHARMACOTHERAPY OF SMOKING

This is the only article I have abstracted which applies to every patient at every consultation. RTJ

1-1 SOLICITING THE PATIENT'S AGENDA

Patients, when asked to describe their concerns by physicians, are often quickly redirected after the first expressed concern. Once redirected, patients seldom return to their agenda and complete their offering of concerns. (Patients, if given the opportunity, express an average of 3 concerns per office visit.) Clinicians often pursue a concern without knowing what other issues the patient might wish to discuss, or if the pursued concern was the most important one. Clinicians often take control of the content of the interview too early in the visit. This increases the chance of ignoring important issues and creating less efficient visits.

This behavior has been termed "interruption" or "redirection". It indicates verbal interventions that direct the focus of the interview before the patient completes the initial statement of concerns.

Most texts on the medical interview advocate soliciting patients' reasons for seeking care and encourage the practice of listening until all concerns are elicited. This "agenda setting" precedes more focused open-ended and closed-ended questions to further clarify each concern. Non-directive, open-ended inquiries such as "Tell me more" or "Anything else?" reduce the risk of missing unstated concerns.

This study examined the extent which experienced family physicians elicited the agenda of concerns patients bring to the office

STUDY

1. Cross sectional survey analyzed 264 patient-physician interviews recorded by audiotape.
2. Determined physician solicitation of patient concerns, rate of completion of patient responses, length of time for patient responses, and frequency of late-arising patient concerns.
3. Noted non-completed sequences when the physician disrupted the patient's statement or initiated discussion of a specific topic without determining if the patient had indeed completed the list of concerns. (This can be done by asking closed questions — eg, "When does your chest pain come?" or making a statement "That sounds serious".) Although such inquiries are designed to facilitate patient disclosure, they have the effect of directing the discussion toward a particular concern.

RESULTS

1. Mean length of the visits was 15 minutes.
2. Physicians failed to elicit any patient concerns in 25% of interviews.
3. Patients' initial statements of concerns were completed in only 28% of interviews.
4. Physicians redirected patients' opening statement after a mean of 23 seconds. Most physician redirections occurred after the first concern expressed by the patient. Following the original redirection, patients went on to state one or more additional concerns in 33% of the interviews.
5. Once the discussion became focused on a specific concern, the likelihood of returning to complete the agenda was very low (8%).
6. Patients given the opportunity to complete listing their concerns took an average of only 32 seconds to do so. (Additional time was needed for the patient to describe the concern in detail.)

7. Visit length was not associated with completion of statements (15 minutes, 18 seconds when concerns were completely stated vs 14 minutes, 52 seconds for non-completed statements.

DISCUSSION
1. Only after allowing the patient to describe the full range of concerns, should the physician then explore further using elaborators, closed-end questions, and statements.
2. Physicians commonly redirect and focus clinical interviews before giving patients the opportunity to complete their statement of concerns. This incomplete agenda-setting misses opportunities to gather potentially important patient data.
3. Complete setting of the agenda at the outset is an efficient manner to open the medical encounter.
4. Asking "Anything else" often reveals additional concerns before moving on to soliciting additional information about a specific concern.
5. The study did not include any indication of non-verbal clues (posture; facial expression) that may have informed the physician that the patient had not completed the initial agenda of concerns.

CONCLUSION

Physicians often redirect patients' initial descriptions of their concerns before the description is fully completed. Once redirected, the list of concerns is rarely completed. Soliciting the patients' complete agenda at the outset of the interview can improve interview efficiency and yield increased data.
Ask — "What concerns do you have" and then "Anything else" to complete the agenda.

JAMA January 20, 1999; 381: 283-87 "The Patient-Physician Relationship" Original investigation , first author M Kim Marvel, Fort Collins Family Medicine Program, Fort Collins, Colorado

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1-2 THE ASSOCIATION BETWEEN CARDIORESPIRATORY FITNESS AND IMPAIRED FASTING GLUCOSE AND TYPE 2 DIABETES MELLITUS IN MEN

The American Diabetes Association defines impaired fasting glucose **(IFG)** as a fasting glucose level between 110 and 125 mg/dL, (6.1 to 6.9 mmol/L), and diabetes as a fasting glucose 126 and above. IFG is a strong predictor of type 2 diabetes.

There is an inverse relation between physical activity and type 2 diabetes. This study asks — Is there an inverse relation between physical activity and IFG as well?
Conclusion: This study reported an inverse relation between physical activity and IFG.

STUDY
1. Population-based prospective study entered over 8500 men (age 30 to 79; mean = 44). Of these, 13% had IFG. None had diabetes.
2. Measured 1) fasting plasma glucose and 2) cardiorespiratory fitness by a maximal exercise treadmill test.
3. Treadmill times were placed in frequency distributions for specific age groups. The least fit 20% of the participants according to treadmill time were classified as low fitness; the most fit 40% as high fitness.
4. Follow-up = 6 years.

RESULTS
1. Over 6 years 2% developed type 2 diabetes; 8% developed IFG.
2. After considering age and other possible confounding factors, the least fit 20% had a 2-fold risk of developing IFG compared with the most fit. And a 3.7-fold risk of developing type 2 diabetes. There was a dose-response gradient between fitness levels and incidence of IFG and type 2diabetes.
3. Older men and those with a higher BMI had increased risk of developing IFG.
4. Men in the highest fitness group had the lowest levels of total cholesterol, triglycerides, BMI, waist circumference, and BP, the lowest prevalence of current cigarette smoking, and the highest levels of HDL-cholesterol.
5. Men with IFG at baseline were 8 times more likely than men with normal fasting glucose to develop type 2 diabetes.

DISCUSSION

1. “The most novel finding in our study was the steep inverse gradient for incidence of impaired fasting glucose across cardiorespiratory fitness categories.”

CONCLUSION

Poor cardiorespiratory fitness was associated with increased risk for developing impaired fasting glucose and type 2 diabetes. A sedentary lifestyle may contribute to progression from normal fasting glucose to impaired fasting glucose, to diabetes.

Annals Int. Med. January 19, 1999; 130: 89-96 Original investigation, first author Ming Wei, Cooper Institute for Aerobics Research, Dallas TX

Comment:

I abstracted this article mainly because of the data about impaired fasting glucose. In screening glucose levels, I believe the most valuable determinant is impaired fasting glucose. Patients with levels between 110 and 125 can be given the opportunity to improve their lifestyles and lessen the incidence of diabetes and its complications. This is a most valuable contribution of primary care. RTJ

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1-3 QUALITY END-OF-LIFE CARE: Patient’s Perspectives.

Quality end-of-life care is an ethical obligation of health care providers.
This study identified and described elements of quality end-of-life care from the perspective of involved patients.

STUDY

1. Analyzed data from interviews with 126 patients, some on dialysis (mean age 48) , some with HIV infection (mean age 40), and some who were residents of long-term nursing care facilities (mean age 76). Interviews were in-depth, open-ended, and face-to-face.
2. Sought their views on end-of-life issues.

RESULTS

1. Participants were White, African American, Hispanic, and Asian.
2. The analysis identified 5 domains of quality end-of-life care:
   1) Receiving adequate pain and symptom management:
      Despite the palliative care movement, pain and other distressing symptoms are still a problem for many dying patients. “Clearer guidelines separating appropriate pain control from euthanasia may also help alleviate clinicians’ fears with respect to pain management. “
   2) Avoiding inappropriate prolongation of dying:
      Many patients with advanced dementia and terminal cancer receive non-palliative treatments. Physicians sometimes feel that the treatments they offer patients are overly burdensome. Conversely, dying patients sometimes overestimate their survival probabilities, and these estimates may influence their treatment choices. The primary focus of discussions about the use of life-sustaining treatment should be on the realistic and achievable goals of care.
      Participants in this survey expressed fear of “lingering” and “being kept alive” after they could no longer enjoy their lives. Many were terrified of becoming “a vegetable” or living in a coma. They adamantly denounced “being kept alive by a machine”. They wanted to be “allowed to die naturally” or “in peace”.
   3) Achieving a sense of control:
      They wanted to retain control of their end-of-life care decisions while they were capable of doing so. And wanted the proxy of their choice to retain control if they became incapable.
   4) Relieving burden:
      Participants were greatly concerned about the burdens their dying would impose on loved-ones. They wanted their loved ones to know what they (the patient) had decided about terminal care. They did not wish to place on their family the burden of trying to decide what the patient would have wanted for care. Some wanted to die in an institution rather than at home (which they might have preferred) because of the burdens placed on family. They also feared the financial burden their terminal care might place on family.

5) Strengthening relationships with loved ones:

For the dying experience to be meaningful, participants desired the full involvement of loved ones. Communication with loved ones was of overwhelming importance. When this intimacy was achieved, relationships strengthened. When dying patients had discussions with their loved ones, they seemed to feel less isolated in the face of death. Dying offers important opportunities for growth, intimacy, reconciliation, and closure in relationships.

The domains of quality end-of-life care described here can be easily used by clinicians at the bedside to review the quality of care of dying patients.

CONCLUSION

From a patient's perspective, quality end-of-life includes: receiving adequate pain and symptom management, avoiding inappropriate prolongation of dying, achieving a sense of control, relieving burden on family, and strengthening relationships with loved ones.

JAMA January 13, 1999; 281: 163-68 "Special Communication" Original investigation, first author Peter A Singer, Toronto Hospital, Toronto, Canada.

The authors comment further: The current approach to end-of-life decision-making in bioethics focuses on the patient's individual rights and choices, and not on his or her social and family ties. This may be too specific, and may not address patients' psychosocial needs in the face of death.

Comment:

We should inform all close family members, on several occasions, not only once, about our decisions concerning terminal care. A chief proxy should be named. There should be no doubt, disagreement, or dissent among the relatives when the time comes. RTJ

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1-4 PATIENT'S PRIORITIES

"A revolution is underway in health care. After decades of patriarchal provision of services, governments are now accepting that patients should have a say in what they are provided." Patients now demand information. Providing patients with accurate, high quality up-to-date information is a priority. Patients hold remarkably similar views about what they want from primary care. Top of the list are: 1) having enough time in the consultation, 2) being able to get quick service in an emergency, and 3) having a general practitioner who listens and provides helpful information about their illnesses and treatment, and encourages them to discuss all their problems. They also want their physicians to keep up to date, and meet their need for confidentiality and advocacy.

The convenience and décor of the medical environment are rated low priorities. Time spent in the waiting room was seen as much less important than the quality of the consultation.

For a "caring profession" to fail to take into account the priorities of those it exists to serve is hard to justify. It makes little sense from a medical or economic standpoint. Evidence suggests that where patients are informed and supported to participate in decisions, health care outcomes are better, services are used more appropriately, patient satisfaction is higher, and there is less risk of litigation.

Defining good quality care is notoriously difficult, but any attempt at definition should incorporate patients' views.

Listening to patients and responding to their needs helps break down the wall between patients and professionals. "Patients always have important insights and priorities that doctors and other health care professionals miss."

The medical mindset needs radical readjustment to accept that patients are partners and that their input into medical education, service provision, research, and policy-making is essential.

BMJ January 30, 1999; 277 Editorial by Tessa Richards, associate editor BMJ

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1-5 BACTERIOLOGIC ANALYSIS OF INFECTED DOG AND CAT BITES

" . . . 3 to 18 percent of dog bites and 28 to 80 percent of cat bites become infected, with occasional sequellae of meningitis, septic arthritis, and septic shock. "

This prospective multicenter study assessed specific criteria for infection and included culturing for aerobic and anaerobic bacteria.

Conclusion: These bites have a complex microbiologic mix.

STUDY
1. Enrolled infected bites in 107 patients (50 dog bites; 57 cat bites). All bites were large enough to permit a miniswab to be inserted to obtain a deep culture.
2. All patients met one of three major criteria for infection: fever, abscess, and lymphangitis; or 4 of 5 minor criteria (associated erythema, tenderness at the wound site, swelling at the site, purulent drainage, and leukocytosis).
3. All were seen in emergency departments and therefore may have had more severe illness than the average patient with a bite.
4. Cultured all on multiple media for aerobic and anaerobic bacteria.

RESULTS
1. Sixty two percent of patients with dog bites were male; 72% of patients with cat bites were female.
2. Fifteen patients had associated medical conditions: diabetes, glucocorticoid use, alcoholism, chronic renal disease, and chronic liver disease.
3. The majority of bites were puncture wounds, with and without lacerations. Most involved the arms, especially the hands.
4. Most had received first aid: soap and water, iodine, peroxide, sterile saline, alcohol.
5. Median interval between bite and collection of specimen = 25 hours.
6. Median number of isolates per culture = 5 (3 aerobes, 2 anaerobes)
7. Mixed aerobic-anaerobic infections were present in 56%; only aerobes in 36%, only anaerobes rarely.
8. Culture results were complex — a whole page of isolates (p 88).
9. Pasteurella species were the most common isolates.
10. Median time from the bite to first symptoms (latency period) averaged 12 hours for cat bites and 24 hours for dog bites.
11. About 1/3 of patients were hospitalized and treated initially with intravenous antibiotics. The regimens varied considerably. Oral regimens also varied. Median duration of treatment until symptoms resolved = 10 days.

DISCUSSION
1. A precise definition of wound infection is critical.
2. An average of 5 isolates was cultured, even from non-purulent wounds.
3. Pasturella species were the most common pathogen. They are among the most common canine and feline oropharyngeal isolates.
4. “Empirical therapy should be directed against pasteurella, streptococci, staphylococci, and anaerobes.
5. Empirical treatment should include 1) a beta-lactam antibiotic combined with a beta-lactamase inhibitor; 2) a second generation cephalosporin with anaerobic activity; 3) combination therapy with either penicillin and a first-generation cephalosporin; or 4) clindamycin and a fluroquinolone.

CONCLUSION
Infected dog and cat bites have a complex microbiologic mix that usually includes pasturella species and may include many other organisms not previously recognized as bite-wound pathogens.

NEJM January 14, 1999; 340: 85-92 Original investigation from the “Emergency Medicine Animal Bite Infection Study Group”, first author David A Talan, Olive View-UCLA Medical Center, Los Angeles.

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1-6 THE MANAGEMENT OF BITE WOUNDS

Editorial Comment — Practical Advice, First Aid and Empirical Antibiotics.

Deciding whether to close a bite wound involves weighing cosmetic benefits against risk of infection. In general, puncture wounds should be treated and left open. Facial lacerations are almost always closed. Subcutaneous sutures should be used sparingly because of the risk of infection.

Prompt adherence to standard principles of wound management provides the best defense — copious irrigation at high pressure and debridement of devitalized tissue.

Cultures obtained at the time of injury are of little value because they cannot be used to predict whether infection will develop, or the causative pathogen.

Whether antibiotics prevent infection remains controversial. Five of 8 studies reported prophylactic antibiotics reduced rate of infection, but in only 1 (amoxicillin-clavulanate [Augmentin] was the difference statistically significant. A meta-analysis found the relative risk of infection after prophylactic antibiotics was 0.56. "Currently, antibiotics are not given routinely, but they are almost always recommended for high-risk wounds (deep punctures, and those requiring surgical repair and those involving the hands). "

For empirical treatment of infection, in most cases a beta-lactam combined with a beta-lactamase inhibitor [eg, amoxicillin-clavulanate] should be the appropriate choice.

Given the risk of tetanus after bites of all kinds, for patients who have previously received two or fewer primary immunizations, tetanus immune globulin should be given combined with tetanus toxoid. Toxoid alone can be given to those who have completed a primary immunization [three shots] and who have not received a booster in the past 5 years.

Consider rabies. Since rabies is endemic in most of the world, all domestic animals — as well as wild animals (if they can be caught)— that behave wildly or erratically, should have their brains evaluated for rabies. Healthy animals can be quarantined for 10 days. Prophylaxis includes rabies immune globulin and a series of 5 doses of human rabies vaccine.

Human bites by individuals possibly infected with viral hepatitis or HIV require specialized prophylactic therapy.

NEJM January 14, 1999; 340: 138-40 **editorial by Gary R Fleisher, Children's Hospital,** Boston MA. Editorial Comment — Practical Advice, First Aid and Empirical Antibiotics.

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1-7 THE CARDIAC INSUFFICIENCY BISOPROLOL STUDY II (CIBIS II)

In patients with heart failure **(HF),** beta-blockade improves left ventricular function and morbidity. This study assessed the impact of bisoprolol on all-cause mortality in patients with chronic HF. Bisoprolol [*Zebeta*] is a highly selective antagonist of the beta adrenoreceptors found mainly in the heart, especially in the ventricles.

Conclusion: Bisoprolol therapy improved survival in patients with stable HF.

STUDY

1. Double-blind randomized, placebo-controlled trial enrolled over 2600 patients (mean age 61). All had symptomatic HF (class III [83%] or IV) with left ventricular ejection fractions less than 36%. All had symptoms of HF lasting for at least 3 months before entry.
2. All were clinically stable and ambulatory.
3. All were receiving standard therapy with diuretics and ACE inhibitors.
4. Randomized to: 1) bisoprolol 1.25 mg daily or 2) placebo. Bisoprolol was progressively increased to a maximum of 10 mg daily, according to tolerance. (The great majority reached 10 mg.)
5. Follow-up a mean of 15 months.

RESULTS

1. The study was stopped early because of a significant mortality benefit.
2. Outcomes over 15 months:

	Bisoprolol	Placebo	NNT(benefit-15 months)
All-cause mortality	11.8%	17.3%	18
Sudden death	3.6%	6.3%	37

3. Treatment effects were independent of severity of HF.
4. Significantly fewer patients in the bisoprolol group were admitted to hospital.
5. 15% in each group withdrew.

DISCUSSION

1. Over a mean of 15 months, beta-blockade with bisoprolol in patients with HF was associated with a lower all-cause mortality, and fewer hospital admissions.
2. Benefits resulted irrespective of the cause of HF.
3. The greatest benefit was in patients with ischemic heart disease and class III HF.
4. Neuroendocrine activation, a compensatory mechanism in HF, may be potentially harmful. The renin-angiotensin-aldosterone system is inhibited by ACE inhibitors, and the increased sympathetic activity

is inhibited by beta-blockers. ACE inhibitors decrease cardiac work and energy consumption by unloading. Beta-blockers slow the heart rate. Both lower BP.
5. It is possible that ACE inhibitors prevent direct toxic cardiac effects of angiotensin II and aldosterone, and beta-blockers prevent the toxic effects of catecholamines.
6. In view of its major effect of reducing sudden death and the lower rate of admission to hospital for ventricular tachycardia and fibrillation, bisoprolol may act principally as an antiarrhythmic agent.
7. "The addition of a beta-blocker to standard therapy with a diuretic and an ACE inhibitor can be recommended in appropriate, stable, ambulatory patients who have heart failure."
8. Administration should be gradual and progressive, starting with low doses.
9. Patients in this trial averaged age 61. This is at least a decade younger than that of patients with HF seen in clinical practice. Information about the effects of beta-blockade in older age groups is inadequate.
10. This should not be extrapolated to patients with severe class IV HF symptoms and recent instability. Safety and efficacy has not been established in these patients.

CONCLUSION
Beta-blocker therapy had benefits for survival in stable heart-failure patients.
Start low — go slow.

THE LANCET January 2, 1999; 353; 9-13 Original multicenter trial by the CIBIS-II Investigators
An editorial in this issue (p 23) comments:
A meta-analysis of 18 double-blind placebo-controlled trials of beta-blockade in chronic heart failure showed an increase in left-ventricular ejection fraction by 29% and a 32% reduction in risk of death.
"For many physicians, the use of beta-blockers in patients with heart failure seems to conflict with their earlier training. To promote use of these agents, guidelines have to be updated."
Comment:
This is a good example of how fashions in medicine change. Beta-blockers heretofore were considered contraindicated in HF. RTJ

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1-8 A TRIAL OF ETANERCEPT, A RECOMBINANT TUMOR NECROSIS FACTOR RECEPTOR:Fc FUSION PROTEIN, IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING METHOTREXATE.

Methotrexate, a disease-modifying drug, is increasingly regarded as the agent of first choice in treatment of rheumatoid arthritis **(RA).** But many patients have persistent disease even when treated with methotrexate. When this occurs, a second disease-modifying drug is usually added.

Tumor necrosis factor (**TNF)** is a proinflammatory cytokine that has a complex role in the pathogenesis of RA.

Etanercept (*Enbrel*), a genetically engineered protein, is similar to the normal TNF-receptor. It binds with and inactivates TNF.

This study asked whether etanercept, added to methotrexate therapy, provides additional benefit to patients whose RA persists despite methotrexate mono-therapy.

Conclusion: The combination was safe and provided significantly greater clinical benefit than methotrexate alone.

STUDY
1 Double-blind trial entered 89 patients with active RA (mean age = 50; mean duration of disease = 13 years). Activity had persisted despite at least 6 months of methotrexate therapy at a stable dose.
2 Randomized to continuing methotrexate plus 1) etanercept 25 mg subcutaneously twice weekly, or 2) placebo.
3 Follow-up = 6 months.

RESULTS
1. The addition of etanercept to methotrexate resulted in rapid and sustained improvement.
2. Outcomes at 6 months according to the American College of Rheumatology criteria:

	Etanercept+methotrexate	Placebo+methotrexate
20% improvement	71% of patients	27% of patients
50% improvement	39%	3%

70% improvement 15% 0

3. At baseline patients had a median of 28 tender joints and 18 swollen joints
4. At 6 months:

	Etanercept	Placebo
Number of tender joints	7	17
Number of swollen joints	6	11
Sedimentation rate became normal	62%	30%
C-reactive protein became normal	44%	13%

5. The median disability-index score improved by 47% in the etanercept group.
6. Safety: etanercept was well tolerated. Reactions at the site of injection (usually mild) were the only events occurring more often in the etanercept group. None required discontinuation.

DISCUSSION

1. At 6 months, 15% of those receiving the combination met the ACR criteria for a major clinical response.
2. Etanercept did not potentiate the toxic effects of methotrexate. It did not induce dose-limiting toxic effects of its own.

CONCLUSION

In patients with persistently active RA while on a stable dose of methotrexate, addition of etanercept was safe and well tolerated, and provided significantly greater clinical benefit than methotrexate alone.

NEJM January 28, 1999; 340: 253-59 first author Michael E Weinblatt, Brigham and Woman's Hospital, Boston MA

Comment: A similar study appeared in the March 16 issue of the Annals. Over 225 patients were randomized. Significant and sustained benefit was reported.
Both studies were supported by Immunex Corp. RTJ

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A Primer on Cytokines

1-9 ANTICYTOKINE THERAPY — A New Era in the Treatment of Rheumatoid Arthritis?

(Thie editorial comments and expands on the preceding.)

Tumor Necrosis Factor:

Tumor necrosis factor **(TNF),** a cytokine, plays a pivotal role in the immune system. It is an important mediator of local inflammation. It appears to keep inflammation localized. Actions included: local activation of vascular endothelium, release of nitric oxide with vasodilation and increased vascular permeability, and increased expression of adhesion molecules on endothelium of blood vessels. It increases platelet activation resulting in local blood vessel occlusion and containment of infection. (The local blood vessel occlusion is probably responsible for the tumor necrosis — hence the name.)

This results in recruitment of inflammatory cells, immunoglobulins, and complement. And also activates T-cells and B-cells. Activation of macrophages produces interleukins.

Although locally the effects of TNF are beneficial, systemically they may be disastrous, leading to septic shock, and disseminated intravascular coagulation. Patients who make excessive amounts of TNF as a response to infection have higher mortality.

TNF has a central role in the pathologic response associated with rheumatoid arthritis (RA). Excess TNF occurs in their blood. Increased levels of interleukins occur in the synovial fluid, correlating with severity of the disease.

TNF Receptors and TNF Receptor-blockers

TNF binds to receptors on neutrophils, vascular endothelial cells, and fibroblasts. These receptors are also found in soluble form in serum and synovial fluid and may act to regulate TNF.

Two TNF receptor blockers are under investigation: 1) infliximab is an antibody to TNF, 2) etanercept is a TNF receptor which, when administered locally, binds TNF, and prevents its action. Infliximab combined with methotrexate also leads to substantial improvement in RA. It has recently been approved for use in Crohn's disease.

"On the basis of data currently available, it appears that patients who have suboptimal response to methotrexate are the best candidates for etanercept or infliximab."

Other cytokines are also important in RA. Anti-TNF alone is not the whole story.

"A new era has begun."

NEJM January 28, 1999; 340: 310-12 Editorial by James R O'Dell, University of Nebraska Medical Center, Omaha

Comment: I am trying to learn more about cytokines. Terminology confuses me. This article helped. RTJ

1-10 BENEFITS OF LIFESTYLE ACTIVITY VS STRUCTURED EXERCISE.

Regular physical activity (bodily movement produced by skeletal muscle contraction which substantially increases energy expenditure) reduces risk of coronary disease and diabetes.

Exercise, a subset of physical activity, is planned, structured, and repetitive bodily movement done to improve or maintain physical fitness.

The term "aerobics" was first adopted as a popular description for endurance exercise in the 1960s. The health and fitness benefits of regular vigorous exercise have been touted ever since.

During the past 5 years there has been a reassessment of the original epidemiologic evidence linking physical activity with health and a growing body of new research demonstrating that lesser quantities and intensities of physical activity also lead to benefits. Focus is now on the important role that moderate intensity physical activity plays in improving and maintaining good health. Epidemiologic evidence clearly indicates that 30 minutes of moderate physical activity yields daily substantial health benefits, but evidence from clinical trials has been sparse.

Two randomized clinical trials in the issue of JAMA [1; 2] compared the effects of lifestyle physical activity vs structured exercise on fitness, body composition, and risk factors for cardiovascular disease.

The studies demonstrated that a lifestyle approach to increasing activity among previously sedentary persons can be effective and has similar effects on fitness, body composition, and blood pressure as a traditional structured exercise program.

The relationship between physical activity and health appears likely to be a continuous one. Some activity is better than none, more is better than some, until at some point it is possible to do too much. Lifestyle modifications support a wide range of choices of physical activity. "Physical activity needs to become not just the right choice, but an easy, sustainable, and enjoyable choice."

JAMA January 27, 1999, 281: 375-76 Editorial by Michael Pratt, Centers for Disease Control and Prevention, Atlanta, GA

1 "Comparison of Lifestyle and Structured Interventions to Increase Physical Activity and Cardiorespiratory Fitness" JAMA January 27, 1999; 281: 327-34 This study compared the 2-year intervention effects of a lifestyle physical activity program vs traditional structured exercise on improving cardiorespiratory fitness, and lowering risk of cardiovascular disease. Over 200 sedentary subjects were entered. Participants randomized to the lifestyle group were advised to accumulate at least 30 minutes of moderate-intensity physical activity on most, preferably all, days of the week in a way uniquely adapted to each person's lifestyle. The mean increased energy expenditure was about 450 kcal/week.

The investigators monitored and advised the group carefully over 2 years. The goal was to increase energy expenditure by 3 kcal/kg per day and to increase fitness (VO2 peak) by 5 mL /minute at the end of 24 months. (Few met the goal.) The study concluded that the lifestyle physical activity intervention was as effective as the structured exercise program in improving fitness and blood pressure.

Benefits were also reported in those who fell well short of the physical activity goal.

2. "Effect of Lifestyle Activity vs Structured Aerobic Exercise on Obese Women" JAMA January 27, 1999; 281: 335-40 This 16-week trial entered 40 obese women. A 1200 kcal/day diet was prescribed in addition to a fitness program. Participants in the lifestyle group were advised to increase their levels of moderate intensity physical activity by 30 minutes daily. They incorporated short bouts of activity into their daily schedules. (Walking instead of driving short distances; taking the stairs instead of the elevator.) Energy expenditure increased by about 1500 kcal/week. The group lost a significant amount of weight. Lipid profiles improved. The investigators concluded that the diet-lifestyle activity program was a suitable alternative to structured aerobic activity for obese women.

Comment:

Note that the increased energy expenditure in the first study was only 450 k/cal per week — not much.

(I double checked this from the text.) Nevertheless, some benefits resulted. Even an enthusiastic, encouraging trial found it most difficult to sustain increased activity.

The challenge for primary care clinicians is to encourage and motivate a sustained lifestyle change. Difficult, but not impossible. RTJ

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1-11 ORAL CONTRACEPTION AND HEALTH

"Oral contraceptives **(OC)** have been studied more intensively than any other medication in history."

A study in this issue of BMJ [1] reports mortality experience in 46 000 women over a 25 year period. Half were using OCs. Most were combined OCs containing 50 ug of estrogens. Over this time 1600 deaths were recorded. OC did not increase or decrease total mortality (RR = 1.0) compared with never-use. Women who used OC had a lower death rate from ovarian cancer (RR = 0.2), and a higher death rate from cervical cancer (RR = 2.5) and cerebrovascular disease (RR = 1.9). These risks were seen while the women were taking the OC and for 10 years after. After 10 years mortality rates were similar to never-users.

There was no evidence of an increase risk of breast cancer (RR = 1.1; CI = 0.8 to 1.8)

"How would one compare the relief of dysmenorrhea in 1000 women with the causation of stroke in one? And how about avoiding the grief of an unwanted pregnancy?"

The evidence suggests that women who do not smoke, who have their blood pressure checked, and do not have hypertension, have no increased risk of myocardial infarction and little risk of stroke when they use combined OCs. (BP should always be measured before starting OCs.)

BMJ January 9, 1999; 318: 69-70 Editorial By David C G Skegg, University of Otago, Dunedin. New Zealand.

1. "Mortality Associated with Oral Contraceptive Use: 25-year Follow-up of Cohort of 46 000 Women from Royal College of General Practitioners Oral Contraception Study" BMJ January 9, 1999; 318: 96-100

Comment: The data about breast cancer are reassuring. The risk of cervical cancer can be reduced by surveillance. RTJ

==========**1-12**

WEIGHT CONTROL AND RISK REDUCTION IN OBESE SUBJECTS TREATED FOR 2 YEARS WITH ORLISTAT

Orlistat (*Xenical*) is a gastrointestinal lipase inhibitor. It reduces activity of pancreatic and gastric lipases, and blocks intestinal uptake of ingested fat by about 30%. Orlistat itself is minimally absorbed.

This study tested the hypothesis that orlistat combined with dietary intervention is more effective than placebo plus diet for weight loss and maintenance of weight loss over 2 years.

Conclusion: Two-year treatment significantly promoted weight loss and lessened weight regain.

STUDY

1. Randomized, double blind, placebo-controlled trial enrolled 1187 subjects. All were obese (BMI = 30 to 43)
2. After a 4-week placebo lead-in period of placebo plus hypocaloric diet, 663 were randomized to continued diet plus : 1) orlistat 120 mg 3 times daily, or 2) placebo. 581 (87%) completed one year.
3. During the second year, 443 were randomized to weight maintenance diet plus 1) orlistat 120 mg 3 times daily, or 2) orlistat 60 mg 3 times daily, or 3) placebo.
4. 403 completed the 2-year study.

RESULTS

1. During the first year, orlistat patients lost more weight than placebo patients (8.8 kg vs 5.8 kg).
2. Subjects taking 120 mg orlistat during the second year regained less weight than placebo group (+3 kg vs + 5.6 kg).

3. Orlistat 120 mg 3 times daily was associated with improvements in LDL-cholesterol and insulin levels.
4. Adverse effects — more were associated with orlistat. At least one GI event (flatus with discharge, oily spotting, fecal urgency, fatty/oily stool, fecal incontinence) was experienced by 79% of orlistat subjects vs 59% of placebo patients.[1] The events typically occurred early in the treatment, were generally mild, and resolved spontaneously. Seven subjects in orlistat group withdrew because of GI events vs 2 in the placebo group.
5. Vitamin D and E levels declined significantly in the orlistat group. Supplementation was required in 14% vs 6% of placebo patients.

DISCUSSION
1. Subjects taking orlistat during the second year while on a weight-maintenance diet regained about 1/3 of their lost weight. The placebo subjects regained most of their lost weight.
2. Lipase inhibition by orlistat prevents absorption of about 30% of fat in a prescribed diet containing 30% of energy from fat. This, in effect, would reduce the intake of fat to about 20% to 24%.

CONCLUSION
Partial inhibition of fat absorption by orlistat combined with a mildly controlled energy diet over 2 years in obese subjects promoted weight loss, lessened weight regain, and improved some obesity-related risk factors.

JAMA January 20, 1999; 281: 235-42 Original investigation, first author Michael H Davidson, Chicago Center for Clinical Research, Chicago, IL

Comment:

1. Hard to believe over half of the placebo patients had these complaints.

The study was supported by funding by Hoffman-LaRoche, Inc.

One way of determining applicability of a study intervention to primary care is to compare subjects originally contacted, then originally enrolled, with the number completing the trial. In this study, 1187 were enrolled, and 306 completed 2 years. Thus only 25% of subjects completed an enthusiastic trial. Applicability to clinical care will be considerably less. In my judgement the benefit/harm-cost of orlistat is too low to justify use in primary care unless a patient specifically requests it. RTJ

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1-13 THE PROTECTIVE EFFECT OF MODERATE ALCOHOL CONSUMPTION ON ISCHEMIC STROKE

Moderate alcohol consumption reduces risk of cardiac mortality and myocardial infarction. The effect on stroke is controversial.

This study was designed to clarify the relationship between alcohol consumption and ischemic stroke.

Conclusion: Moderate consumption was independently associated with a decreased risk of stroke.

STUDY
1. Population-based case-control study entered over 1800 persons.
2. Cases (n = 677; mean age 70) had experienced a first ischemic stroke.
3. Controls (n = 1139) matched by age, sex, race/ethnicity. None had history of stroke.
4. Assessed alcohol consumption in both groups.

RESULTS
1. Moderate consumption (up to 2 drinks daily) was significantly protective. After adjustment for other stroke risk factors, the odds ratio of risk of ischemic stroke in moderate drinkers (1 to 2 drinks daily) vs abstainers = 0.51 (CI = 0.39 to 0.67).
2. The protective effect was detected in both sexes, young as well as old, blacks, Hispanics, and whites equally.
3. No differential protective effect among the types of alcohol consumed.
4. The risk of stroke rose in those consuming 7 or more drinks daily (OR = 3.0).

DISCUSSION
1. “Our results demonstrate a protective effect of moderate alcohol consumption on ischemic stroke in a multiethnic population.”

2. The Nurse's Health Study also found a protective effect among women consuming up to 1.2 drinks per day.
3. The National Stroke Association Stroke Prevention Guidelines also support the beneficial effects of moderate consumption.

CONCLUSION

Moderate alcohol consumption was independently associated with a decreased risk of ischemic stroke. Heavy alcohol consumption was deleterious.

JAMA January 6, 1999; 281: 53-60 Original investigation, first author Ralph L Sacco, Columbia University College of Physicians and Surgeons, New York

Comment: Another example of the benefits of modest alcohol intake. If alcohol was not associated with abuse and dependence, it would be one of the most frequently prescribed drugs. RTJ

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Reference Article

1-14 COX-2 INHIBITORS

Cyclo-oxygenase-1 and cyclo-oxygenase-2 are enzymes very similar in structure. . The prostaglandins they produce are different.

1. COX-1 acts constantly (not inducible). It predominates in the stomach. It is the predominant source of the gastric mucosal prostaglandins which protect the stomach. NSAIDs tend to selectively inhibit COX-1, reducing the protective effect of the prostaglandin, leading to acid-producing gastric mucosal injury.
2. COX-2 is inducible by inflammation. Its prostaglandin is associated with pain, swelling, and stiffness.

The idea then is to inhibit the "bad guy" — COX-2 while preserving the "good guy" — COX-1. Inhibiting COX- will relieve some symptoms of inflammation.

Several COX-2 inhibitors have been developed and approved. They are as effective as aspirin, naproxin, and diclofenac for pain relief. They have been reported to improve quality of life in patients with osteoarthritis. COX-2 inhibitors will not replace aspirin's cardiovascular protective effects.

Endoscopic studies report the degree of gastric injury in patients taking COX-2 inhibitors is similar to placebo, much less than with other NSAIDs .

There are several circumstances where COX-2 may be important for homeostasis in health or disease. In theory, their use could be deleterious. Many concerns and questions remain about the benefit/harm-cost ratio.

"COX-2 inhibitors are likely to have a major impact on prescribing in inflammation and analgesia. As their strengths and weaknesses become clear, non-selective NSAIDs with or without co-prophylaxis of misoprostol, or omeprazole may establish alternative niches. "

THE LANCET January 23, 1999; 353; 307-14 Review article by C J Hawkley University of Nottingham, UK

Comment: This is a simple working scheme to clarify the actions of COX 1 and 2. The reality is much more complicated. RTJ

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Read the Original!

1-15 NARRATIVE IN MEDICAL ETHICS

"Narrative contributes to medical ethics through the content of stories (what they say) and through the analysis of their form (how they are told and why it matters)."

"Patients and their family members and friends are not the only ones who write important "narratives of witness" (autobiographical accounts). By writing narratives from their personal experiences, doctors and other healthcare professionals can also have a powerful effect on the public discussion of ethical issues." Stories are important as case examples for teaching the principles of medical ethics and as moral guides to living a good life (not just the practice of medicine, but in all aspects of one's life). Narratives may compel re-examination of accepted medical practices and ethical precepts.

"Unlike analytic philosophers who are trained to work deductively from general principles to the particular case, doctors are trained to work in the opposite direction, beginning with the particular case

and then seeking general medical principles that might apply" This practice is not inductive, but abductive, as doctors tack back and forth between a particular case and the generalized realm of scientific knowledge.
Narrative ethics focuses on the patient as narrator of his of her own story, including the ethical choices that belong to their story. The doctor must work as coauthor with the patient to construct a joint narrative of illness and medical care. "Narrative practice is relational and requires the doctor to be an empathic witness to the patient's suffering. "

"In its ideal form, narrative ethics recognizes the primacy of the patient's story, but encourages multiple voices to be heard and multiple stories to be brought forth by those whose lives will be involved in the resolution of a case."

BMJ January 23, 1999; 318: 253-56 Essay by Anne Hudson Jones, University of Texas Medical Branch, Galveston.

==========**Read the Original !**

1-16 NARRATIVE BASED MEDICINE IN AN EVIDENCE BASED WORLD

There is an art to medicine as well as an objective science. This article explores the dissonance between the "science" of objective measurement and the "art" of clinical proficiency and judgement. It attempts to integrate these different perspectives.

The limits of objectivity in clinical method

Science uses reproducible methods allowing construction of generalizable statements about how the universe behaves. Conventional medical training teaches students to view medicine as a science. The doctor is an impartial investigator who builds differential diagnoses as if they were scientific theories, while excluding competing possibilities in a manner akin to the falsification of hypotheses. This is a tenuous assumption — that diagnostic decision-making follows an identical protocol to the scientific inquiry — that the discovery of "facts" about a patient's illness is the equivalent to the discovery of a new scientific truth.

The evidence-based approach to clinical decision-making is often incorrectly held to rest on the assumption that clinical observation is totally objective and should, like all scientific measurements, be reproducible. But, the founding fathers of evidence-based medicine made no such claim for objectivity of the clinical method. Clinical judgements are usually a far cry from the objective analysis of a set of eminently measurable "facts". Doctors do not simply assess symptoms and physical signs objectively. They interpret them by integrating the formal diagnostic criteria of the suspected disease (that is, what those diseases are supposed to do in "typical" patients as described in textbooks) with the case-specific features of the patient's individual story and the doctor's accumulated professional case experience.

Evidence-based clinical decision making involves the somewhat counterintuitive practice of assessing the current problem in the light of the aggregated results of hundreds of comparable cases in a distant population sample, expressed in the language of probability and risk — the stuff of clinical epidemiology and bayesian statistics.

How can we square the circle of upholding individual narrative in a world where valid and generalizable truths come from population derived evidence? "Truths" established by the empirical observation of populations in randomized trials and cohort studies cannot be mechanistically applied to individual patients (whose behavior is irremediably contextual and idiosyncratic) or to episodes of illness.

In large research trial, an individual's unique and multidimensional experience is expressed as a single dot on a scatter plot to which we apply mathematical tools to produce a story about the sample as a whole. The generalizable truth that we seek to glean from research trials pertains to the sample's (and hopefully, the population's) story, not the stories of individual patients. There is a serious danger in erroneously viewing summary statements as hard realities.

"Misplaced concreteness" is an apt description of the dissonance we experience when we try to apply research evidence to clinical practice. Medicine lacks rules that can be generally and unconditionally applied to every case, and even in every case of a single disease. Thus, although there are certainly "wrong" answers to particular clinical questions, it is often impossible to define a single "right" answer that can be applied to every context.

The frustration that health professionals experience when trying to apply evidence based research findings to real life case scenarios occurs most commonly when they abandon the interpretive framework and attempt to get by on evidence alone.

Stories within stories:

The doctor-patient encounter takes place in a highly structured transactional space in which the behavior of both parties is determined by socialized expectations. The diagnostic encounter differs from other human narratives. It is the story about a "person as ill". This integrates 4 separate secondary texts: 1) the experiential text — the meaning the patients assigns to the illness; 2) the narrative text — what the doctor interprets to be the problem from the story the patient tells; 3) the physical or perceptual text — what the doctor gleans from the physical examination; and 4) the instrumental text — what the X-ray and laboratory say. The search for the "objective" analysis of a diagnostic test (eg, looking at an X-ray or laboratory test without a clinical or social history) is doomed to fail. The results of diagnostic tests must be interpreted judiciously on the basis of bayesian pretest probabilities determined by the history and physical examination.

There is also a therapeutic narrative: the formulation of a plan of what to do next and the enactment of that narrative. This is a shared decision-making involving both doctor and patient.

Conclusion:

Appreciating the narrative nature of illness and the intuitive and subjective aspects of the clinical method does not require us to reject the principles of evidence-based medicine. Genuine evidence- based practice actually presupposes an interpretive paradigm in which patients experience illness in a unique and contextual way. It is only within such an interpretive paradigm that a clinician can reach an integrated clinical judgement and meaningfully draw on all aspects of evidence — his or her own case based experience, the patient's individual and cultural perspectives, and the results of rigorous clinical research trials and observational studies.

BMJ January 30, 1999; 318: 32325 The last of a series 5 articles on narrative based medicine presented in BMJ, this one written by Trisha Greenhalgh. BMJ books has published "Narrative Based Medicine" from which the article was adapted.

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Read the Original !

1-17 THE TROUBLE WITH FAMILIES: Toward an Ethic of Accommodation

Many health care professionals, when asked what creates the most difficult situations in end-of-life care, reply "Families". Paradoxically, the health care system can not exist without family members. They provide emotional and physical support and assistance, and implement and monitor high-tech procedures at home. Cost containment is largely the shifting costs of care of patients to families.

Conflicts are most likely to occur in an acute care hospital when the patient is seriously ill or dying, and the family is in crisis. When families fail to conform to expected behaviors (eg, failing to appear at critical moments or being unable to make decisions), or disagree with medical professionals and among themselves, they are casually labeled dysfunctional.

Although some clinicians and administrators are extraordinarily sensitive to the legitimate needs and interests of families in medical crisis, a persistent tendency exists to equate families with trouble.

Some problems may derive from western medicine's almost exclusive focus on the individual patient's autonomy. Patient autonomy and a physician-patient relationship based on trust are primary elements in the ethical framework of medical care. Nevertheless, a complete understanding of the patient's personhood must consider the social network that helps define the patient's core identity. Most persons have some deeply meaningful relationships with others— the patient's "beloved people". One of the most significant sources of tension between professionals and families lies in differing perceptions of the roles that family members should play and how they should play them.

Family members as advocates and trusted companions:

1. May become extremely vigilant when their relative is admitted.
2. May experience extreme stress.

3. May have previous negative experiences with the health care system and fear neglect or improper and insensitive treatment of the patient

4. May feel they need to be present at all times to explain the patient's special needs and to prevent improper care.

5. May have dealt with the patient's chronic illness and be familiar with the patient's care. Yet their expertise is rarely accorded respect.

6. May request assistance that they feel is important for the patient, but which may be inconvenient for the staff.

7. May upset institutional routines in ways that patients do not.

8. Have strength in numbers

9. Are not subject to the vulnerabilities of patienthood, but are extremely vulnerable in other ways, particularly with respect to hospital routines and policies.

10. Accompany a relative through the journey of illness and death, bearing witness and sharing and responding to the patient's experiences.

For some patients, especially the seriously ill or cognitively impaired, the family is their primary point of contact with the health care system. Institutional requirements which limit the presence of family members at a critical moment become barriers to family participation. The family may see their presence as a sign of fidelity; staff members may see them as interlopers and may be concerned that their presence will interfere.

Families as surrogate decision makers:

Most commentators, at least in theory, support the idea that family members are likely to know the patient's wishes and to act in the patient's best interest. The reality is that surrogates are often unclear about the real choices available and about how to participate meaningfully.

Other sources of conflict:

Underlying some conflicts between caregivers and families is the often unsubstantiated belief that family members who face financial or care burdens will always put their own self-interest above that of the patient.

Clinicians are frustrated when family members disagree about decisions. Few families are perfectly cohesive. Hidden tensions are common. They can erupt under the strain of the illness of a family member.

The family is often expected to speak immediately with one voice, without the benefit of discussion, or a full understanding of the implications.

Rather than acknowledging the impact of the illness on the family, many clinicians distance themselves from the sometimes palpable emotional atmosphere. This makes the family feel abandoned, and rightly so.

A related source of conflict is the professional's fear of litigation from angry family members. Clinicians may shield information or prevent family members from observing the direct administration of care lest something go wrong — this despite the numerous studies that have clearly shown that litigation is less, not more, likely when communication is direct and honest.

Conflicts are magnified when the family comes from a religious, cultural , or ethnic background that differs from the one that is dominant among providers. "If families and professionals metaphorically do not speak the same language, consider how much more difficult communication is when they literally do not speak the same language."

Recommendations: Toward an Ethic of Accommodation:

Working with families means developing an ethic of negotiation and accommodation when interests compete or diverge. This is a foundation on which to build solid partnerships among clinicians, patients, and families. Patients have both interests and preferences. The well-being and vital interests of their family members also come into play. No simple formula exists that will establish which interests have primacy.

A first step: Physicians should explore how involved the patient wants the family to be in care and decision making. And should explore the expectations of the family as well. Caregivers say that what they need most is understandable, timely information; better preparation and training for the technical and emotional aspects of their role; compassionate recognition of their anxiety, suffering, and hard work;

guidance in defining their roles and responsibilities in patient care and decision making; and support for setting of fair limits of their sacrifices.

Communication is the single most important aspect of working with patients and their families. It involves active listening as well as talking. It requires time and patience.

Conclusion:

A system that saves lives or prolongs lives only to cast patients and families into the abyss of fragmented chronic care and financial and emotional ruin, while at the same time criticizing them for being "too emotional", is unjust. Many families are willing to make enormous sacrifices, but martyrdom is not a good basis for health care policies or practice. When families are pushed beyond their limits, the patient's care is jeopardized, the caregiver's health is at risk, professionals are frustrated, and the health care system is burdened by greater costs. "Our recommendations focus on human relationships, not technology." A health care system that depends so heavily on the patient care provided by families should involve families as partners rather than define them as problems.

Annals Int. Med. January 19, 1999; 130:148-52 "Perspective" ; Commentary by Carol Levine, and Connie Zuckerman, Beth Israel Medical Center, New York.

Comment:

Don't abandon the patient. And don't abandon the care-giver. Anyone who has spent lonely hours sitting in an intensive-care waiting room, where hours creep by, will understand.
Until a clinician has a loved one, especially a young one, in a life-threatening situation, he may not fully understand how helpless and vulnerable care givers feel, and how any word of support and understanding, however slight, will be grasped tightly.

Gaining the trust of the family is as important as gaining the trust of the patient. RTJ

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1-18 NICOTINE NASAL SPRAY WITH NICOTINE PATCH FOR SMOKING CESSATION:
Randomized trial with six year follow up

Nicotine replacement therapy more effectively results in cessation than placebo.

This trial compared efficacy of nicotine patch vs spray. The spray permits a higher level of nicotine substitution and provides a more flexible method of substitution compared with the patch. Patches release nicotine slowly; spray delivers it more rapidly, enabling the smoker to respond rapidly to any smoking urges.

Conclusion: The spray was superior.

STUDY

1. Placebo-controlled, double blind trial entered 237 smokers (all nicotine dependent) who volunteered for the trial. All were motivated to quit.
2. Randomized to: nicotine patch plus nasal spray for 1 year, or 2) nicotine patch plus placebo spray for 5 months.
3. Patches included 15 mg nicotine for 3 months then 10 mg for the 4^{th} month and 5 mg for the 5^{th} month. The spray was available for 1 year even though it was not always used daily.
4. Both groups received supportive treatment.

RESULTS

1. Patch plus spray was associated with a sustained abstinence rate at 1 year of 27% vs 11% in the patch plus placebo. [NNT(benefit-1year) = 6]; after 6 years, 16% vs 9% [NNT(benefit-6years) = 14].
2. At 1 year, of the 32 of 120 participants assigned to patch plus spray who were still abstinent, only 4 were still using the spray. These four were using it at high doses.
   (This suggests it is not cost effective to use the spray for longer than 7 months after stopping the patch.)

DISCUSSION

1. Even at day 15, the spray plus patch was more effective than the patch alone.
2. The spray may have been more successful because of the high level of substitution and the rapid response to the smoker's need.

3. It must be acknowledged that the majority of smokers relapse within one year regardless of the method of substitution. (Only about 1 in 4 who used the patch + spray.)

CONCLUSION

Combination nicotine spray plus patch used for 1 year was more effective than the patch used alone. Most subjects attaining cessation had stopped using the spray at 1 year.

BMJ January 30, 1999; 318: 285-88 Original investigation, first author Thorsteinn Blondal, National University Hospital , Reykjvik, Iceland.

An editorial in this issue (p. 289) comments: No replacement therapy mimics the extremely rapid, rewarding, high arterial nicotine concentrations derived from inhaled tobacco smoke. This may explain the low success rates of substitution. Dosing with nasal spray, buccal inhalation, and chewing gum are under the control of the smoker, and include some behavioral activity. It allows users to adjust the dose, albeit with less control and more slowly than with cigarettes. Underdosing occurs mainly because smokers cannot master the correct technique for their use, or because they find the irritant effects unpleasant.

The study provided evidence that combination therapy is more effective. Part of the benefit may have been due to the higher concentrations of nicotine in the circulation and the more flexible mode of delivery.

Comment: Does "success" in promoting cessation depend on permanent cessation? Does intermittent cessation (ie, stopping for 6 months from time to time) reduce the risk of complications? I suspect it does.

The study was supported by Pharmacia-Upjohn RTJ

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Reference Article

1-19 RECENT ADVANCES IN THE PHARMACOTHERAPY OF SMOKING

This article reviews the new pharmacotherapies for smoking and makes recommendations for changes in physician practices.

"Phamacotherapy should be made available for all smokers. "

" All currently available therapies appear to be equally efficacious, approximately doubling the quit rate compared with placebo."

" Concomitant behavioral or supportive therapy increases quit rates and should be encouraged but not required.

"Combining patch with gum or patch with buproprion [Zyban] may increase the quit rate compared with any single treatment.

"The best treatment choice for an individual should be guided by the patient's past experience and preference and the product's adverse effect profile.

"Recent prospective data indicate that use of nicotine gum for as long as 5 years, even with concurrent use of cigarettes, does not increase risk of cardiovascular or other diseases.

"Every physician should intervene with every patient who smokes. In the future, failure to treat smoking will keep someone out of the "good doctor's club" just as much as failure to treat hypertension.

"Physicians should remind patients that most smokers make many (often over 5) attempts to stop before they succeed.

"Search for poor medication compliance and comorbid psychiatric problems (especially alcohol abuse and depression) which might be interfering with cessation.

" Simple retreatment with the same method achieves little success. A new treatment should be considered, ie, nicotine nasal spray, nicotine inhaler, or bupropion. Choice should be based on patient preferences. Combination therapy should be considered."

JAMA January 6, 1999; 281: 72-76 "Special Communication" review article, first author, John R Hughes, University of Vermont, Burlington.

Comment:

It's not the method, it's the motivation.

Glaxco-Wellcome markets bupropion under 2 trade names, Zyban and Wellbutrin—Zyban for smoking cessation, and Wellbutrin for treatment of depression. I can think of no other drug so marketed. RTJ

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1-20 MANAGING SMOKING CESSATION

This week BMJ publishes smoking cessation guidelines.[1] Primary health care teams are central to this effort. They should adopt a systematic approach towards ascertaining and documenting smoking status in medical records.

Most time and resources should be spent on individuals who are motivated to stop. After raising the issue of smoking clinicians should assess smokers' motivation to stop and tailor any further discussion accordingly.

The recommendation that general practitioners should always advise smokers to stop and constantly repeat this advice at every opportunity is questionable. This has never been adequately tested. Motivated smokers differ from unselected ones consulting general practitioners and are more likely to stop. "We do not know whether this is because of their increase motivation or the repeated advice. "Fewer than half of all smokers consider that their smoking is a problem."

Patients do rate their general practitioners' lifestyle advice highly. But would discussing cessation at every encounter be effective?

Only about 30% of smokers who have seen a general practitioner in the previous year recall doctors' antismoking advice.

BMJ January 16, 1998; 318: 138-39 Editorial, first author Tim Coleman, University of Leicester, UK
1. " Smoking Cessation: Evidence Based Recommendations for the Health Care System" BMJ January 16, 1999; 318: 182-85

1-21 CALCIUM SUPPLEMENTS FOR THE PREVENTION OF COLORECTAL ADENOMAS

Dietary patterns have repeatedly been associated with risk of colorectal neoplasia. A diet rich in vegetables and fruits is associated with a lower risk; animal fat and red meat with increased risk. Changes in risk may be due in part to alterations in bile acids, which are carcinogenic in animals.

Calcium binds bile acids in the bowel lumen — thus, the hypothesis that calcium may be protective.

This trial assessed the effect of calcium intake on risk of recurrence of colorectal adenomas.

Conclusion: Calcium supplementation was associated with a significant reduction in risk of recurrent adenomas.

STUDY

1. Multicenter randomized trial entered over 900 subjects (mean age 61). All had a history of colorectal adenomas.
2. Randomized to: 1) calcium carbonate 3 g (1200 mg elemental Ca) daily, or 2) placebo.
3. Follow-up with colonoscopy at 1 year and at 4 years.

RESULTS

1. Most patients had 1 or 2 adenomas removed at baseline.

2.	Calcium	Placebo	Relative risk
A second adenoma was found at 4 years:	31%	38%	0.85 (CI — 0.74 to 0.98)
3. Mean number of adenomas	0.55	0.73	0. 76 (CI — 0.60 to 0.96)

4. The effect of Ca was independent of initial dietary fat intake.

DISCUSSION

1. Calcium supplementation was associated with a significant, though moderate reduction in risk of recurrent adenomas.
2. The reduced risk became apparent as early as the first colonoscopic follow-up (after 9 months of treatment).
3. In animals, calcium inhibits mucosal injury and hyperproliferation induced by bile acids or carcinogens.
4. The trial did not directly assess the effect of calcium on development of a first adenoma or on progression to invasive cancer.

5. Since the toxicity of this simple and inexpensive agent appears to be minimal, and since it may reduce the risk of osteoporosis, the benefit/harm-cost ratio may be high.

CONCLUSION

Calcium supplementation was associated with a significant — though moderate— reduction in risk of recurrent colorectal adenomas.

NEJM January 14, 1999; 340: 101-07 original investigation from the Calcium Polyp Prevention Study Group, first author J A Baron, Dartmouth-Hitchcock Medical Center, Lebanon, N.H.

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1-22 SEVERE MENTAL ILLMESS AND SUBSTANCE ABUSE

"Evidence from the United States suggests that half of all patients with schizophrenia also have a substance misuse disorder." In one inner district in London, 36% of psychotic patients misused drugs or alcohol.

The term "dual diagnosis" is used increasingly in psychiatric practice to describe the combination of severe mental illness (mainly psychotic disorders) and substance misuse. "We prefer the term 'comorbidity' (the simultaneous presence of two or more disorders), though even this may fail to capture potential causal interactions between psychosis and substance misuse."

Whether there is any causal relation between substance misuse and psychotic disorders remains controversial. Some types of substance misuse, particularly alcohol, cannabinoids, hallucinogens, and stimulants (such as amphetamines) can produce psychotic symptoms directly without mental illness. They may also precipitate psychotic disorders among people with predisposition.

BMJ January 16, 1999; 318: 137-38 Editorial, first author T Weaver, Imperial College of Science, Technology, and Medicine, London UK