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BEYOND AIDS

Moderator: MELVIN C. MCFALL
Panelists: HENRY C. GEORGE*
GREGG R. SADLER
ROBERT J. SPELLMAN**
Recorder: MELVIN C. MCFALL

o The medical community provides insight into developments which could affect mortality in the future. The panel will explore the projected impact of advances in the diagnosis and treatment of major impairments. An update on the latest developments in underwriting tests will be included.

MR. MELVIN C. MCFALL: Actuaries, underwriters, and life insurance company medical directors have been understandably preoccupied with AIDS for the last few years. AIDS will continue to consume much of our time. But there are a number of other health and medical developments that will also affect future mortality. Although none of these developments individually is nearly as important as AIDS, collectively they could have a significant impact. Our panel will discuss these developments, concentrating on those that relate to the more common causes of death among insured lives -- heart disease, cancer, diabetes, etc. We will also touch on new technology that may affect the way we underwrite in the future.

Our first speaker, Dr. Robert Spellman, is Medical Director for the Northwestern Mutual Life Insurance Company. Dr. Spellman is a summa cum laude graduate of St. John's University and received his medical degree from Johns Hopkins Medical School. He joined Northwestern Mutual in 1976 and was promoted to his current position in 1985. He is responsible for all medical operations at Northwestern Mutual and has authority for life and disability income medical standards and requirements.

Dr. Spellman is board certified in internal medicine and became an FLMI in 1982. He is one of the principal authors of the "Underwriter's Guide to Medically Impaired Risks," which is currently a Society of Actuaries study note. He is also an active contributor to the journal *Medical Risks*. Dr. Spellman's major subspecialty interest is in rheumatology.

Our second speaker, Henry C. George, is Vice President, Technical Services for Home Office Reference Labs. Hank is a frequent speaker at underwriting, medical, and actuarial conventions. If you haven't heard Hank before, you will understand why he is in such demand.

* Mr. George, not a member of the Society, is Vice President-Technical Services at the Home Office Reference Laboratory, Inc. in Lenexa, Kansas.

** Dr. Spellman, not a member of the Society, is Medical Director at Northwestern Mutual Life Insurance Company in Milwaukee, Wisconsin.

Hank is an honors graduate of the University of Wisconsin at Milwaukee and is a CLU, an FLMI, and a Fellow of the Academy of Life Underwriting. He is the founder and editor of *On the Risk*, the professional journal for underwriters. He has served on the executive committees of both the Institute of Home Office Underwriters and the Home Office Life Underwriters Association.

Hank spent about 15 years with Northwestern Mutual and worked with Manufacturers Life and Lincoln National Management Services before assuming his current position earlier this year. He has published a number of papers on medical and underwriting topics.

Our third speaker, Gregg R. Sadler, is Senior Vice President, Risk Appraisal and Customer Service at Business Men's Assurance. Gregg is a Phi Beta Kappa graduate of the University of Nebraska, where he majored in math and minored in actuarial science and economics.

Gregg is an FSA and a Member of the American Academy of Actuaries. He served on the part 8 examination committee from 1978 to 1980. He has been active in both the Institute of Home Office Underwriters and the Home Office Life Underwriters Association, and he currently serves as a member of the Risk Classification Committee of the American Council of Life Insurance.

Gregg is a member of the Board of Directors of Home Office Reference Laboratory and is one of a relatively small number of actuaries with extensive experience and expertise in risk appraisal.

DR. ROBERT J. SPELLMAN:

STATISTICAL TRENDS

Cardiac and Diabetic Mortality in the U.S.

The May 27, 1988 Volume 37 No. 20 *Mortality and Morbidity Weekly Report* indicates that heart disease is the leading cause of death in the U.S. and the third leading cause of years of potential life lost (YPLL) before the age of 65. Ischemic heart disease accounts for 71% of all deaths due to heart disease and 27% of all mortality. This is based on data from the National Center for Health Statistics-Mortality Public Use Data tapes for 1985. Cause-specific mortality rates in 1986 per 100,000 were: all causes 871, heart disease 319, malignant neoplasm 192, cerebral vascular disease 61, diabetes mellitus 15. Estimated YPLL for persons dying in 1986 were all causes 12,000,000, unintentional injuries 2,400,000, malignant neoplasms 1,800,000, diseases of the heart 1,500,000, suicide-homicide 1,350,000, and diabetes mellitus 127,000. Diabetes was 13 on the list of YPLL for persons dying in 1986.

Heart Facts

Heart disease and stroke and their related disorders account for almost 1 out of every 2 deaths in America. Heart disease is in prevalent in 1 of 4 of Americans; i.e., more than 60,000,000. By far the single largest cause of heart disease is atherosclerosis. Based on 1984 statistics for the U.S. (population at that time approximately 236,000,000) about 57,000,000 Americans had high blood pressure, 4,810,000 had coronary artery disease, 2,120,000 had rheumatic heart disease and 1,960,000 had had a stroke. Of the 986,000 people that died of cardiovascular (CV) disease in 1984, 1/5 were under the age of 65. There were over 6,000 general hospitals in the U.S. with coronary care capability, i.e., specialized coronary care units (CCUs). Estimates are that these CCUs can reduce in-hospital deaths by about 30%. Over 200,000 coronary artery bypass surgeries were done in 1984. Cost of cardiovascular disease in 1987 was

estimated by the American Heart Association at $85,000,000,000. This included the cost of physician and nursing services, hospital and nursing home services, cost of medications and lost productivity from disability. Heart attacks caused 540,000 deaths in 1984 and was the single leading cause of death in America; 350,000 people that year died of a heart attack before they reached the hospital, and the average victim waited approximately 3 hours before deciding to get help. Based on Framingham National Institute of Health heart data, 5% of all heart attacks occur in individuals under 40, and 45% occur in individuals under 65. Stroke killed 155,000 in 1984; approximately 500,000 people suffer strokes each year. Despite the dramatic recent decrease in rheumatic heart disease, it still afflicts 100,000 children and 2 million adults. About 6,900 Americans died of rheumatic fever or rheumatic heart disease in 1984; compare this however to more than 22,000 deaths in 1950. There are 35 recognizable congenital heart defects. About 25,000 babies each year are born with heart defects. Postnatal mortality from heart defects was more than 6,000 in 1984.

If one were to look at the cumulative percentage change in age-adjusted death rates for major CV diseases in 1972 through 1984, total cardiovascular disease would be down 32.5%, stroke would be down 47.8%, hypertensive disease would be down 45.7%, coronary heart disease would be down 33.9% and rheumatic fever and rheumatic heart disease would be down 47.4%. About 1 in 5 coronary events is sudden death, evidenced as the first, last and only manifestation of the disease.

In looking at a longer time frame from 1963 through 1983, the overall death rate for CV disease declined 36% in the U.S. and was the principal factor accounting for the 26% decline in total mortality. There were about 500,000 fewer deaths in 1982 than 20 years prior. The Intersociety Commission for Heart Disease Resources concluded that a 60% decline based on the 1963 benchmark could be achieved by the early 1990s, through continued nationwide avoidance or correction of established risk factors. In a well-done study by Goldman and Cook in the *Annals of Internal Medicine* in 1984, they estimated about 30% of the estimated decline in mortality was due to reduction in serum cholesterol levels, 24% to reduction in cigarette smoking, 13.5% to coronary care units, 10% to medical treatment of ischemia heart disease, 8.5% to treatment of hypertension, 4% to prehospital resuscitation and care, 3.5% to coronary artery bypass surgery and about 6.5% that they couldn't explain.

CORONARY ARTERY DISEASE (CAD)

Risk Factors

The cardinal triad of modifiable risk factors for coronary disease is hypertension, cigarette smoking and hyperlipidemia. Add genetic susceptibility (family history) and you have the primary risk factors for coronary disease. Secondary factors would include aging, maleness, obesity, lack of exercise, stress, diabetes mellitus, oral contraceptive agents and thrombogenic disorders. Of the approximately 60 million hypertensives in America, about half are receiving treatment. Approximately 29% of our population still smokes, though that number is slowly ebbing downward as educational programs aimed at altering lifestyle begin to take hold. Recently the National Institute of Health changed the upper limits of "normal" for cholesterol. For adults, their current recommendation is to have total cholesterol less than 200 mg percent with a low-density lipoprotein (LDL) of less than 130. Borderline high risk is defined as between 200-239% mg percent total cholesterol and 130-159 LDL; and high risk is greater than or equal to 240 mg percent total cholesterol and greater than or equal to 160 LDL. Recent medical therapy trends include use of Angiotensin Converting Enzyme (ACE)

inhibitors, e.g., Capoten because of its low degree of side effects, and the use of more palatable lipid lowering drugs, e.g., Lovastatin (major side effect is liver toxicity).

Diagnostic Testing

The double Masters exercise test has been out of vogue for quite some time. The graded exercise test using Thallium or a so-called Multiple Uptake Grated Acquisition (MUGA) study are currently in vogue. The focus in the near future will be on silent ischemia. It has been shown to occur in about 80% of patients with diagnosed angina, 50% with asymptomatic infarctions, and in 2.5% of individuals who are totally symptomatic and have no coronary events. Since 50% of patients with CAD present initially with an acute Myocardial Infarction (MI) or sudden death, it would be important if silent ischemia could be detected and managed before end point events occurred. Since ST segment analysis, that portion of the electrocardiogram involved in the detection of ischemia, is more accurate, there will be more ambulatory (Holter) monitoring, especially in high-risk groups who are asymptomatic, e.g., diabetics.

Medical Therapy

Current treatment of stable angina pectoris includes avoidance of precipitating factors, diet, no smoking, nitrates, beta blockers, calcium blockers, aspirin, and exercise. Unstable angina is treated by hospitalization using the same medications for stable angina: intravenous nitroglycerine, aspirin and intraaortic balloons.

Data from close to 14,000 patients in one study showed an overall one-year mortality that was 24% lower in a beta blocker group compared with a placebo group. Further data has indicated that high-risk Myocardinal Infarction (MI) patients are prime candidates for long-term beta blockade therapy and that lower risk patients may also receive some benefit. Since beta blockers unfortunately have a side effect that increases serum cholesterol and triglycerides, as well as lowering high-density lipoproteins, there will be increasing efforts to find drugs which are more selective in reducing adverse side effects.

Surgical Therapy

Data was recently gathered from 1,800 consecutive percutaneous transluminal coronary angioplasty (PTCA) procedures performed in 15 centers and compared with earlier data. It was noted that PTCA is now attempted in patients with a larger number of diseased vessels, poor left ventricle function, and a greater number of other risk factors such as advanced age, diabetes, hypertension, history of MI, bypass surgery and congestive failure, so it is difficult to compare the technique with internal mammary or saphenous vein bypass. Currently over 90% of patients have one or more lesions successfully dilated and there has been quite a drop in the emergency bypass surgery after PTCA. One study that is being carefully looked at is the Emory Groups data of a 5-8-year follow up after the first 169 angioplasty patients. At 6 years cardiac survival was 96% with 67% remaining asymptomatic. Stenosis occurred in 30% during the first 6 months following angioplasty. Patients with single vessel disease had a better long-term outcome than those with multiple vessel disease. PTCA is growing in popularity. It has become a first choice (versus coronary bypass) in property-selected populations where cardiac surgery is considered the best option.

With respect to coronary artery bypass surgery, there is a general feeling that the internal mammaries are better than saphenous veins as surgery is considered to be a more important prognosticator for overall mortality than the number of

vessels bypassed. While their symptoms improve or disappear, controversy still exists as to its overall effect on cardiac mortality when compared to medically treated groups. There seems to be some agreement that patients with "left main" disease or their equivalent do benefit from cardiac surgery. There is some growing evidence that with improvements in surgical technique and postoperative care, surgery may be better than medical therapy in carefully chosen populations.

VALVES AND CARDIOMYOPATHY

Rheumatic Fever

As recently as the early 1970s, 1,000-2,000 new cases of rheumatic fever were reported in the U.S. Over the next decade it became a rare disease. In 1985, however, there was a nation total of 250 cases which reflected a resurgence of rheumatic fever, with reports coming in from Utah, Columbus, Akron, Pittsburgh, Dallas and Denver. The reasons for this outbreak still are unclear, as are the reasons why it has declined. Everyone has their favorite factor or theory which generally means the answer is multifactorial or there simply is no answer that we can prove from a scientific view. Rheumatic fever until the 1970s has always been considered the major cause of valvular heart disease, especially mitral and aortic. Current thinking now focuses on the congenital bicuspid aortic valve as the principal cause of aortic valve disease and subsets of mitral valve prolapse which lead to mitral regurgitation; i.e., the shift has been from infectious to genetic. There is some intriguing data though that there is a type of Group A streptococcal infection called mucoid with specific types 3, 5 and 18 that may have been responsible for this resurgence of rheumatic fever.

Replacement

Basic types are prosthetic, e.g., the St. Jude valve versus Xenograft. Porcine xenografts are the most common when utilized, but can not be used for children since they tend to calcify. The major problem with valves revolve around coagulation, infection and mechanical failure.

CARDIOMYOPATHY

Basics and Definitions

An intrinsic abnormality of the heart muscle, they can be genetic or acquired. They can be restrictive, obstructive or dilated. The most important is Idiopathic Hypertrophic Subaortic Stenosis (IHSS) which is a genetic disease inherited as an autosomal dominant.

Progress in this area has been slow with septotomies for asymmetric septal hypertrophy having some degree of success, as well as treatment of ventricular rhythm disturbances. The real hope lies in either genetic manipulation or transplantation. Currently the major use of mechanical devices lies in the realm of "bridge transplantation" in which a suitable donor is being sought, but the patient's condition is so poor that without a Jarvik-7 the patient would die.

THE FUTURE

Genetic Testing -- Markers are becoming available for cardiomyopathy, abnormal apolipoprotein and possibly susceptibility to hypertension and those most prone to the bad effects of cigarette smoking. Identification of abnormal apolipoproteins seems to be the area most fruitful for the near future.

Laser Therapy -- In this particular case, we are basically talking about "Star Wars in the coronaries." Laser therapy to dissolve plaques in coronaries is being looked at critically in a number of centers. The major problem is

perforation and adequate visualization -- and having the right shooting touch? All those years at the video arcade machines may finally pay off. At the current time there are 4 different types of lasers with different properties being tested and it seems that it will have its usage in peripheral arteries, most notably the legs, before it really has widespread application in the coronaries. This one bears watching.

Prosthetics -- In this context, prosthetics means artificial hearts or artificial valves. While both of these hold promise, there is really nothing new in the last decade of great significance and I would expect that there would be slow but steady progress in both areas, largely dependent upon progress in prevention of graft rejection for the Xenograft and fine tuning of anticoagulation for the mechanical valves.

Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) -- with respect to MRI, the basic operating principal is that within a magnetic field, atomic nuclei vibrate at characteristic frequencies called a resonant frequency. To get an image, radiologists expose the tissue to a pulse of radio wave frequency energy at the resonant frequency of the nuclei. When the pulse stops, the nuclei release characteristic types of energy. This energy "signal" is then converted mathematically into images. It has the advantage of no radiation with relatively distinct detailed images and can measure to some degree blood flow. It definitely can not be used with patients with pacemakers. In a PET study, researchers expose the tissue to a tracer chemical that binds with specific tissue sites and emits positrons. Multiple detectors pick up the resultant gamma ray radiation which computers translate into distribution maps. While currently being used mostly on the brain, it has some unique advantages with respect to selecting out viable tissue. It requires an accelerator to produce the tracer materials necessary, is highly expensive and is certainly the wave of the more distant future.

Autodefibrillator -- Recent introduction of a fully automatic implantable cardioverter-defibrillator (AICD) has definitely improved the prognosis for patients with recurrent drug-resistant sustained ventricular arrhythmias. These life threatening ventricular arrhythmias which can cause sudden death are currently being treated by new investigational anti-arrhythmic drugs, anti-tachycardia surgery, catheter ablation techniques, anti-tachycardia pacing, internal low-energy conversion and high-energy defibrillation. Unfortunately the AICDs have a variety of potential complications related to the surgical procedure for implantation, the size of the leads in generator and AICD drug and AICD-pacemaker interactions. In one study over a mean follow-up period of about one year, give or take 10 months, the authors studied 25 patients who underwent primary implantation of an AICD system. Two died in the hospital, one interoperatively and the other of sepsis, congestive heart failure and asystole 11 days after implantation. While in the hospital 6 patients had 10 complications and 17 had none. These included wound infections, interoperative heart attacks, and failure of the AICD to convert induced ventricular fibrillation. After the patients left the hospital, 4 required battery replacement due to device failure with a mean replacement time of about 8 months. During the long-term follow-up, one patient died as a consequence of ventricular tachyarrhythmia, one died of cerebral hemorrhage, and one died of a ruptured abdominal aortic aneurysm. While these may not sound like great results, without these devices the prognosis would be far more dismal.

Pacemakers
Over 120,000 permanent cardiac pacemaker implantations are performed every year in the U.S. In one study of 382 pacemaker implants, 44% were definitely indicated, 36% were possibly indicated and 20% were not indicated. Permanent pacing is indicated in patients with symptomatic proven bradycardia. The most common causes requiring pacer insertion are the sick sinus syndrome, with or without tachycardia and bradycardia and symptomatic high atrioventricualr (AV) block. Sophisticated pacemakers will continue to abound but there will be a higher and more stringent threshold for pacemaker implantation.

ANGIOGENIC FACTORS

Angiogenic factors refer to substances which facilitate and cause new blood vessel formation. The potential in this area for progress in preventing abnormal cardiahypertrophy, tumor growth and abnormal retinal vessel proliferation and diabetes, for example, is enormous. These factors work on endothelial cells causing them to elongate, proliferate and move towards the angiogenic stimulus. New capillaries then arise as offshoots of parent venules or other capillaries.

LYTIC THERAPY

The control of clotting (hemostasis) involves an interplay between clotting factors and platelets which form the clot (thrombus) and lytic factors which tend to dissolve the clot, e.g., plasmin. In addition to prevention of clots on valves which was mentioned before, clots play a major role in precipitating myocardial infarctions, probably in the majority of them. The concept is that there is an atherosclerotic plaque which cracks and a clot is superimposed creating further obstruction of the opening of the artery leading to cell death as the blood supply is compromised. The major lytic drugs in use are Streptokinase, Urokinase and tissue plasminogen activator (TPA). TPA is very expensive -- $2,000 for the usual treatment versus $150 for streptokinase. The results at this point in time are not dramatic with respect to cardiac mortality though they are encouraging and better than without treatment. The thrombolytic therapy must be started within 4 hours of the onset of chest pain. The major side effect is bleeding. After the initial infusion of the thrombolytic agent, heparin therapy must be started immediately.

Of more practical significance is the use of aspirin in heart disease and as a prophylactic measure in the general population. Aspirin is an antiplatelet agent. It has been shown that it is effective in a subgroup of high risk patients with "unstable angina." A recently completed study involving physicians indicates that the use of aspirin, 1 tablet every other day, is of help in preventing heart attacks, though the data is still fairly new and a person should be certain that there is no contraindication to the use of aspirin.

Being a rheumatologist by nature, I feel I can now rest in peace since I have basically advocated the use of aspirin from a cardiologist's perspective as well! As always, check with your doctor before you undertake any long-term drug usage, even if they are over-the-counter.

Diabetes -- Future Directions
Basic Facts:
- o Approximately 6 million people in the U.S. have diabetes.
- o An additional 5 million have the disease but is has not yet been diagnosed.
- o Each year 500,000 new cases of diabetes are identified.
- o In 1984, diabetes was listed as the cause of death in 35,500 Americans.

- o Diabetes was listed as a significant contributing cause in an additional 95,000 deaths.
- o Compared to the general population, heart disease is twice as common and more often fatal in diabetics. The risk is five times greater in diabetic women compared to nondiabetic women.
- o Of people with diabetes in the U.S. 50% have hypertension, compared to 20% in the general population.
- o Diabetes is the leading cause of new cases of adult blindness -- almost 6,000 people each year.
- o Diabetes is the cause of about 30% of end-stage kidney disease in the U.S.
- o Fifty percent of all nontraumatic amputations in the U.S. occur in diabetics.
- o Pregnant diabetic women have children with three to five the times frequency of birth defects and other complications that require intensive medical care.
- o Forty percent of diabetics have detectable loss of nerve function after 25 years; greater than 90% are affected.
- o Diabetes in an enormous economic burden: it accounts for 25 million hospital days and a total annual cost of $13.8 billion.

Diabetes -- Definition and Major Types -- Diabetes mellitus is a general term applied to diseases which share a primary disorder of carbohydrate metabolism that involves absolute or relative insulin deficiency, insulin resistance, or both, with hyperglycemia as the hallmark.

Descriptive Phrases	**Insulin-Dependent Diabetes Mellitus (IDDM)**	**Non-Insulin Dependent Diabetes Melitus (NIDDM)**
Synonym	Type I	Type II
Age of onset	Usually less than 30 years old (11-13)	Usually greater than 40 years old
Ketosis	Common	Rare
Body Weight	Not obese	80% obese
Prevalence percentage	0.2-0.3	2-4
Genetics		
HLA antigens	Yes	No
Percentage of concordance in identical twin studies	40-50	Nearly 100
Circulating islet cell antibodies	Yes	No
Insulin necessary	Always	Usually no
Complications	Frequent	Frequent
Insulin secretion	Severe deficiency	Moderate deficiency > normal levels
Insulin resistance	Occasional	Usual

Complications of Diabetes --

1. ketoacidosis > to coma > to death (IDDM)
2. macrovascular disease-medium arteries, e.g., coronaries > accelerated atherosclerosis
3. microvascular disease-retinopathy and cataracts, nephropathy, and neuropathy
4. increased susceptibility to infections

Mechanisms of Diabetes -- Not Clearly Known and Probably Multifactoral

1. Polyol pathway: glucose > sorbotol. Most are implicated in neuropathy and retinopathy.
2. There is an increased glycosylation (glucose attachment) to certain proteins; it forms the basis of hemoglobin A1c as measure of ambient glucose level for the preceding 8 weeks.
3. LDL-glucose is not recognized by normal LDL receptor and the longevity in the blood stream is increased. Conversely high-density lipoprotein (HDL) glucose turns over more rapidly than native HDL.
4. The major structural protein collagen attached to glucose traps LDL at rates 2-3 times the normal. The combined effect could be a mechanism for increased atherosclerosis.
5. The thickened altered basement membrane of tissues leaks proteins into kidney or eye leading to nephropathy or retinopathy.

Progress

1. Home monitoring -- We are seeing less painful lancets, more accurate colorimetric strips, automatic glucose level reading devices.
2. Insulin pumps
   a. Open loops: a basically sophisticated insulin delivery system. The results are somewhat disappointing; tedious, wound infection, controversy surrounding some unexplained deaths. It is reserved for special patients and for pregnant mothers, especially in the first trimester.
   b. Closed loops: the concept is a device which could monitor glucose and deliver insulin in response to the glucose level, i.e., function like an artificial pancreas. The problem is miniaturization with an accurate glucose-sensing device remaining to be the major obstacle.
3. Hemoglobin A1c glucose in the bloodstream for extended periods of time bonds irreversibly to hemoglobin. This fact enables clinicians to measure glucose control over the preceding 8 weeks or so. Many companies are using hemoglobin A1c as a surrogate test for the glucose tolerance test. Hemoglobin A1c is less sensitive, but probably more specific than the glucose tolerance test. It is not yet clinically accepted as a diagnostic tool for diabetes but rather as an indicator of diabetic control.
4. Dialysis-transplantation -- peritoneal versus hemodialysis is used as a bridge to renal transplantation or when renal transplantation is not a viable alternative. Greater than 100,000 people are on renal dialysis. There were more than 10,000 kidney transplants by 1987.

The Future

In genetics, there will be more widespread human leukocyte antigent (HLA) testing in relatives of Type I diabetics; an intensified look at chromosome 11 in the locus where insulin is made; and attempts to identify genetic markers for me Type II diabetic. The view will be eventually to genetically manipulate the abnormalities to reverse the diabetic problem. Trying to identify environmental factors in Type I, where the basic thought is genetic predisposition followed by an environmental trigger, most likely viral will be important. The key viral candidates are congenital rubella, Coxsackievirus B4, and certain strains of encephalomyocarditis.

There have been advances in autoimmunity and it is now fairly well established that Type 1 diabetes is an autoimmune disease. The presence of circulating islet cell antibodies are the hallmark of the disease. Monitoring formation of these islet cell antibodies in high-risk families will become more widespread to diagnose the disease in an early stage.

Regarding angiogenic factors, one of the hallmarks of retinal disease is the proliferation of new vessels. These may be possibly linked to the polyol pathway and if their formation could be prevented, many eye complications could be arrested or prevented. Currently laser photocoagulation as a therapeutic tool and fluorescein angiography as a diagnostic tool are commonly used.

Pancreatic transplantation for diabetes has been a reality in insulin-deficient patient diabetes for over 20 years. By April 1987, approximately 1,200 such operations had been done. About 300 were done in 1987 alone. The major technical breakthrough, called the "Bladder Technique," was introduced at the University of Wisconsin. In this technique, digestive enzymes from the pancreas are drained to the bladder. Over 90% of U.S. pancreas transplants in the past two years have utilized this technique. Immunosuppressive drugs, including Cyclosporine A, prednisone, Antilymphocyte globulin and Azothlaprin, have improved survival rates but graft rejection still is 45% within one year, with diminishing graft survival continuing on thereafter. Thrombosis fistula and infection also are problems.

At an international meeting in February 1988, Dr. Groth of Stockholm said that after careful review he felt that pancreatic transplantation at this point in time was very disappointing and doubted that it should be continued. He suggested that future efforts in pancreatic transplantation should be devoted to attempts to prevent diabetic complications, or at least their progression at an earlier stage than advanced renal failure. My prediction is that pancreatic transplantation will continue, mostly in patients who have received or are in the process of receiving a renal transplant. Future trials will be better controlled, but I am not excited that this is the answer at least for the next 10-20 years.

The chief killers in diabetes are nephropathy and accelerated atherosclerosis. All those modalities which result in lowered cardiac mortality and morbidity will be helpful in this diabetic complication.

Tight control is considered good but hypoglycemic episodes are to be avoided. No one yet knows the optimum control level and ongoing prospective studies will help clarify this.

The central and most fundamental controversy in diabetology is the extent to which diabetes is a genetic disease with independent mortality and morbidity, versus a disease in which the final outcome and complications are the result of the degree of hyperglycemia. Strong evidence that metabolic abnormalities cause complications comes from the observations that kidneys from donors who have neither diabetes nor a family history of diabetes develop characteristics of diabetic nephropathy within three to five years of transplantation to a diabetic recipient. Moreover diabetic kidney disease usually does not develop when a kidney is transplanted into a diabetic subject whose disease has been reversed by pancreatic transplantation prior to renal transplantation. Some sporadic reports indicate that kidneys with lesions of diabetic nephropathy showed reversal of their lesions when transplanted into normal recipients.

Additional work for the future includes antiglucagon compounds, insulin by nasal route, genetic amplification of native data cells, and early immunosuppression in Type 1 diabetics.

MR. HENRY C. GEORGE: Now that my friend Bob Spellman has totally reworked your perception of the life insurance medical director, let me do my

best to persuade you that the concept of an underwriter as a public speaker is not altogether oxymoronic!

I'd like to begin by picking up on a point Bob alluded to briefly, regarding apolipoproteins. Apolipoproteins are the carrier proteins which transport lipids like cholesterol and triglycerides between tissues. Apos, as we call them, are literally bound up with combinations of lipids in macromolecular complexes known as lipoproteins.

HDL is the "good" lipoprotein which helps to remove excess cholesterol from arteries, thus inhibiting the formation of atherosclerotic plaque lesions in coronary arteries. LDL is the "bad" lipoprotein directly associated with coronary disease.

In a paper published in the *Mayo Clinic Proceedings* in 1986, Kottke and his Mayo coworkers describe one of the apolipoproteins, known as APO A-I, as "an excellent marker for the presence of clinically significant CAD . . ." They found APO A-I discriminated between patients with coronary disease versus healthy controls better than cholesterol, triglycerides or HDL. Just as high levels of HDL are favorable from a longevity point of view, the same is true for APO A-I. Healthy controls in this Mayo Clinic study had consistently higher APO A-I readings than the patients with known CAD, and the difference was statistically significant.(1)

The other apolipoprotein which has been the focus of great attention is apolipoprotein B-100, or, simply, APO B. Sniderman, at Royal Victoria Hospital in Montreal, discovered that APO B discriminated better than traditional lipid markers (cholesterol and HDL) in screening for cases of familial (genetically-determined) hyperlipidemia.(2) APO B is the apolipoprotein associated with low-density lipoprotein (LDL) and, like LDL, high APO B readings are associated with an increased risk of coronary artery disease.

Not all patients with coronary disease have high cholesterol and triglycerides readings. Indeed, when we are limited to traditional lipid markers for risk-selection purposes, we miss a significant percentage of cases. They will be masked, so to speak, by normal cholesterol, triglycerides and HDL readings. Bittolo and his colleagues found they could unmask these cases by screening with APO B. When comparing APO B readings in three groups (patients with prior heart attacks, patients with anginal chest pains and healthy controls), all of whom had normal cholesterol and triglycerides readings, they found APO B levels were significantly higher in both cohorts with CAD, than in the disease-free control group.(3)

Home Office Reference Laboratory (HORL) is making APO A-I and APO B available to clients as a confirmatory screening test. We envision using apolipoproteins to further define the CAD risk in applicants who have elevated cholesterol and triglycerides readings and/or abnormal cholesterol to HDL ratios. From rapidly accumulating evidence in the medical literature, it appears apolipoproteins are destined to make a significant improvement in our capacity to screen for coronary artery disease -- a major step forward when you consider that this disease remains our number one cause of death!

The next topic I'd like to discuss, albeit briefly, is psychiatric impairments. I wish I could tell you I expect a major improvement in mortality from affective

disorders like major depression, bipolar disease (manic depressive psychosis) and from schizophrenia, but I really don't.

When I addressed the Institute of Home Office Underwriters at their 1984 meeting, I quoted a paper by Babigian and Odoroff which reported on mortality in psychiatric disease. In that paper, the authors said "The relative risk of death for the psychiatric care group is 2.5 to 3 times that of the comparable general population; psychiatric illness does take its toll on life."[4] Let me update that citation with an excerpt from *Scientific American*, published in 1976: "Major depressive illness involves serious mortality and a substantial risk of death. Among patients with recurrent depression, 15% commit suicide; the remaining 85%, regardless of age, experience higher mortality than age-matched controls because they have a greater incidence of other illnesses."[5]

Medical scientists are slowly evolving a better understanding of the causes of psychiatric impairments, which should eventually lead to more effective therapies. One noteworthy recent advance was the introduction of a new anti-anxiety drug, buspirone, which I understand is not addicting, making it a potential replacement for valium and other abusable benzodiazepine drugs (which have been the mainstay of the medical treatment of anxiety for many years).

The so-called eating disorders -- anorexia nervosa and bulimia nervosa -- are now more prevalent. These conditions occur primarily in adolescent and young adult females, and, whereas anorexia, characterized by extreme weight loss and multiple physical complications, is often a readily-apparent diagnosis, the same cannot be said of bulimia. Indeed, bulimia is a deceptive disorder, making the job of the doctor and the underwriter more difficult.

Bulimia is referred to as the "binge-purge" syndrome. These female patients, who tend to be of normal build or even a bit stocky, are secretive about their binge eating and self-induced vomiting (purging). A recent paper in the *Annals of Internal Medicine* provided needed clues to identifying bulimic applicants on the basis of physical findings and medical histories.[6]

We also now know both anorexia and bulimia are associated with a significant incidence of alcohol and drug abuse[7] so underwriters need to be knowledgeable about these increasingly-prevalent impairments. An excellent place to start learning more, I might add, is a superb paper written by an underwriter, Barbara J. Lutz, FALU, of Century Life (Waverly, Iowa). Barbara earned a Fellowship in the Academy of Life Underwriting for her thesis titled "Underwriting the Anorexic and Others with Eating Disorders."

Cancer is the second leading cause of death in our society and, as such, it is also an exciting prospective source of mortality improvement. Unfortunately, I see little reason to get excited. Why? Because there has been no significant progress in developing curative treatments for the most common metastatic visceral carcinomas, that is, cancers of the lung, breast, colon, pancreas, ovary, esophagus, stomach, bladder, prostate, liver, etc., which has spread to lymph nodes, internal organs and other sites. Nearly all of the major advances in cancer therapy have impacted pediatric neoplasms and cancers occurring in young adults, ages 20-35. I am referring to acute lymphocytic leukemia of childhood, Hodgkin's disease arising before age 50, rhabdomyosarcoma and Wilm's kidney tumor, carcinoma of the male testis, osteogenic sarcoma and

Ewing's sarcoma of bone, and a once-hopeless placental malignancy called choriocarcinoma.

Consider embryonal cell carcinoma of the testicle, as an example. Two decades ago, this diagnosis was a virtual death sentence. The two-year death rate was 60%. Only an occasional patient with metastases ever survived. Now contrast those gloomy statistics to a report just published in *Cancer*, detailing the outcome of 479 cases of embryonal cell carcinoma diagnosed and treated since the mid-1970s. The cure rate in Stage I (localized) and Stage II (metastasis to regional lymph nodes) was 98%! Even in Stage III, with metastases to the lungs, three out of four patients walked away from chemotherapy with no residual cancer, survived three years thereafter and are felt to be cured.[8] There are similar success stories in Hodgkin's disease, acute lymphocytic leukemia diagnosed in children (not adults!), etc., and nearly all of these successes are due to advances in multidrug chemotherapy protocols, a matter I will come back to a bit later.

Don't misunderstand, I don't think the situation is hopeless where cancers in adults over 35 are concerned. There are many encouraging developments in research which could, potentially, impact outcomes significantly in the next decade. Let me describe a couple of these.

You have probably heard of interferon. Interferons are proteins, part of a larger group of hormone-like proteins referred to as cytokinins. Cytokinins can impact a variety of bodily responses to viral infections, cancers and other diseases. Discovered in London in 1957, recombinant (manufactured) interferons are now being used to treat certain cancers as well as AIDS patients, chronic hepatitis and even rhinoviruses which cause the common cold! Although the anticancer effects of interferons may not have satisfied everyone's expectations, they have produced impressive results in several tumors, most notably in chronic leukemia called hairy cell leukemia, plus kidney carcinoma and malignant melanoma.

Recently, cancer therapists have combined interferons with another cytokine, interleukin II, and realized unexpected favorable results.[9] Interleukin II, or, T Cell Growth Factor, stimulates the proliferation of supercharged killer T lymphocytes which go off and fight cancers, viruses and other invaders. Interleukin II helps restore essential cellular immunity in cancer patients and AIDS patients, a vital step in fighting back against disease.

A cytokine dubbed Tumor Necrosis Factor, or caseation, may have a key role in future cancer perscription. Caseation appears to be capable of blocking the blood supply to a cancer, leading to hemorrhagic necrosis (death) of the tumor. Like interleukin II, cachetin may also be useful in combating syndromes associated with HIV-1 infection, such as ARC and AIDS. A recent editorial in the *New England Journal of Medicine* opines that Tumor Necrosis Factor may hold the key to many unsolved mysteries in medicine, with the answers "just around the corner."[10]

You may have heard of "magic bullets" (oncotoxins), a promising new cancer treatment. This innovation utilizes manufactured (monoclonal) antibodies which block the uptake of vital growth factors needed by cancer cells. Without these growth factors, the tumors appear powerless to grow stronger, invade normal tissues and metastasize.

One of the basic characteristics of cancer cells is that they suffer from arrested development. That is, they are biologically less mature than normal cells. Cancer pathologists will grade tumors according to their degree of immaturity. Grade I (well-differentiated) tumors contain cells which largely resemble normal cells from the tissue of the tumor's origin, whereas grade IV (undifferentiated) cancers are bizarre-looking. Tumor grading even has prognostic significance. Grade I tumors spread more slowly than grade IV tumors, while grade IV tumors are more vulnerable to radiation and cytotoxic drugs than their more mature (grade I) relatives.

From time to time you may see articles in the press about cancer patients who make seemingly miraculous recoveries from terminal malignancies. In many cases, the biological process which causes this unexpected (and exceedingly rare) event involves spontaneous differentiation (maturation) of a malignant tumor. If cancer researchers could find a way to induce the differentiation (maturation) of a malignant tumor while it was ravaging a patient, they could stop it in its tracks and, depending on how much damage has already been done, possibly save the patient's life. Wishful thinking? Maybe not. A functioning Tumor Differentiation Factor has already been isolated. Using injections of this substance, researchers have been able to save the lives of two out of three baby rats given lethal injected doses of leukemia cells.(11)

I have one last observation about cancer. As I said earlier, advances in chemotherapy have led to dramatic improvements in the cure rates for tumors occurring in children and young adults. One of the watershed effects has been an increase in life and health insurance applications from successfully treated, apparently cured patients. I have done a great deal of research, in part to write my thesis to earn my Fellowship in the Academy of Life Underwriting, on the late effects of chemotherapy and I can assure you some of these late effects will have a significant impact on the mortality and morbidity results of insured cancer patients. For example, several studies have documented a 3-10% incidence of a virulent form of acute nonlymphocytic leukemia which develops one to ten years after curative chemotherapy for Hodgkin's disease. This leukemia appears to be directly induced by the effects of certain anticancer drugs, primarily those in the family known as alkylating agents. Underwriters who are too aggressive in making offers on some cancer cases will get burned, if you will, by excess claims from treatment-related disabling and fatal complications. The key to the puzzle, of course, is knowledge. Cancer underwriters must acquire extensive knowledge which allows them to make sophisticated distinctions between cases. And, above all, they must be splitters, not lumpers. Splitters make essential distinctions between individual cases based on the whole risk. Lumpers arrive at premature conclusions and pay for it later!

My concluding remarks have to do with impairments related directly to how we choose to live our lives, but I will shy away from the misunderstood and hence oft-maligned term "lifestyle underwriting." According to a short article in a recent issue of the *U.S. Journal of Drug and Alcohol Dependence*, Americans consume, on a DAILY BASIS(!!), almost 348 million cups of coffee (of which 83% are caffeinated), 1.3 billion cigarettes, 11.5 million pounds of sugar, 75 acres of pizza, and my friends back home in Milwaukee will be relieved to note no less than 28 million six packs of beer!(12) And we call ourselves the most advanced society in the world?!

Have you ever heard of "caffeinism?" It describes a syndrome associated with acute and chronic toxicities of consuming large quantities of caffeine, most often in the form of coffee. Several recent papers have reviewed the medical implications of caffeinism. If you are interested, you may want to review them. Indeed, if you drink more than four cups of caffeinated coffee per day and suffer from irritability, diarrhea, palpitations or frank panic attacks, you should probably make a point of reading at least one of these papers![13]

Cigarette use is declining. Roughly 29% of men and 24% of women continue to freebase nicotine, excuse me, smoke cigarettes despite overwhelming evidence of the enormous health consequences. Will we realize a smoke-free society by 2000 A.D.? I doubt it, if your definition is complete disappearance of smoking. It's hard to tell what percentage of smokers are hard-core addicts who will find it agonizing, if not impossible, to quit.

There is some good news, however. There may be a major advance in prevention/early treatment of emphysema, particularly in susceptible individuals who suffer from a predisposing disorder known as alpha-1 antitrypsin deficiency. A paper in the *Annals of Internal Medicine* relates how normal lung function depends on the dynamic interaction of two enzymes, protease and antiprotease. Too much protease causes emphysematous damage. Recombinant gene technology may enable us to make therapeutic antiprotease, which could be used to prevent lung damage, or at least limit damage in smokers.[14]

Trauma, which means accidents, suicides and homicides, accounts for a large share of select period death claims. It is the leading cause of death under age 45 in North America. It accounts for more years of productive life lost than coronary artery disease! And, unfortunately, many people still view trauma as largely a matter of adverse serendipity! I believe trauma is a disease, much of it being caused by aberrant, destructive behavior. I believe alcohol is the #1 cause of such behavior. I know alcohol abuse can be underwritten and, therefore, I am convinced trauma-related mortality and morbidity can be controlled.

An article in the 1987 *Archives of Surgery* revealed that in 65.8% of 152 trauma centers nationwide, more than half of all trauma patients were injured or killed as a direct result of alcohol consumption.[15] The same report concludes that alcohol abusers, 85% of whom are undiagnosed, die annually as a result of trauma rather than the long-term effects (cirrhosis, cancer) of their disease.

The insurance-sensitive HORL blood chemistry profile contains a test which is very helpful in screening for occult alcohol abuse. The test is a liver enzyme known as gamma-glutamyl transpeptidase and is variously referred to as GGT, GGTP or Gamma-GT. I won't recite chapter and verse about GGT. I will however, refer you to two papers which detail the incredible value of this test. One appeared in the clinical literature[16] and the other, written by yours truly, has published in the *Journal of Insurance Medicine* a few years ago.[17]

One last note on alcohol. A paper in the *Journal of the American Medical Association* by Pollack reported on a Centers for Disease Control (CDC) study which revealed that, among army veterans, the incidence of alcohol-related deaths was understated by a factor of six! They looked at 426 deaths. Although 133 were clearly alcohol-related, only 21 were so labeled on the death certificates![18]

Recent reports now tell us that marijuana smoke is a major airway carcinogen. In addition, it contains more carbon monoxide than cigarette smoke. And, the effects of marijuana and tobacco cigarettes are apparently synergistic. The bottom line: it makes no sense for marijuana users who don't smoke cigarettes to be issued at nonsmoker rates. One could even speculate that the mortality of smoking both substances is much more than additive![19]

I'd like to conclude by making a quick reference to several drugs. Several of the newest drug fads are the so-called "designer drugs." One drug is Crack, a freebase form of cocaine which can be smoked without the hazards of conventional freebasing. Crack has been linked to serious lung damage. More ominously, it carries with it a very high risk of (almost instant) addiction to cocaine.

The other two "designer drugs" we may be seeing in insured populations are China White and Crystal. China White is a synthetic opiate said to be thousands of times more potent than morphine. It's main ingredient is fentanyl, an opiate used in certain anesthetics. Crystal is methamphetamine, which is also known as Speed. Some experts believe the amphetamine is making a comeback in some urban areas, capturing a small share of the cocaine trade. There is also a rock form of Crystal called Glass, suitable for freebasing. If you want to know more about "designer drugs" there is a fine new book on the subject which you can find in shopping mall bookstores.[20]

My last point relates to cocaine testing. At HORL, we use the state-of-the-art confirmatory test, gas chromatography with mass spectrometry (or, GC/Mass Spec.). This test method was reviewed recently by "heavy hitters" in the legal community who are involved in going to court over drug abuse lawsuits, etc. They rated only one confirmatory method as "fully defensible" and that method was GC/Mass Spec. If your company, like so many companies, tests for cocaine with every urinalysis, I thought you'd appreciate being reassured about the reliability of our test.

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MR. GREGG R. SADLER: I'm the token actuary on the panel -- I'm not an expert underwriter, although I've spent my last five or six years in underwriting at my company. My objective is to focus on how you can spend your underwriting dollar most effectively. I spend a lot of my time talking to our

agents about underwriting tools and the information we receive. Of course, my agents tell me that our underwriters get everything on everybody, but obviously we can't do that -- we've got a limited budget and we've got to spend our dollars most effectively.

Number one on my list is paramedical exams. It's no surprise to this group that the use of paramedical exams is increasing, particularly with the AIDS epidemic and companies dropping their testing and nonmedical limits. Paramedical exams have been around for a long time, and they've proven to have an excellent cost benefit ratio. You get a good medical history, blood pressure, blood profile and urinalysis. If you're using the major, national, or regional paramedic companies, the information is very consistent and can be handled easily by your underwriter. With the additional testing that is being done now, the paramedica firms have been very convenient for both the agent and the applicant.

Second on my list is the blood chemistry profile -- that will be no surprise in light of the HIV testing that is being done now, but there's also a lot of other information that is contained in the blood chemistry profile. Certainly the immune system profile is an important part of it. Hank referred earlier to the liver enzyme testing that many companies, including my own, are using. The most useful liver enzyme is called GGT; I'll talk more about it a little bit later. Bob mentioned cholesterol and HDL as being valuable in evaluating coronary artery disease risks. A number of other tests are useful in this area as well.

First let me mention the immune system profile that's currently in use. The protocol starts with an HIV antibody test using the ELISA method. After two out of three positive ELISA tests, we go to a Western Blot test for the further confirmation. In California, you can't do the ELISA or Western Blot tests right now, so the T-cell test is used instead.

I know the program says "Beyond AIDS," but please let me spend a couple of minutes giving you some statistics on underwriting for HIV infection. If your underwriters are underwriting for AIDS, they're underwriting for the wrong thing. There are only a little over 50,000 diagnosed cases of AIDS as of February 1, 1988. Yet there are over a million and half people with the HIV infection. At first the CDC estimated that 5-19% of those that were infected by HIV would ultimately develop AIDS and die. Now the estimates are running 75-99%, and in every study you see it seems the estimate was increased.

The mortality for HIV infection is very high. Compared to the mortality of a standard risk at 100%, smoking is double, diabetes is 400%, and myocardial infarction is 500%. Of course there's no doubt -- if you have an individual who is HIV positive, she/he is not an insurable risk.

Let me mention a few important facts for any successful testing program. We'll discuss these facts in the context of HIV testing, but they could apply to a number of other tests contained in a blood profile or urinalysis as well.

First, of course, you've got to have reliable and timely results. From time to time you read in the newspapers that the insurance departments have questioned the reliability of HIV testing. Obviously, test accuracy is essential to all parties involved, and I think the facts are now fairly clear. According to Dr. James Allen of the U.S. Center for Disease Control, the probability of a false positive test -- he's talking about the HIV antibody test protocol that is used by the major laboratory vendors in the insurance industry -- in a population with a low

prevalence of infection is only one in 100,000. That is an excellent number; I wish a number of our other tests had such a low false positive rate as well.

Second, your results have to be consistent.

Third, confidentiality is a major concern, especially with regard to HIV underwriting. Many of the state insurance departments are passing special regulations. The legislatures are looking at special laws, and they seem to be targeting more on disclosure and confidentiality, and hopefully less on whether or not insurance companies should be allowed to test. I think our industry has had a good track record on maintaining the confidentiality of medical information, but any company that just assumes what was done in the past is adequate could be making a mistake. You really have to take a second look at your confidentiality procedures.

Fourth, and finally, a successful testing program has to have a large protective value per dollar of the cost. I'm associated with Home Office Reference Laboratory. The percent of HIV positive by age group for the entire year of 1987 is as follows: Ages 20-29-.30%, ages 30-39-.21%, ages 40-49-.11%, ages 50-59-.06%. The first thing that strikes any underwriter about the hit rates is that the highest rates are at just the ages where companies traditionally have required the least amount of underwriting information. That's one of the reasons most insurance companies have levelized their nonmed limits and their testing limits.

In California the percentage of abnormal T-cell ratios by age group is as follows: Ages 20-29-1.1%, ages 30-39-1.4%, ages 40-49-1.1%, and ages 50-59-0.9%.

The discounted present value cost of insuring an HIV-positive individual is really over $530 per thousand dollars of insurance. If you've just issued a one million dollar policy to someone that does not have AIDS but is positive for the HIV, the present value cost of that transaction to you today is over $530,000. I think if I redid my calculation with some of the new information from the studies that have been released recently, the present value cost would be even higher than that. "AIDS, HIV Mortality and Life Insurance," the landmark study Michael Cowell and Walter Hoskins published a few months ago; suggested that HIV screening might be cost effective for amounts of insurance as low as $10,000.

Using some of my own numbers, in a population with a 1% HIV prevalence rate, I've picked an arbitrary 10,000 policies with an average size of $200,000. The present value of AIDS claims, using my $530 per thousand factor, is in excess of $10 million. The cost of testing -- not just the cost of the HIV test alone, but the cost of a full battery of blood profile tests -- is around a half million dollars. That's a protective value -- a present value return -- of almost $20 per $1 spent, and that ignores all the other value of the blood profile. It is unbelievably high for a routine requirement -- a requirement where you're testing everybody above a certain threshold. There is a large amount of protective value to blood chemistry profiles on the non-HIV items as well. A study by Northwestern Mutual has estimated the protective value of the non-HIV items to be in the neighborhood of 30 to 1, so you can see the value is dramatic.

Even though the insurance industry is facing higher levels of claims due to the HIV epidemic, because companies have dropped their testing limits and are getting better information for the non-AIDS impairments, one might assume that there will be some mortality savings from accident risks, cardiovascular risks,

etc., that we wouldn't have had otherwise. These savings may offset much of the additional costs attributable to HIV.

Hank talked briefly about liver enzyme testing. GGT is the one that's most sensitive to long-term alcohol consumption. I think if your company is using the liver enzyme test -- especially GGT -- in your underwriting when you get a blood profile, then you can expect to reduce your early year accidental death mortality.

The percentage of elevated GGTs by age group is as follows: Ages 20-29-0.3%, ages 30-39-0.6%, ages 40-49-1.2%; and ages 50-59-1.7%. There are some medical factors other than alcohol that cause GGT to be elevated, but if you look at these numbers and you're an underwriter, most commonly they're not the kind of things you'd want to insure anyway.

Dr. Spellman talked about the cholesterol risk, so I'll breeze through this quickly, but certainly that's an important part of the blood chemistry profile and it has a high protective value. Some of the studies that are being released now at Framingham National Institute of Health, and there are others, suggest a rule of thumb that for every 2% change in your cholesterol, there's a 1% change in your coronary artery disease risk.

Urinalysis is another effective underwriting tool. Several components of that are useful, particularly the nicotine screen and the cocaine screen. For 1987, the overall HORL hit rate for positive nicotine screens was 23%. My company has dropped our testing threshold dramatically at the younger ages, so we're getting more nicotine screens as well as blood profiles. It's amazing how our mix of business between smoker and nonsmoker has changed now that our agents and applicants know we are going to be doing the nicotine screen. Our applications are coming in much more on a smoker basis than before, so in a sense our mix of business is much more favorable than it was earlier. The cocaine screen is the second important component of urinalysis. The percentage of positive cocaine tests by age for HORL in 1987, are as follows: Ages 20-29-1.8%; ages 30-39-1.0%; ages 40-49-0.4%; and ages 50-59-0.1%. Once again, note that the use is the highest at the younger ages, which is traditionally where we've done the least amount of underwriting.

Another underwriting tool I wanted to mention is the personal history interview (PHI). I know a number of companies, including my own, who have a program where we pick up the telephone and call our applicant. We tell our agents to tell any applicant that they may be called. We then have some internal underwriting criteria that tell us when a PHI might be most valuable. We tend to call an applicant more often if there are certain risk factors shown on the application, or if the amount of insurance is particularly high.

The information we're getting from these telephone calls is excellent. The cost to us is about $10 per interview. Our interviewers are trained in medical terminology and telephone techniques. The average call lasts about eight minutes, and about 60% of the calls are completed within four days. The biggest problem we have is finding the applicant or the spouse of the applicant at home. When we do, the information we get is dramatic.

I will give you an example of the frequency with which we learn something in the PHI that was not on the application. In over 8% of the interviews, we developed a medical condition that was not stated on the application. In our

statistics we try to rule out sore throats, colds, flu, etc., so the 8% "hits" represent significant medical conditions -- obviously not all that would have been rated, but conditions that probably should have been on the application. Also, 4.4% of the time we come up with a hospitalization that was not on the application; over 4% of the time additional doctors were named; and 3.5% of the time applicants tell us they are currently taking a medication that wasn't stated on the application. It's amazing the information people will tell you on the phone. We've had several people tell us that they've had AIDS! Drug usage is another area where we get a lot of information on the telephone.

We also get motor vehicle information from the PHI, which we request particularly at the younger ages, especially if we've got some elevated liver enzymes or other suspicion. The information we're getting on the PHI is very useful in determining motor vehicle problems. In about 10% of the phone calls, people tell us they've had some sort of a violation. That may not be too unusual, but 3.5% tell us they've had an accident recently; 3.4% -- and I double-checked this number because this seems high to me, and actually in the first quarter of 1988 it was higher than 3.4% -- but in the fourth quarter of 1987, 3.4% of the people we called said they had their driver's license suspended at one time in the past (not currently, but sometime in the past). Finally, 1.7% admit they've been DWI sometime in the past. You can reduce your accident mortality with information like this.

The last item on my list of effective underwriting tools is the EKG. A colleague of Bob Spellman at Northwestern Mutual performed a protective value study recently and found that treadmill EKGs provide a 13 to 1 protective value over age 45. That's excellent, especially if you're dealing with a very large amount of insurance.

Another widely used underwriting tool is the attending physician's statement (APS). This is one that we're probably never going to be able to get along without. But I do think we're becoming more and more dependent on our own paramedical exams, blood profile information, and urinalysis information, because there are a lot of instances where the APS doesn't necessarily tell you everything. I know there may be some doctors that have their medical files, and then they have their *confidential* medical files. When you order that APS you may not get the total picture of that individual, so we need to spend a little more money developing our own medical information.

Application information, of course, is important in underwriting. Physicians' exams can be valuable, particularly if you're ordering an exam for a cause, when you suspect there might be a problem and you want an MD to check out a specific condition of possible importance. Inspection reports are still useful, particularly for large amounts of insurance. Chest x-rays have just about been eliminated as a routine requirement, but once in a while they are appropriate for cause.

Next let's turn briefly to tools of the future. New HIV tests may improve the current antibody tests. There is still a "window" period from the time of infection until the time your body develops antibodies, and there are also a number of tests in the current testing protocol that are indeterminate. The new HIV tests may give you better information on whether a result is a true positive or a true negative. The new tests also may shorten the "window" period so that you can pick up more of those that are infected.

Sometime down the road we may have a cancer tumor marker. There are some markers out there, but the false positive rate right now is high enough that there is no way that they could be used as an insurance screening exam. At a point in time when the false positive rate is very low, we might be able to work with a very important tool that would impact one of the leading causes of mortality.

Last on my list is expert systems in underwriting. Certainly a number of companies are experimenting with those. Some are using them, and they are another tool that will allow the underwriter to spend his time more cost-effectively in the future.

MR. BRADLEY D. LEONARD: Two questions come to mind. First of all, we are getting a lot of conflicting advice from different sources as to future mortality improvement. On the one side, AIDS is a significant additional risk. On the other hand, there are lots of things on the horizon for future mortality improvement. How do those balance each other off?

DR. SPELLMAN: Over the last two-three decades, there's been about a 35% decrease in cardiovascular mortality. I don't think we've seen the nadir of that; I think it will go down even further, and I think it will be a slow steady trend. I don't see anything really dramatic happening in the area of diabetes. So I would tell you that I think that you will see that the AIDS mortality will be counterbalanced to some extent by improvements in cardiovascular mortality. I think that Hank probably is the best man to talk to you about cancer.

MR. GEORGE: I don't think much is going to happen with cancer. I think we are going to see the outlook for some of the childhood and young adult neoplasms improve as new combinations of second- and third-generation chemotherapy improve our cure rates without having a lot of potentially fatal side effects. But when you're talking about the kinds of cancers that kill the big numbers of people -- the lung, the breast, the colon -- it seems unlikely that anything in the offing the rest of this century is going to change the outcome for those individuals to a degree that would affect insurance company mortality.

MR. LEONARD: What about pricing? I know there are still some companies pricing for improving mortality. A "wash" between cardiovascular mortality improvement and AIDS isn't necessarily accurate. Some are talking about systems to price increases in mortality, others are pricing for decreases. What's BMA doing, for example?

MR. SADLER: I don't know. Since I've been in the underwriting community, they haven't gotten me involved in the pricing.

MR. LEONARD: In the area of applications, of course, the really accurate information comes from all the underwriting tests. There's a tremendous desire for simplified apps from the field, and so you're always trying to condense the most useful questions in the smallest space. What are the big ticket items -- obviously cancer and heart disease, but beyond that?

MR. SADLER: Obviously you want to focus on the leading causes of mortality, particularly in an insured population, and those are not necessarily the same as in the general population. One thing we've done with our personal history interviews is to try to design our application questions to hit the "biggies," and

then we can follow up with our telephone calls and ask detailed questions using people that know how to probe and know how to ask the open-ended question in such a way that we can develop additional information.

MR. LEONARD: You mentioned the marijuana situation earlier. We have a question in our applications that says "Have you used any form of tobacco in the last twelve months?" Might you be suggesting that the question should be expanded to include both tobacco and marijuana? Or is marijuana prevalent?

MR. GEORGE: I don't know if you really care about it. First of all, most people who use marijuana aren't going to take out an ad in the newspaper to tell you about it. It is a misdemeanor to use it; even if it's been decriminalized, there is still a still a stigma associated with it. I think your best investment is to ask questions on the key impairments -- the key heart questions, the key cancer questions, and obviously all the major stigmata of HIV infection. A question on weight loss is absolutely indicated now. It is also a good idea to ask the general question: "Have you seen a physician within five years, and if so, why?" I think this question remains intrinsic to what we do.

MR. MCFALL: When inquiring about tobacco use on the application, it makes sense to me not to focus strictly on the last twelve months, even if your nonsmoker discount is defined in those terms. You may look at a proposed insured differently, for example, if he or she quit smoking thirteen months ago on the doctor's orders. Information about tobacco use history can also help you evaluate an applicant's coronary risk profile.

MR. GEORGE C. CROSBY: The Pap smear has resulted in earlier detection of cervical cancer. Don't you think that the hemoculture stool test will give a likewise reduction in colorectal cancer deaths?

MR. GEORGE: That's a very interesting hypothesis that has been raised by a number of individuals over the last few years as techniques for doing studies of stool samples looking for cult blood have improved. The bad news is that there are a whole lot of physiological reasons, like meat ingestion and others, that produce a positive stool cult blood. If you follow a large number of people with expensive gastroscopies, barium enemas, etc. the yield rate of neoplasms and even noncancerous polyps is not very encouraging. In fact, most of the people in screening and surveilliance program testing right now are not very encouraged about screening large populations with these kinds of tests because the hit rates are so low that you wind up paying an unacceptable price for each hit. I think there's some potential in high-risk individuals -- people with very positive family histories of colorectal cancer occurring in young age groups, for example. But as an overall screening of large populations that would impact insurance, I fear that cost would be prohibitive for the hemocult stool test, mammography, or sputum cytology for heavy cigarette smokers.

DR. SPELLMAN: I think there's another pretty crucial factor, and that's going to be the incredible increase in the use of aspirin in this country as an antiplatelet factor. I didn't get much of a chance to talk about lytic therapy, but there recently was a five-year study which included 22,000 physicians that looked at the overall infarction rates on basically healthy people from age 40-84. There was a 50% reduction in heart attacks in those people that had taken an aspirin once every other day. I know plenty of physicians who advocate, for themselves as well as for their patients, the taking of an aspirin or half an aspirin every other day. Once you start doing that you're going to have a lot

more stool cult bloods that are going to be positive. I think you're going to see a big surge of lytic therapy or antiplatelet therapy in this country. This therapy will mean small amounts of blood in the stool, for which you will have a lot of false positives. I think also you've got to recognize that when you're looking at a lot of polyps those can cause bleeding in the rectum. With polyps, you have to keep surveying those people's colons by colonoscopy and other means, because it's not one individual polyp that's going to be the cancer; in most cases, it's going to be a so-called fertile colon that's creating polyps over time, and you have to keep on looking at them. In summary, I don't think the hemocult stool test is that great a test in the long-run.

I do want to mention that I think the next great battlefield for testing in this country is going to be in genetic testing. I think we could spend a lot of time talking about that, but if you wanted a cost-effective tool besides tumor markers, it would be genetic markers. However, I think that the whole AIDS era has super-sensitized the population to false positive rates. Because of concerns over false positive readings, I don't think we're ever going to get into genetic testing as an underwriting tool.