

FIFTY CENTS

MARCH 19, 1973

# TIME

## Toward Control of CANCER

**Immunologist  
Robert Good**

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## A LETTER FROM THE PUBLISHER

**C**ANCER, mankind's most feared disease, has been stubbornly resisting the onslaught of medicine since the days of Hippocrates. It is today the second leading cause of death in the U.S. (after heart disease) and a subject of intensive study by researchers around the world. One of the foremost of these is this week's cover subject, Dr. Robert Good, director of New York's Sloan-Kettering Institute for Cancer Research. Dr. Good specializes in immunology, using the body's own natural defenses to fight cancer. In recent weeks, he has been sharing his experiences with Medicine Writer Peter Stoler who, aided by Reporter-Researcher Andrea Chambers, wrote and did much of the reporting for this week's cover story.

Stoler and Good, it turned out, have more in common than their interest in immunology. The scientist, a onetime country boy, and the reporter, an incurable morning jogger, are both early risers. Their initial meeting was over lunch, but they subsequently had most of

DAVID BURNETT

their discussions in Good's office from 6 a.m. to 8 or 9 a.m. Last month both attended a Florida conference on immunology, and while fellow conferees slept, Stoler and Good continued their talks over chilled orange juice, watching the sun rise over St. Petersburg.

Not all of Stoler's sources greeted the day at dawn, however, and during more civilized hours he interviewed cancer researchers from the University of Wisconsin, the University of California and the National Institutes of Health, as well as representatives from a number of cancer treatment centers. What began to emerge was solid evidence that immunology might well lead to a successful control of cancer. "The problem now," cautions Stoler, "is that doctors can't make it work all the time or with everybody. There's no 'magic bullet' yet for cancer, but this seems to be one of the most encouraging developments in years."

PETER STOLER & DR. GOOD

A former newspaper reporter and radio-documentary writer, Stoler began writing TIME's Medicine section 2½ years ago and now cuts his way through eight to ten medical journals a week. "I reduce things to terms that I can understand, and I figure if I can understand them, I can make the reader understand them," he says. "The challenge is to take a fairly complex procedure and explain it in simple, everyday language without losing any accuracy."

His early interviews with Good behind him, Stoler is back to running two miles before breakfast each weekday morning, sometimes seven or eight miles on the weekends. "I suppose everybody has got his hang-up," he says a trifle defensively. "I'm hooked on exercise." And on early mornings.

Ralph P. Davidson

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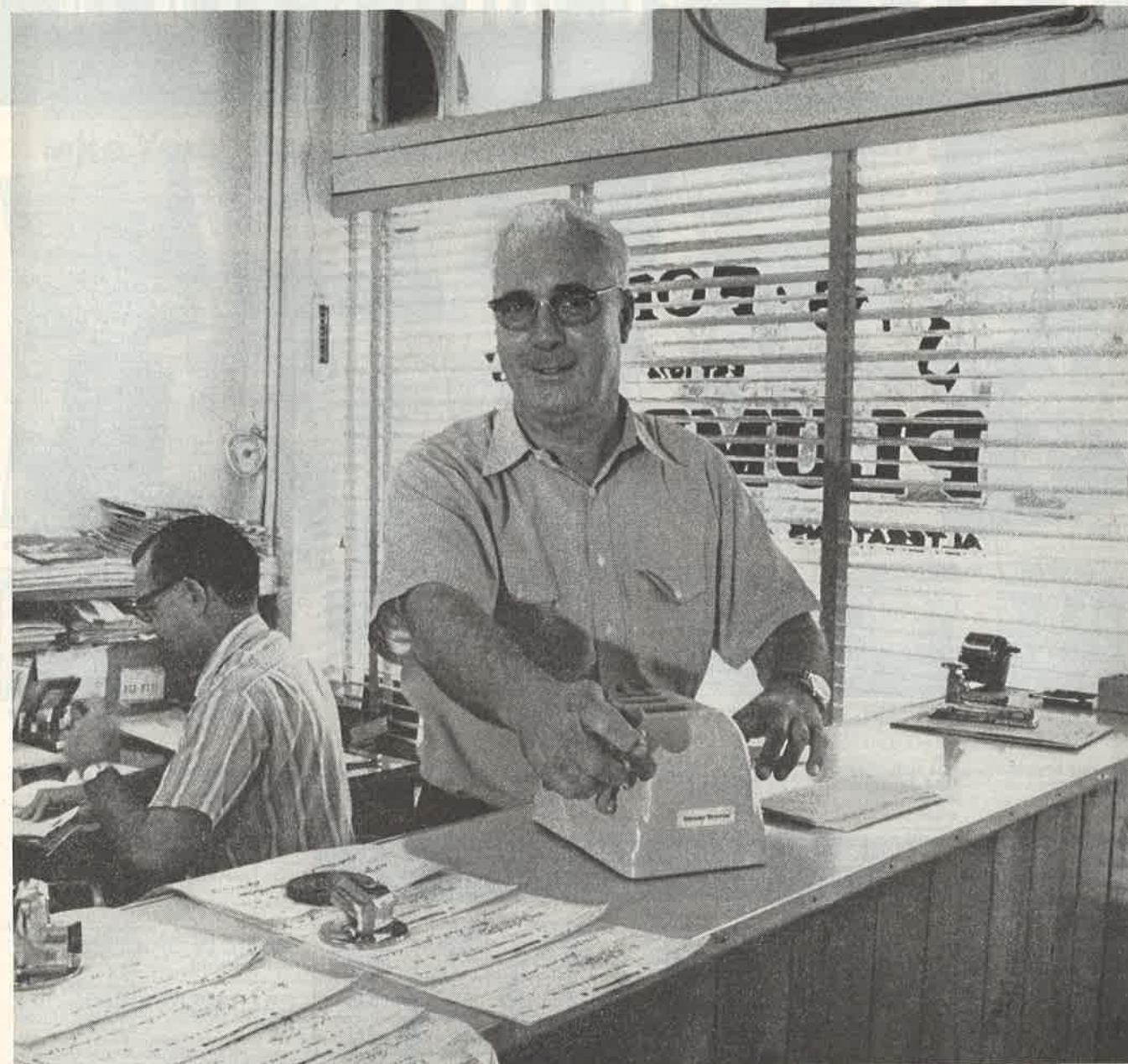
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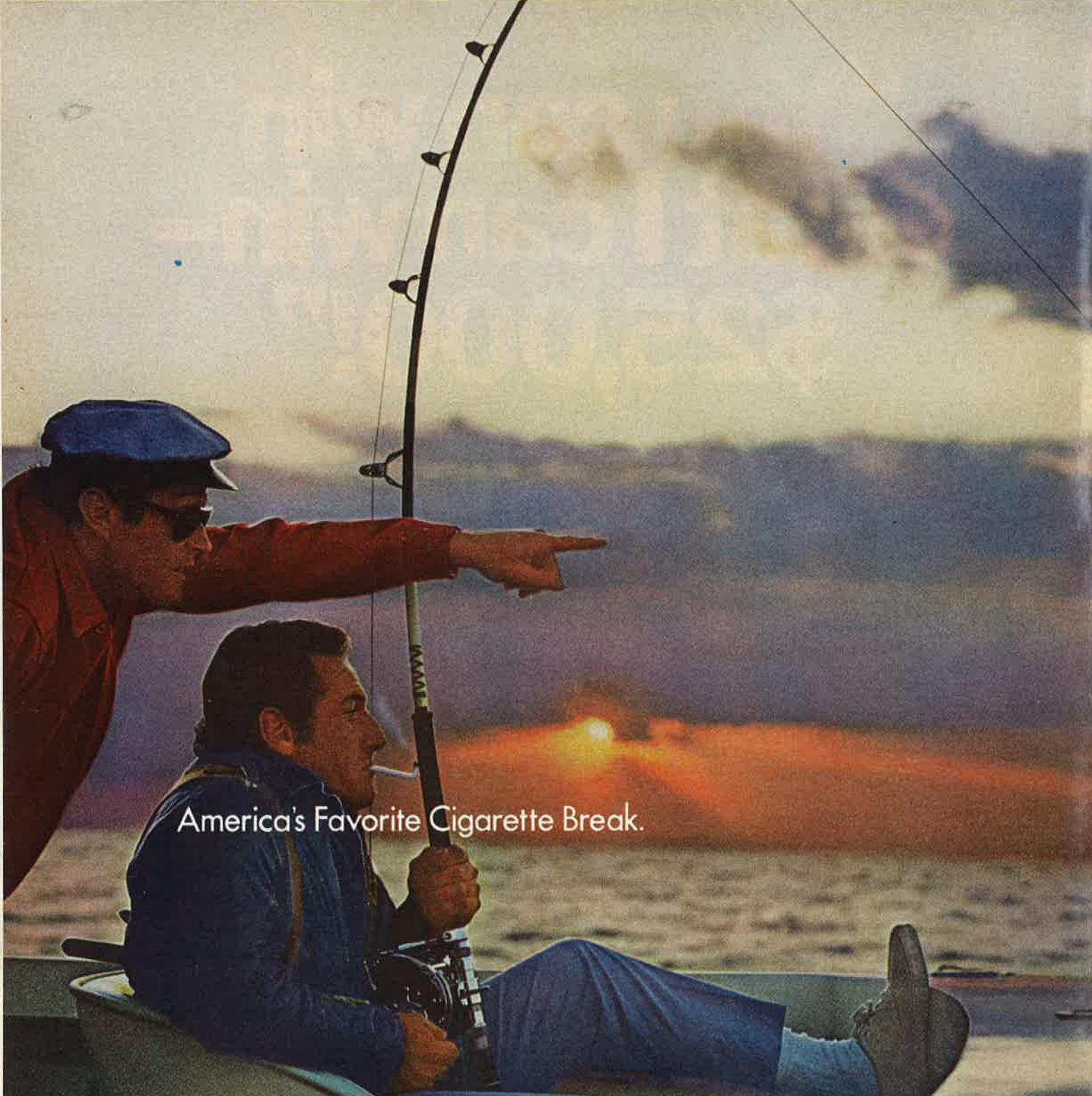
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## LETTERS

when students have been attacked and injured there this year?  
 Why not blame the thugs who try to terrorize everyone, black and white, student and teacher alike, and quit whipping the middle class? We have tried to stay in the public school system and in an integrated neighborhood, but we are being literally pushed out of the public schools and may well be pushed out of our neighborhood some day. I hope not.

MRS. DOUGLAS W. KIRKLAND  
 Dallas

## Cleaning Out the Fold

Sir / Re the evangelical campaign Key 73 [Feb. 19]: I suggest that the churches eager to win souls for Christ should start by first cleaning out their own folds. If Christian virtue—as practiced, not as preached—is going to be the reason for conversion, then Judaism and other persuasions need not be concerned about the possible loss of their numbers.

JOSEPH VINCI  
 North Dartmouth, Mass.

Sir / We Jews already live in an overwhelming Christian environment and are bombarded with its message day and night. To heighten that bombardment, however, and seek the destruction of the Jewish faith is a negation of this country's basic beliefs.

Key 73 will not succeed.  
 BARBARA ANN SHELTON  
 Peoria, Ill.

Sir / There are more than 6,000,000 Jews in the U.S. representing more than 6,000,000 completely different interpretations of their faith.

Should Christians ever be successful in converting the Jews, they will rue the day.

EDDIE GERSHATER  
 Dallas

Sir / The Christian evangelical movement exists not to force-feed those who do not wish to be fed, but to share the joy of our faith with those who are hungry.

STACY MACLEOD  
 Brookline, Mass.

Sir / The rabbis against Key 73 might be the spokesmen of the majority of Jews. I as a Jew, however, have come to believe in Christ, and I'm thankful for all of the gentle Christians who dealt with me kindly and lovingly when my own response to their religion was one of hostility. The rabbis don't speak for all of the Jews, and they certainly don't speak for me.

MOISHE ROSEN  
 Corte Madera, Calif.

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IRISH TERRORIST BOMB EXPLODES OUTSIDE GOVERNMENT BUILDINGS IN WHITEHALL



rad's protagonist in *The Secret Agent* schemed to blow up the Greenwich Observatory, just as the hero of a novel recently published in London, *The Patriot Game*, plans to blast the headquarters of the British secret service.

Last week the electorate of Northern Ireland was asked to vote on whether it wanted to remain part of the United Kingdom. The result was inevitable—almost 99% voted yes since Ulster's population is two-thirds Protestant, and since many Catholics had decided to boycott the British government's referendum. On that very day, Irish extremists made themselves heard in another way—once again bringing the violence to London.

The first "Belfast Special"—a car loaded with 175 lbs. of gelignite time bombs—destroyed the back of the Old Bailey court building and its year-old \$17 million annex and wrecked a three-story hotel and pub across the street. An hour later, 1½ miles to the west, a second car exploded in Whitehall, badly damaging the Ministry of Agriculture and the main army recruiting center. Whole walls were stripped of windows, the frames twisted and buckled. The two blasts injured 194 people, including five policemen, but miraculously caused only one death. The victim was a 60-year-old caretaker who was treated for head wounds and was returning home when he suffered a heart attack.

SHATTERED OFFICE BUILDING WINDOWS

## THE WORLD

Throughout the rest of the day, squad cars and ambulances chased through the city, evacuating buildings and trying to deal with a rash of hoaxes; the rumored targets included Windsor Castle and the Royal Opera House. Police blocked off Trafalgar Square for several hours and, taking no chances, exploded four locked suitcases that were found on the steps of the National Gallery; the suitcases, as it turned out, contained old clothing.

The explosions brought out the city's best blitz spirit. Medical workers suspended their strike and returned to St. Bartholomew's Hospital, which treated most of the casualties.

"Well, it's one way to go free," reflected one man, grinning despite a swollen lip, a cut nose and two loosened teeth. At the time of the explosion, he had been on trial at the Old Bailey for receiving stolen goods. He added: "Maybe they'll give me good conduct for this."

Most I.R.A. leaders in recent years have strongly opposed the opening of a new campaign of terror in London. The rebels are far more isolated there than they are in Northern Ireland, and the damage they can cause is not so great. Last year's I.R.A. attack on a paratrooper base at Aldershot, 35 miles from London, backfired humiliatingly; of the seven people killed when a bomb went off in a mess hall, all were civilians, five were women and one was a Catholic priest. Both bombers were caught and convicted. Last week's terrorists seemed to fare no better. Within hours, seven men and three women were arrested at London airport as they tried to board planes for Belfast and Dublin.

Almost forgotten in the turmoil was the referendum in Northern Ireland, which for once seemed almost tranquil in comparison with London. Ulster managed to get through its first polling day in seven years with only eleven explosions, two people injured, and one soldier killed by a sniper.

## The Lollipop Budget

First the gas workers walked out, cutting service to 4,000,000 homes. About 3,500 business firms, 1,700 schools and 400 hospitals were shut down—either because of lack of heat or because their own employees were also on strike. Some hospitals even had to burn their soiled bedsheets because their laundries were closed.

As the strike for higher wages spread, stoppages and slowdowns seemed to succeed one another almost at random. The customs inspectors at London's Heathrow Airport returned to duty within 24 hours, but the rail strike that was supposed to last one day dragged on for four. Queen Elizabeth II herself had to rearrange a train trip to Wales (she went by plane instead). Scotland Yard warned travelers: "Do not come into London unless your presence is absolutely essential." In some



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## SPORT

often beat the boys in climbing, skiing, even schoolyard brawling.

That spirit carried her through her one major setback so far: failure to win in the 1972 Winter Olympics at Sapporo. The Austrians went into that competition confident of success, and Annemie was expected to pick off a gold medal or two with little trouble. The team's morale was destroyed, however, by the controversial disqualification of Star Skier Karl Schranz (TIME, Feb. 14, 1972), and Annemie had to settle for a pair of silver medals. After that setback, she thought of giving up skiing, but the mood lasted only a short time. Then she threw herself into her harsh training regime, modeled after that of a prizefighter—long-distance runs, shadow boxing and rope jumping—and had a metal plaque made for the dashboard of her car: NEVER FORGET SAPPORO. Said Proell to a friend: "When I'm second, I see red."

**Kid Sisters.** If anything ever lures Proell away from skiing, auto racing might do it. Romance for the moment runs a poor third. Her current car is a hopped-up Ford Capri, painted black and gold in the colors of Brazil's World Champion Emerson Fittipaldi. She is renowned for flogging it along slippery Alpine roads at speeds of up to 160 m.p.h. Whenever her training schedule permits, she flies off to Grand Prix races to watch the progress of such motoring pals as Fittipaldi, Jackie Stewart and Jackie Ickx.

But her skiing days seem far from ended. Last week she was racing in World Cup competition in Alaska, after a painful fall that knocked her out of a cup weekend in Quebec. Beyond the current North American tour there is next year's World Cup and, in 1976, the Olympics in Innsbruck, Austria. How long will she continue to ski? "I don't know," she says, "but there will be Proells on the slopes for years to come. Wait until you see my kid sisters—they'll be the best yet."

## Designated Success

Score one for the American League and its "designated hitter" experiment (TIME, Jan. 22). In the first game of the 1973 exhibition season last week, which matched the American League's Minnesota Twins and the National's Pittsburgh Pirates, each team played according to the rules of its own league. Thus the Twins had the advantage of putting a hitter in the pitcher's batting-order spot without removing the pitcher from the game. The Twins' designee, Outfielder Larry Hise, drove home seven runs with a pair of homers as Minnesota won 12-4.

"It's a wonderful rule," said Hise, whose career batting average is a modest .236. Pirates' Manager Bill Virdon, who will not have to contend with the innovation once the regular season begins, had a different view: "It's not fair, playing nine men against ten."

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## CINEMA

as is the only one who really makes things work. He performs *Funky Chicken*, strutting smartly about the stage splendidly attired in shocking-pink cape with matching shirt and Bermuda shorts and white vinyl boots as if he will never come home to roost. It is a performance of ebullient self-parody, one that the kids in the stadium seem to enjoy. It is unfortunate that the Code and Rating Administration will not let kids see it in theaters unless their parents (or "an adult guardian") can get them past *Wattstax's* R classification. Such a harsh rating was assigned presumably because of the scruffy slang in the film, the sort of language street kids hear and use every day. It is a part of life that they all share, but one that the censors, by some convoluted hypocrisy, would forbid them on-screen. ■J.C.

## Now This Message

### SLITHER

Directed by HOWARD ZIEFF  
Screenplay by W.D. RICHTER

There is a fairly promising plot notion here, a little like one of Thomas Pynchon's wonderland allegories. A motley but not unlikable crew of misfits chases around rural California in quest of a greenback grail: \$312,000 in cash embezzled from a talent agency years earlier. James Caan, Sally Kellerman, Peter Boyle and Louise Lasser barrel



KELLERMAN & CAAN IN "SLITHER"  
Greenback grail.

over the back roads towing an Airstream Land Yacht, pursued by two absurdly sinister motor homes painted deadly black and piloted by unseen, relentless drivers.

But Director Zieff does not make the fantasy of the script quite abstract enough, nor his odd, self-consciously cute characters quite believable enough. Whimsy and reality, neither fully realized, cancel each other out. Caan, a perennially baffled ex-con, basically plays

straight man to Boyle as a bunko artist-bandleader and Lasser as the band-leader's addled spouse, both of whom are amiably funny throughout. Kellerman, a souped-up Bonnie Parker, pushes much too hard, perhaps in reaction to Zieff's almost laboriously studied direction, which favors lingering takes and long pauses.

Still, *Slither* is intermittently interesting and almost always diverting. There are some quiet laughs, and those ominous black campers exert a weird, compulsive kind of suspense, although they are a lot more intriguing in their cryptic malevolence than in the mundane explanation eventually dispensed by the scenarist.

The movie boasts some of Cinematographer Laszlo Kovacs' customarily exquisite work and an abundance of character actors chosen for their rather too picturesque physiognomies. Zieff was formerly a prominent director of TV ads (*Slither* is his first feature), and he has cast most of the small parts with the sort of eccentric types who are generally seen on TV urgently requiring an Alka-Seltzer. This may be the reason why every candy bar, every can of beer or other easily identifiable product is conscientiously wrapped in brown paper or covered with a phoney label. Zieff must have worried that any time one of the supporting cast picked up a prop, *Slither* might look like a commercial. ■J.C.

## MILESTONES

**Married.** John A. Scali, 54, former newsman and new U.S. Ambassador to the United Nations; and Denise St. Germain, 38, who once worked for the CIA in Paris and Rome, and most recently served as an assistant to TIME's Washington bureau chief; he for the second time, she for the first; in Washington.

**Divorced.** Gilbert ("Mr. 100,000 Volts") Becaud, 45, intense, high-energy French singer-composer (*What Now My Love*, *The Day the Rains Came*, *Let It Be Me*) and Monique ("Kiki") Nicolas Becaud, fortyish; after 20 years of marriage, three children; in Paris.

**Died.** Fourteen members of the U.S. Army's Golden Knights, the precision parachuting team that since 1959 has been performing at Army air shows across the U.S.; when their plane exploded and crashed while carrying the team to an exhibition; between Silver City and Silk Hope, N.C.

**Died.** Ron ("Pigpen") McKernan, 27, scruffy blues singer and harmonica player with the Grateful Dead, the San Francisco rock group whose loud, countrified rhythm-and-blues has been a staple of the West Coast counterculture since the mid-'60s; from as yet undetermined causes (he had recently been under treatment for liver disease); in Corte Madera, Calif.

**Died.** Robert L. Conly, 55, senior assistant editor of the *National Geographic* magazine, who under the pen name Robert C. O'Brien wrote a prize-winning children's book (*Mrs. Frisby and the Rats of NIMH*) and last year's top-rated cloak-and-dagger tale for adults, *A Report From Group 17*; of a heart attack; in Washington, D.C.

**Died.** The Rev. Robert J. McCracken, 68, minister of Manhattan's interdenominational Riverside Church for 21 years; while on a world cruise; near Bangkok. A wry, Scots-born Baptist, McCracken succeeded the nationally famous radio preacher, Dr. Harry Emerson Fosdick, at Riverside in 1946. In understated but eloquent sermons, he was an ardent advocate of both ecumenism and civil rights.

**Died.** Paul Kletzki, 72, Polish-born violinist and conductor, music director of the Dallas Symphony (1958-61) and Geneva's l'Orchestre de la Suisse Romande (1967-70); after collapsing while conducting a rehearsal of the Liverpool Philharmonic; in Liverpool, England.

**Died.** Pearl S. Buck, 80, whose compassionate novels about life in pre-Communist China (*The Good Earth*, *A House Divided*) earned her both the Pulitzer and Nobel Prizes (see Books).

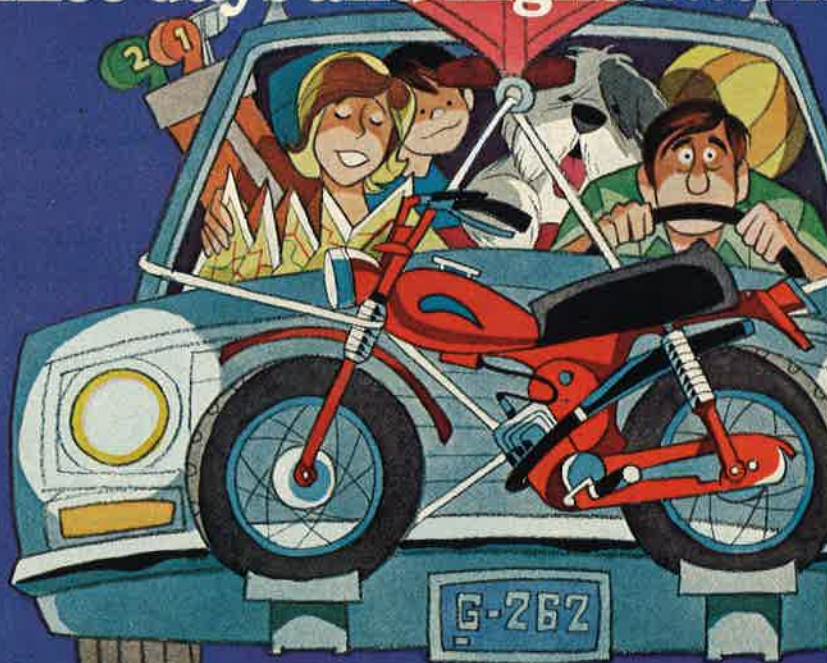
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### THE PRESS

#### Subpoenas (Contd.)

Will there be a federal "shield" statute to protect the confidentiality of newsmen's sources? If so, how strong a measure will be enacted? There was still no firm consensus in Congress last week despite the protracted debate. However, Representative Robert Kastenmeier, chairman of a House Judiciary Subcommittee holding hearings on the dispute, made a cautious prediction: "The odds favor our coming out with some kind of recommended legislation." In the House generally, he said, "proshield forces are definitely stronger than anti-shield forces at this time."

Kastenmeier meanwhile was getting varied opinions from journalists. Investigative reporters would be the prime beneficiaries of a shield law, but Clark Mollenhoff of the Des Moines Register, who has won a Pulitzer Prize for his investigative work, testified that journalists should fight subpoenas on an individual basis, relying on the Constitution for their defense. A law giving absolute protection, he said, could impede law-enforcement agencies and would give newsmen privileges "beyond anything enjoyed today by anyone except absolute monarchs." Anyone could get protection, Mollenhoff added, by claiming to be gathering information for a publication. (Actually, many of the bills that have been introduced attempt to clarify this question by limiting privilege to those "regularly employed" in newsgathering.)

Mollenhoff is in a tiny minority within the trade. Stanford Smith, president of the American Newspaper Publishers Association, and A.M. Rosenthal, managing editor of the New York Times, were among those arguing for absolute protection of confidential sources and unpublished material. "I say flatly," Rosenthal contended, "that without the guarantee of confidentiality, investigative reporting will disappear. The erosion of confidentiality will mean the end of the exposure of corruption as far as the press is concerned."

Last week Time Inc. proposed a strong federal statute that would apply to state cases as well. However, the company did not urge absolute immunity in all circumstances.

The statement, issued by Editorial Director Ralph Graves, pointed out that Time Inc. would prefer to rely on constitutional defenses of newsmen's privilege. But the refusal of the Supreme Court last June to protect newsmen and the frequent issuance of subpoenas has

made the company conclude "reluctantly" that "the First Amendment now needs legislative support."

Specifically, Time Inc. proposed that the law cover both the issuance of subpoenas and conditions under which confidential information would be disclosed: "A subpoena for a reporter's testimony and material should not be issued unless it is established at a prior court hearing that the reporter has relevant information that cannot be obtained from any other source, and that the information is so important that lack of it might result in a miscarriage of justice."

Even if a subpoena is then approved, "a reporter should not be compelled to disclose confidential sources unless it can be demonstrated that there is imminent danger of loss of life if he



"What do you need a shield law for?"

does not disclose such information, or that he has essential information on a violent crime such as murder, kidnaping or skyjacking. Another criterion, which the Congress will no doubt consider, is overriding danger to the national security, though this concept is easily abused and extremely difficult to define."

Essential as legislative protection has become to assure unfettered newsgathering, it is crucial that the law be clear and comprehensive. Said Time Inc.: "A complex, heavily circumscribed shield law, leaving the question of privilege open to a wide variety of judicial interpretations, would be worse than nothing and might well invite a new wave of exploratory subpoenas." The statement also stressed the broad issue in the current debate: "The freedom of the press guaranteed by the U.S. Constitution does not belong to journalists; it belongs to the public. It exists only so the public can have the opportunity to know what the press is able to report."

#### Making of a Nonperson

At the wedding three years ago of Journalist Peter Niesewand and Nonie Fogarty in Salisbury, Rhodesia, one of the guests quipped to the bride: "If he doesn't look after you, my dear, I'll have him restricted." The jocular threat came from Desmond Lardner-Burke, Minister of Justice, Law and Order. Niesewand has looked after his wife well enough, but for the past month he has been in jail under an order signed by Lardner-Burke. The vague grounds: the freelance reporter was "likely to commit acts prejudicial to public safety or public order." Free translation: the white-supremacist government of Ian Smith did not like what Niesewand had been writing, and has the dictatorial powers to squelch him.

The early-morning arrest and the incarceration at Gwelo Jail hardly came as a surprise. Niesewand, 28, was one of the few enterprising and influential newsmen still reporting regularly from Rhodesia. He ran a bureau representing the BBC, the Australian Broadcasting Commission, United Press International, Agence France-Presse and a number of London and South African newspapers. It was Niesewand who broke the story in 1971 of the arrest of former Prime Minister Garfield Todd, who was also considered a threat to public order. Niesewand published exclusives on government action against the African National Council, a black political group opposed to white rule.

**Grinding Pressure.** His phone has been tapped, his office and home searched by police, his official sources restricted by Information Minister P.K. van der Byl. In a letter to a friend before the arrest, Niesewand said: "The worst part is the grinding social pressure—not knowing whether one or both of us will be attacked for being Commie rats. As one lady put it at a recent dinner party, why don't I pull myself out of the slime in which I wallow?"

Van der Byl, one of the most extreme members of the government, obviously intends to eliminate all journalistic criticism. Several other newsmen have been expelled, prevented from re-entering the country or otherwise silenced. Late last week, in a proceeding closed to the public, Niesewand was charged with violating the Official Secrets Act. That could result in a jail term of up to five years. Because he is South African by birth, he could be deprived of Rhodesian citizenship and deported.

Meanwhile, he languishes in modified solitary confinement. His wife, pregnant with their second child, drives 340 miles each day to see him for one hour. Says Nonie: "He's bearing up well under the circumstances, but for a man as active as Peter, the routine is boring him to death." Back in the capital, he has already become a nonperson. Local newspapers and the government broadcasting system are forbidden to discuss his case or even mention his name.





DR. ROBERT GOOD SILHOUETTED AGAINST CELL SLIDE

## MEDICINE

### COVER STORY

# Toward Cancer Control

WHEN Mrs. Mary Brown, a plump, cheerful housewife from Dallas, had her first bout with breast cancer seven years ago, her doctors knew exactly what to do. Following the accepted procedure, they performed a radical mastectomy, removing the affected breast, the underlying muscle tissue and the nearby lymph nodes. Then they subjected her to intensive radiotherapy, hoping that the X-ray bombardment would kill any residual cancer cells. But when cancer recurred at the operation site two years ago, and raised reddish, golf-ball-sized lumps on the flat area where her left breast had been, the doctors were stymied. Surgery was out of the question; the lumps were evidence that the cancer had spread too far. So was X-ray treatment. Mrs. Brown (not her real name) had already had so much exposure to X rays that any more could do serious damage to her healthy tissues. Thus, when even anti-cancer drugs failed to halt the spread of the disease, Mrs. Brown turned in desperation to a new and still experimental treatment.

The treatment, called immunotherapy, uses a biochemical strategy designed to trick the body's own natural defenses into fighting cancer. In Mrs. Brown's case, doctors deliberately ex-

posed her to attenuated tuberculosis bacilli, figuring that if they could make her body resist them, it might resist the cancer as well. The strategy worked. Shortly after treatment began, her lesions began to shrink and disappear. Today Mrs. Brown has only a few lumps on her chest. None of her doctors will say that she is cured, but all agree that without immunotherapy she probably would not be alive today.

Mrs. Brown's treatment is one of the most dramatic applications of the rapidly expanding science of self-immunology—the study of the body's natural defenses against disease. That science is one of the most promising weapons yet developed by doctors in their long fight against cancer, which this year alone will afflict an estimated 650,000 Americans and kill more than 350,000. The older techniques—surgery, radiation and chemotherapy (drug treatments)—have been used successfully in bringing some cancers under control. But surgery usually results in unsightly and handicapping mutilation, radiation can destroy healthy as well as cancerous tissue, and chemotherapy produces unpleasant and dangerous side effects. Immunotherapy, which so far seems to have none of these disad-

vantages, could thus prove to be the ideal approach.

Whether immunology fulfills this promise and becomes a major part of medicine's approach to cancer depends in large part on a hard-driving, affable egotist named Robert Alan Good. A lanky (6 ft. 2 in.), generally rumpled man with an insatiable curiosity and an almost uncanny ability to assimilate any information that passes his way, Good, 50, is both a pediatrician and a Ph.D. in anatomy. He believes that immunology holds the key not only to controlling cancer but to preventing and curing many of man's other ills.

Good is the foremost student, practitioner and advocate of immunology in the U.S. today. His own research, most of it carried out at the University of Minnesota, has been responsible for much of medicine's current knowledge about how the immune system functions. His writings have helped spread the word about the new science; he is co-author or editor of at least a dozen books on the subject, including two that are considered standard texts, and well over 1,000 articles. His clinical work has led to the development of techniques that successfully overcome malfunctions of the immune system.

Good recently moved from Minnesota to New York to become director of the largest privately operated cancer-research operation in the country. As the new president and director of the Sloan-Kettering Institute for Cancer Research and director of research at the Memorial Sloan-Kettering Cancer Center, he will continue his work in immunology, aiming toward understanding and controlling cancer. Those who are familiar with his ingenuity and energy predict that he will ultimately achieve his goal.

**Fifth Column.** Good's achievements in immunology rest on a broad foundation of work by other scientists dating back to 1796, when the British Physician Edward Jenner inoculated an eight-year-old boy with fluid from a cowpox pustule in a successful attempt to give him resistance against the more virulent smallpox. Jenner knew nothing about the immune system, but he had recognized that milkmaids who frequently came in contact with cows suffering from cowpox seldom contracted smallpox. Scientists began to suspect that the body had a mechanism for identifying and combatting disease agents only after Louis Pasteur discovered the existence of bacteria and in the 1850s propounded the germ theory of disease.

That mechanism was still a mystery in 1891, when Dr. William Coley, an American surgeon, first observed the beneficial effects of certain infections on patients with cancer. Coley began injecting patients with mixed bacterial toxins to induce responses that might alter the course of the malignancy, and without fully understanding what he was doing, succeeded. In 1893, he injected his toxin into a 16-year-old boy

with inoperable cancer and was rewarded with a demonstrable success: the tumor shrank and, over a period of a few months, disappeared. He treated some 250 other patients who also improved and survived for another five to 72 years. But despite the results, Coley's work, which was far ahead of its time, generally went unrecognized.

**Outlaws.** But immunology was gradually becoming a science. The existence of antibodies—agents produced by the body in response to the challenge of disease-causing organisms—was discovered at the end of the 19th century. In the 1940s, doctors finally recognized that a badly functioning immune system, or the absence of one, can leave the body virtually defenseless against infection from without. But it was not until the early 1950s that Sir Frank MacFarlane Burnet, an Australian, theorized that the way the body manages to cope with the enormous range of disease organisms is through its ability to recognize itself and to reject everything that is non-self (see box page 67).

A few years later, Burnet and Dr. Lewis Thomas, who has just been appointed president of Memorial Sloan-Kettering Cancer Center, suggested a relationship between the immune system and cancerous growth. They postulated that in addition to protecting the body from invaders, the immune system has the duty to police cell growth and prevent the survival and replication of abnormal or "outlaw" cells.

As Burnet and Thomas saw it, the body, in which cells are continually replicating themselves, produces anywhere from tens to hundreds of abnormal, genetically different and potentially cancerous cells each day. Ordinarily, the immune system recognizes these biological fifth-columnists as "foreign" because they are genetically different; it destroys them before they begin dividing and reproducing. But when the defense mechanism is weakened, for whatever reason, it fails to do away with the errant cells, either because it cannot recognize them or because it is incapable of attacking them. That gives the outlaw cells (which are apparently not under the same genetic restraints as normal cells) the opportunity to run wild. They reproduce themselves at an extremely rapid rate, invade normal tissues, and, if not destroyed, cut out or arrested, eventually kill.

Some of the evidence that cancer thrives when the immune system is defective is purely circumstantial. For example, the disease strikes hardest at the aged or very young, the two groups whose immune systems tend to be weakest. Cancer on rare occasions has also been known to undergo spontaneous remission, an indication that some mechanism has acted to inhibit its growth.

But much of the evidence is more scientific. Good and his co-workers have observed a high correlation between cancer and the so-called

immunodeficiency diseases, which leave their victims unable to resist infection. They speculate that eventually it will be found that all cancer patients suffer from some impairment of their ability to resist disease. "In order for cancer to occur and persist, there must be a failure of the immunological process," says Good. "We've never found a cancer patient in whom something wasn't screwed up immunologically."

Other research tends to support Good's theory. A study conducted at the University of California at Los Angeles showed that only one out of three patients about to undergo surgery for cancer was able to respond to a skin test used to determine if normal immune reactions occur. Kidney-transplant patients, whose immune systems are suppressed by drugs to prevent rejection of the new organ, are more susceptible to certain malignancies than others in the same age groups.

The American College of Surgeons/National Institutes of Health's organ-transplant registry studied more than 8,000 transplant patients and found 77 cases of cancer, 17 of which were a bone-marrow malignancy called reticulum cell sarcoma. Significantly, that disease occurs about 100 times more frequently in transplant patients than it does in members of the general population, according to a report by doctors at the Medical College of Virginia of the Virginia Commonwealth University.

Why these immunological problems occur has long been a mystery. But lately researchers have been finding some clues that could lead to its solution. Doctors at Sloan-Kettering Institute have

discovered that some cancer cells fail to produce antigens, or markers identifying them as foreign, and thus avoid the body's recognition mechanism. There is also speculation that larger cancers shed so many antigens that they simply overwhelm the immune system.

Drs. Karl and Ingegerd Hellstrom, Sweden's husband and wife team now working at the University of Washington in Seattle, have found that in some cancer patients there are complexes known as "blocking factor" that prevent the immune system from attacking cancers. They have also discovered "unblocking factor" as well, raising hope that some method may be developed to free those immune systems inhibited by blocking agents.

Other doctors, meanwhile, have borrowed a leaf from Coley's book and have been trying, with some success, to awaken sleeping immune systems to combat cancer. The techniques of this approach vary widely. Some doctors still use Coley's bacterial-toxin formula; others inject vaccine made from killed mumps virus and diphtheria bacteria. Many, however, prefer a live-bacteria tuberculosis vaccine called BCG (for *Bacillus Calmette-Guérin*, after the Frenchmen who developed it).

**Memory Jogger.** BCG is not an anti-cancer drug as such. But it does appear to be a powerful immunopotentiator, or tool for turning on the immune system. When injected into patients with either natural or acquired immunity to tuberculosis, it jogs their immunological "memory" of the disease and produces a generalized immune response. Injected directly into cancer lesions, it can cause a responsive immune system to send anti-tuberculosis antibodies to the scene to fight the invaders. In some patients, this defense against bacterial attackers destroys cancer cells as well.

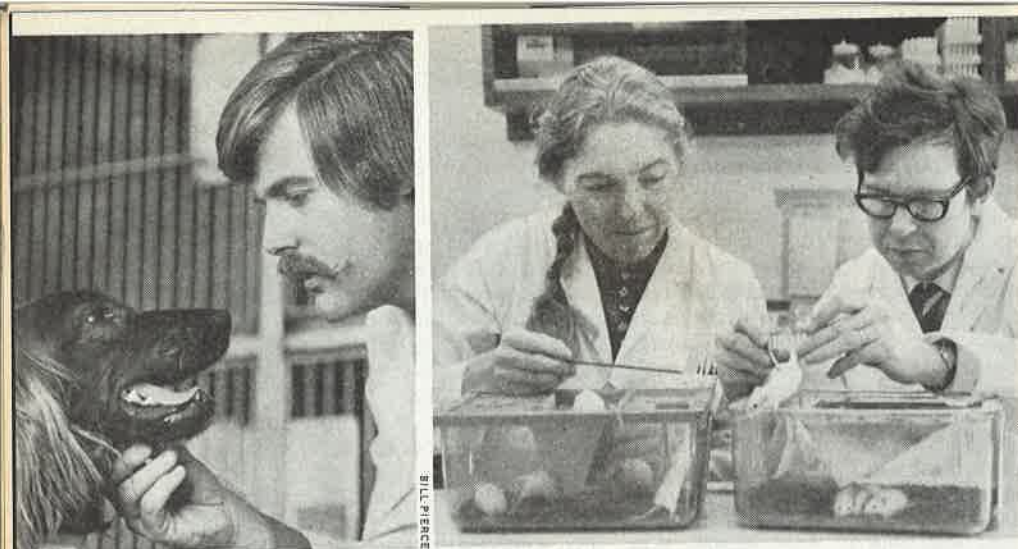
Several doctors are now using BCG for cancer immunotherapy. Dr. Donald Morton of U.C.L.A. has used BCG to hype up the immune systems of patients suffering from malignant melanoma, a cancer that first appears on the skin and spreads rapidly to other parts of the body; some of his patients have been free of the disease for two years or more.

Dr. Georges Mathé, a leading cancer researcher at the Paul Brousse Hospital at Villejuif, near Paris, has been using BCG since 1964. He administers it as part of a double-barreled approach to treating patients with acute lymphoid leukemia, a cancer of the blood-forming tissues that tends to further depress and obliterate the patient's already weakened immune responses. Mathé begins with chemotherapy, using cell-destroying drugs that kill rapidly proliferating cells (and thus destroy cancer cells more quickly than normal ones) to reduce the size of cancers from billions of cells to 100,000 or so. Then he uses

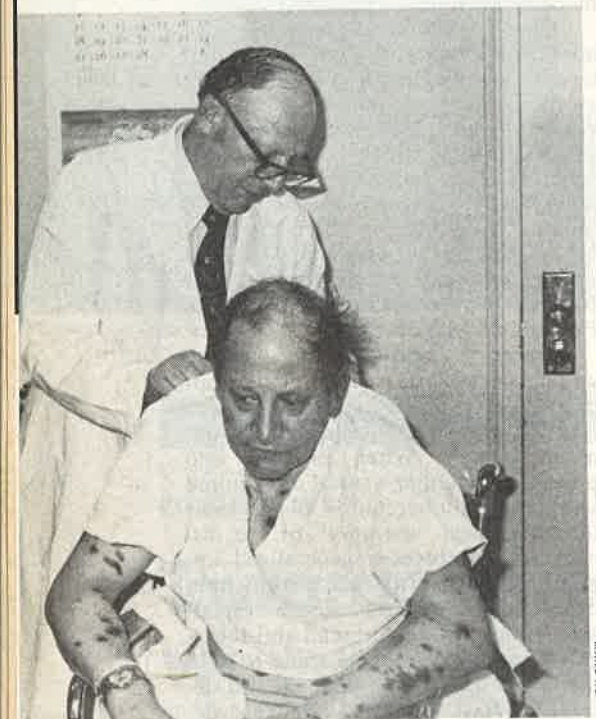


JENNER INOCULATING HIS SON





HARDY WITH TEST SUBJECT INGEGERD & KARL HELLSTROM IN LABORATORY



KLEIN EXAMINING CANCER PATIENT  
Establishing an equilibrium.

immunotherapy in an effort to make the body root out the residual cancer.

Dr. Edmund Klein of Roswell Park Memorial Institute in Buffalo has used BCG to stimulate an immune reaction against malignant melanoma, mycosis fungoides and other cancers that originate on the skin, as well as against such deep-seated tumors as breast cancer. He has also experimented with vaccines made from tumors similar to those of the patient, injecting the substance into cancer victims in the hope of triggering not a general immune reaction but one that is specifically directed against the cancer. Of those patients who responded immunologically, most showed marked improvement.

Dr. Virginia Caspe Livingston of the University of San Diego has also used such vaccines in patients with breast cancer and cancer of the thymus, and has achieved remissions. Dr. Loren Humphrey, chairman of the department of surgery at the University of Kansas School of Medicine, has eval-

uated 96 patients who have received injections of cells from people with tumors similar to their own; more than 20 have had partial remissions and three now appear completely free of disease.

Results like these have led some researchers to regard immunotherapy as one of the most encouraging developments in decades, and an important tool for the physician. "Immunotherapy used to be a dirty word in cancer," says Klein. "No one thought it worked. Now it has become respectable."

**Overkill.** But it still has a long way to go. Doctors are not yet sure whether the commonly used methods, which rely primarily on nonspecific immune stimulation to produce selective tumor destruction, represent a form of immunological overkill. Says Klein: "It's sort of like alerting the whole damned U.S. Navy to keep one foreign destroyer from entering one harbor. It's effective, but it may be unnecessary." Furthermore, doctors cannot make immunotherapy work for all patients. They have no sure way of knowing who will respond until they begin treatment.

Even when such problems are solved, no one sees immunotherapy as completely supplanting other, more traditional methods of treatment. The technique seems to work best against small, localized cancers; surgery, radiotherapy and chemotherapy are still the preferred methods for dealing with large or widespread malignancies. But even when these methods are used, immunotherapy may still be necessary to cope with residual cancers. Says Dr. Lloyd Old, vice president and associate director of Sloan-Kettering Institute: "What we can do well right now is eliminate massive amounts of cells. But getting rid of 90% of a cancer, even 99%, isn't enough; if there's one cell left, it can produce millions more cells. Immunotherapy offers a way of getting at these residual cancers and preventing them from spreading."

Despite the heady progress, few researchers think in terms of "curing" cancer, particularly in light of the widely held view that the body is constantly producing abnormal cells. "Let's think of control of cancer rather than cure," says Old. "Cancer is not a killing dis-

## MEDICINE

ease; what kills is progressive cancer. What we're trying to do is not eliminate cancer but establish an equilibrium between cancer and its host."

That, in essence, is what Good is uniquely qualified to do. He first became interested in medicine at the age of five when his father, a Minneapolis high school principal, developed what proved to be a fatal cancer. "I was very impressed with the doctor who came to take care of him," says Good. "I never wanted to be anything but a doctor after that."

The path to a degree in medicine proved arduous. The second of four sons in a fatherless family, Robert Good had to earn his own way through the Depression by raking leaves, shoveling snow and running a newspaper route. Impressed by Good's ambition and industry, a Minneapolis businessman helped pay his way through medical school at the University of Minnesota.

While a student, he was stricken with a paralytic disease (doctors diagnosed it as poliomyelitis but Good thinks it was Guillain-Barré syndrome, which generally produces a less permanent form of paralysis); whatever it was, it left him partially paralyzed. Dropped from the class roster by professors who felt he would be unable to keep up his grades, he was restored only after he promised to withdraw voluntarily if his grades dropped below A. They never did. Through exercise, Good rehabilitated himself to the point where he has only a slight limp to show for his illness. He generally wears ankle-high sneakers, which he finds more comfortable than shoes, around the lab. His preference for another Good sartorial trademark—a turtleneck sweater instead of a shirt and tie—is purely personal. Says he: "I've never been convinced that a necktie has any real function except to get in the way."

**Toughness.** Good's interest in immunology dates from a chance discovery during medical school. Lacking enough fresh, uninfected rabbits for some research he was conducting, he used some animals he had infected with herpes viruses in an earlier experiment. His experiment, designed to elicit an allergic reaction, instead depressed the animals' immune systems, which had kept the viruses under control. As a result, the viruses became active and the rabbits developed encephalitis. The results so intrigued Good that he combined studies in biology with his medical education and received his Ph.D. and M.D. degrees together in 1947.

Convinced that good research starts at the bedside rather than in the laboratory, Good opted for pediatrics because it would give him an opportunity to study immune system defects, which are most often found in children (victims usually die of disease well before adulthood). "Besides," says Good, who admits that he has been tempered by his own battle with disease, "I like kids. They're tough."

So is Good, who combines painstaking laboratory work with gutsy speculations, or "probes," much in the manner of a medical Marshall McLuhan. On one occasion, while treating a patient whose inability to resist infection coincided with the growth of a massive thymic tumor, Good began to speculate about the link between the thymus and agammaglobulinemia, a disease caused

by a deficiency or lack of the major antibodies. He—together with others in his laboratories—conducted a series of experiments in which he removed the thymus from newborn rabbits. The results of the test—all of the animals failed to develop normal immune systems—led to recognition of the thymus' role in the development of immunity.

Another example of Good's intu-

itive flashes occurred while he was working with Dr. Henry Kunkel at New York's Rockefeller University in 1950. Good observed that patients with different types of tumors suffered from different types of infections. Those with Hodgkin's disease, a cancer of the lymphoid system, were particularly susceptible to TB, fungus and viral infections; those with multiple myelomas, or can-

## Defending Against Disease

*Man lives in a sea of microorganisms; the immune system is his license to survive.*

ROBERT GOOD's metaphor may be mixed, but it is apt. As a swimmer in an ocean of organisms, man must have a means of identifying and resisting the ones that can harm or kill him. The major mechanism that does this, and enables man to survive, is the immune system, designed by nature to quickly recognize, attack and destroy any foreign matter that enters the body. The system is complex and depends for its function on a wide variety of highly specialized substances. Its main agents are cells called lymphocytes, which are produced by the so-called "stem cells" of the bone marrow, the mushy, reddish substance that manufactures blood components. Once formed, the lymphocytes develop into two distinct types of cells, each of which plays an important role in the immune response. Those that pass through the thymus—a small organ located just under the breastbone in children (it shrinks and virtually disappears by puberty)—become T-cells, the main agents of what immunologists call "cell-mediated immunity." They are responsible for maintaining the body's biological uniqueness by rejecting foreign matter, including transplanted tissue and organs.

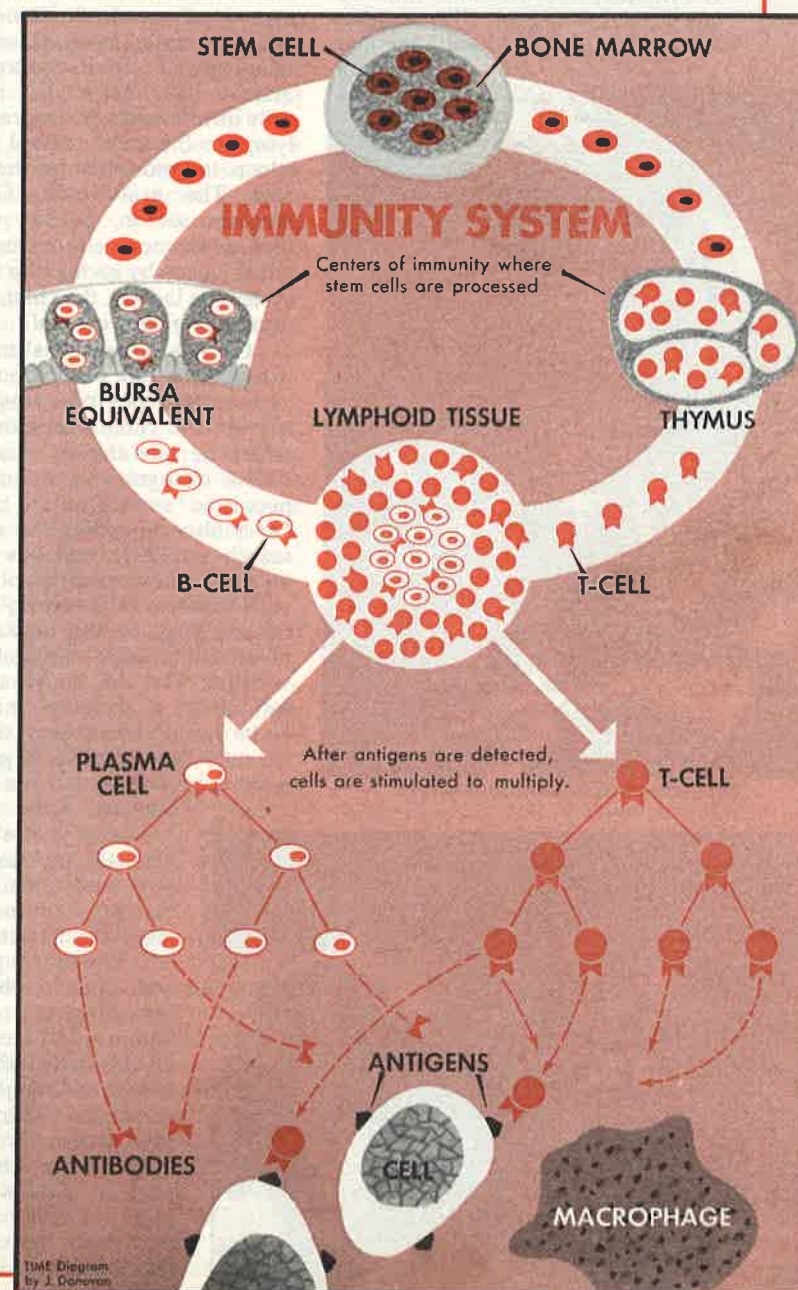
The other type of lymphocyte, the B-cell, undergoes differentiation, in chickens, at least, in an organ called the bursa of Fabricius. (Where that transformation takes place in man has not yet been positively determined, but it can be assumed that the human body contains an equivalent of the bursa.) B-cells are called the agents of humoral immunity because they synthesize antibodies that circulate freely in the blood. The antibodies, actually globular proteins, help the body resist disease-causing organisms. Both the B-cells and T-cells reside primarily in the body's lymphoid tissues, which are found under the arms, in the groin, behind the ear, in the abdominal cavity and other locations. From these tissues, the cells recirculate through the body and continually monitor for the presence of potential attackers.

When a foreign organism enters the body, the lymphocytes work like an internal anti-ballistic-missile system. Coming in contact with the invader, they recognize it by means of its biochemical flag, or identification marker. Every cell and microorganism is believed to carry at least one such flag on its surface; it fits, like a key in a lock, into a site on the lymphocytes. Thus lymphocytes, which know their body's own cells, recognize others as foreign and trigger an immunological alarm.

When the alarm is sounded, the immune system swings into action, sometimes dispatching both T- and B-cells, sometimes just one variety. T-cells multiply and attack; the foreigners are soon surrounded and isolated by rings of angry lymphocytes that cause inflammation and chemically destroy the invaders. The T-cells may also call up macrophages, large scavenger cells that literally devour and digest foreign cells.

B-cells, meanwhile, are stimulated to produce antibodies, which immunologists believe can be tailor-made to interact with each of the millions of different organisms a human may encounter in his lifetime. The antibodies lock onto foreign substances, making them far more susceptible to ingestion by macrophages and other scavenger cells.

Once an antibody has locked onto an invading cell, it can interact with a series of blood proteins called "complement," which aids in destroying the invader and makes it even more attractive to scavenger cells. By one or a combination of these actions, the intruder is broken down into chemical components that are recycled by the body or excreted as waste.





## MEDICINE

cers of the bone marrow, were vulnerable to such bacterial infections as streptococcus and pneumococcus. Subsequent observation and experiments at the University of Minnesota convinced Good that there were not one but two basic immune responses. One, controlled by the thymus, was responsible for delayed hypersensitivity, or certain types of allergic responses, and the rejection of foreign tissue. The other, involving blood-borne antibodies, helped the body to battle bacterial invaders.

Presented by Good and his group in the mid-'60s, the "two component" theory became the foundation of modern immunology, and led to new experiments and ways to understand the phenomenon of immune response. It also led to another of Good's contributions—the first successful use of bone-marrow transplants to correct immunodeficiency disease.

Doctors had experimented with bone-marrow transplants in the mid-'50s, primarily to combat leukemia. But their efforts proved generally unsuccessful. Immunologically sound bone mar-

row contained cells that recognized the recipient of this gift as "foreign." The new cells, in a phenomenon known as "graft v. host" reaction, thus rejected the host, producing lymphocytes capable of reacting with and destroying his tissue. In fact, the reaction, combined with infection and other factors, could prove fatal to the recipient whose immune system was either weak or absent.

**Legacy.** Good tried a different approach with five-month-old David Camp, who was suffering from hereditary immunodeficiency disease, which had already killed twelve infants on the maternal side of his family. Thinking back to work that he himself had done in 1956, Good remembered that mice given bone marrow from donors whose cells were genetically similar suffered from graft-v.-host reaction but never died from it. He reasoned that David, too, would survive if a good tissue match could be found.

Luckily, the infant had four sisters; one of them had cells similar to his. Using a local anesthetic, Good's team inserted a needle into the bone of the sister's leg and withdrew about a billion marrow cells. Then, they injected the cells into David's peritoneal cavity, relying on the cells' natural homing instincts to guide them to the bone marrow. The graft took. Graft-v.-host reaction set in, peaked and finally passed. The new cells overcame David's lethal legacy by giving him the immune system he lacked; the child, now five, is immunologically normal.

Good's accomplishments have made him a folk hero at home in Minnesota. He hopes to be equally productive at the Sloan-Kettering Institute, where he has already made administrative changes and, as one associate puts it, is "stirring up the reservation." He is also expanding the scope of research at S.K.I., and has taken over an entire floor that he plans to staff with the best immunology researchers he can find at the institute or woo away from other hospitals and universities. The lab, he says, will study just about everything immunological—the immunodeficiency diseases that he calls "spontaneous experiments of nature"; allergies; and the relationship between aging and cancer.

Good's most ambitious undertaking, however, will be a study that could make cancer immunotherapy a more exact science. At present, attempts to administer and evaluate the relatively new form of treatment are hampered by medicine's lack of knowledge about the full nature and range of immune response. "What we need," says Good, "is a workable system by which we can determine what is normal immunologically, a yardstick by which we can measure and evaluate immune re-

sponse." To arrive at that system, Good plans to run tests on every patient, employee and staff physician at S.K.I. and Memorial Sloan-Kettering Cancer Center, recording the various blood components, allergic reactions and response to common disease agents.

The result of such a study, involving thousands of people, says Good, will be a complete profile of the immune response, and a set of guidelines for those attempting to manipulate it to fight disease. "We know we've got a hell of a weapon in immunotherapy," says Good. "This study will help us write the instruction manual so that we can use this weapon effectively."

An early riser who can honestly echo Ernest Hemingway's claim to have seen the sun rise every day of his life, Good is usually up by 4 and at his desk by 5 a.m. (he generally retires by 11 p.m.). He freely confesses to being a "work addict," and concedes that his addiction may have contributed to the breakup of his first marriage. The marriage, by which Good has four children, ended in divorce in 1965. (He was remarried in 1967 to Joanne Finstad, a phylogeneticist—a specialist in evolutionary relationships—who worked with him in Minnesota.)

**Theory.** An ardent advocate of unhampered creativity, Good encourages his students and colleagues to try a wide variety of approaches in their search for answers. "Hypotheses," he tells them, "are instruments. It doesn't matter if they are right or wrong as long as they stimulate thought." Thus, he reasons, no one need feel chagrined when his pet theory is shot down. "Right now, our theories are widely accepted," says he, "but I'm sure that some young bastard will come along and make us mad as hell with some intellectual leap that postulates a completely new theory. Whether he's right or wrong doesn't matter. Just trying to find out if he is or isn't should force us to think, to examine, to do new experiments. That's what science is—or should be—all about."

Good has detractors. Some find him too ambitious for their taste, viewing him as a scientific Sammy Glick who occasionally lets his ego get in the way of his intellect. "He uses the pronoun we a bit too freely," says one immunologist who feels that Good has taken credit for work done by members of his team. "He has a terrible ego drive and occasionally forgets what other people do," says another, who is admittedly annoyed by Good and jealous of his ability to attract research funds and keep his name before the public.

But even Good's severest critics acknowledge his accomplishments. "I'll forgive Good any excess," says a colleague and sometime competitor, "because he's such an enormous stimulator of ideas. Even his bad papers have been well conceived." Most agree and credit Good with being able to recognize an error and abandon it faster than anyone else in medical research. "Good

never gets married to his hypotheses, so he doesn't go through the pangs of divorce when one is proved wrong," says a Minnesota associate. "He learns from everything and everyone."

Good, who often acts as if he is running for the Nobel Prize, does not deny their charges. "Of course I'm an operator," he admits. "I'm the most self-centered person in the world. I'll use whatever there is to get things done the way I want them done." At S.K.I., he says, "I hope I can be an effective operator when it comes to cancer."

There is a good chance that he will be. Most researchers believe that the time is ripe for major discoveries in cancer research. Cancer, they believe, could be the first major killer to be controlled by immunological engineering.

Immunology has already led to the control of many serious illnesses. Immunological research resulted in the development of vaccines against polio, once a majorcrippler of children, and rubella, or German measles, which can cause serious birth defects in the children of women who contract it while pregnant. It has led to a broader understanding of allergies and an effective method of preventing erythroblastosis fetalis, a blood condition that can prove fatal to infants shortly after birth.

**Hope for Lepers.** Doctors can now use "transfer factor," a substance first isolated from the white cells of blood by New York University's Dr. H. Sherwood Lawrence in 1948, to transfer specific immune responses from a normal individual to another who has an immune system deficiency.

Drs. Martin Schulkind and Elia Ayoub of the College of Medicine of the University of Florida have used transfer factor to treat effectively chronic mucocutaneous candidiasis, a severe fungal infection of the skin and mucous membranes; others have used it successfully to treat agammaglobulinemia and Wiskott-Aldrich syndrome, a hereditary defect that leaves its victims unable to resist certain infections.

Immunology has even provided hope to victims of leprosy, one of man's oldest and most dreaded diseases. Last month, Dr. Soo Duk Lim of Seoul National University, Korea, told an international workshop on immunodeficiency diseases at St. Petersburg, Fla., that he has used immunotherapy successfully on 14 patients with lepromatous leprosy, the most severe form of the disease. Lim, who worked closely with Good's Minnesota group, infused the patients with large doses of white cells from unmatched donors weekly for periods of up to 16 weeks, in an attempt to stimulate an immune response against the bacillus responsible for the disease. The treatment, used on patients who had failed to respond to other therapy, helped in all cases, switching on idling immune systems. All patients are now disease free, and one has been so for a year and a half.



GOOD IN OFFICE

In addition to these dramatic results, doctors now know more than ever before about what happens in such autoimmune diseases as rheumatoid arthritis and systemic lupus erythematosus, in which the immune system goes haywire, recognizes certain of the body's own tissues as foreign, and destroys them. They can also treat these illnesses with drugs that suppress the immune system, relieving the symptoms at the risk of leaving the body open to infection. But they have yet to learn the exact causes, let alone the cures for these diseases, which affect more than 5.5 million Americans.

There are other major mysteries to be solved in immunology. No one, for example, has figured out how to overcome completely the phenomenon of tissue rejection that plagues transplant surgery. Serum that inhibits the production and action of lymphocytes, the cells responsible for rejection, may cause severe reactions; immunosuppression, which is now the mainstay of transplant surgery, reduces the body's ability to resist both infection and some cancer.

Research is now going forward to find the answers to these questions. Dr. William Hardy, an S.K.I. veterinarian, is conducting research in animal leukemias that could lead to better understanding of the disease in man. Dr. Philip Paterson and his colleagues at Northwestern University Medical School are trying to identify the viruses they believe are responsible for autoimmune diseases and develop specific agents to combat them. Scientists are seeking to improve existing techniques of tissue typing to facilitate transplants.

A former Minnesota researcher, meanwhile, has made a discovery that may well make tissue typing unnecessary. Dr. William Summerlin, now at S.K.I., has found that when skin is kept in tissue culture for several weeks, its antigens are somehow lost. As a result, the immune system of the patient can no longer recognize the donor's skin as foreign. The skin can then be grafted onto any patient without being rejected. Summerlin's work, which is still exper-



GETTING TO KNOW HIS PATIENTS



LECTURING ON IMMUNOLOGY  
An affable operator.

imental, could eventually eliminate both the rejection problem and the need to match donor and recipient, enabling transplant surgeons to make wider use of organs taken from cadavers.

No one appreciates this potential more than Good, who sees immunology as the key to understanding—and ultimately controlling—almost all diseases that afflict man. "Understanding the immune system will enable us to do far more than treat allergies or immunodeficiency diseases, or to control cancer," says Good. "It will enable us to understand the basic processes of life." Good will not predict when this millennium will occur; immunologists are still groping for answers to questions that have puzzled scientists for centuries. But there is little doubt that they are groping in the right direction.



SURGEONS TRANSPLANTING KIDNEY



IMMUNODEFICIENT BABY IN GERM-FREE TENT