LEWIS THOMAS 1913-1993

A Biographical Memoir by GERALD WEISSMANN

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LEWIS THOMAS

November 25, 1913–December 3, 1993

BY GERALD WEISSMANN

The LIFE OF LEWIS THOMAS spanned a golden age of American medicine, an era when, in his words, "our oldest art became the youngest science." Thomas played a major role in that transformation; he was known among scientists as an innovative immunologist, pathologist, and medical educator. He became known to the wider public as a deft writer whose essays bridged the two cultures by turning the news of natural science into serious literature. Witty, urbane, and skeptical, he may have been the only member of the National Academy of Sciences to win both a National Book Award and an Albert Lasker Award. He is certainly the only medical school dean whose name survives on professorships at Harvard and Cornell, a prize at Rockefeller University, a laboratory at Princeton, and on a book (*The Lives of a Cell*) that is eleventh on the Modern Library's list of the best 100 non-fiction books of the century.

Thomas made several important discoveries in the field in which he was a pioneer, immunopathology. He found that neutrophils were important mediators of fever and shock brought about by bacterial endotoxins or antigen/antibody reactions; these launch cascades of limited proteolysis in the blood. Therefore, if animals are depleted of neutrophils or given heparin they are protected against tissue injury

as in the Arthus reaction or Shwartzman phenomenon. He made the dramatic observation that intravenous papain causes collapse of rabbit ear cartilage; similar damage results when excess of vitamin A induces host cells to release endogenous proteases. The search for endogenous, papain-like ferments pointed to neutrophils, complement, and immune complexes as the culprits in rheumatoid arthritis. With Philip Y. Paterson he contributed to our understanding of acute allergic encephalomyelitis, and he teamed up with H. Sherwood Lawrence and John David to define soluble mediators of delayed hypersensitivity: the first inklings of what we now call "cytokines." A prescient suggestion, published only in conference proceedings years before the HIV pandemic, was that our immune system constantly surveys our body to find and destroy aberrant cancer-prone cells; we now attribute Kaposi's sarcoma and other AIDS-related tumors to defects in Thomas's "immune surveillance." Those discoveries resulted from a very intense period of bench research (1946-1964) at Johns Hopkins, Tulane, Minnesota, and NYU before he turned his attention to broader issues of medical education and to his writing.

THE EDUCATION OF LEWIS THOMAS

Lewis Thomas grew up as a bright lad in a loving family in a comfortable house in Flushing, Queens. His father, Dr. Joseph Simon Thomas (Princeton, 1899; Columbia P&S, 1904), was a good-natured, hard-working doctor who had met and married the love of his life, Grace Emma Peck of Beacon Falls, Connecticut, at Roosevelt Hospital, where she was a nurse and he was an intern. They were married in New York City on the 30th of October in 1906, and thereafter, in the words of her son, Emma Peck's nursing skills were "devoted almost exclusively to the family."

Lewis Thomas was born on November 25, 1913. As were

his three older sisters and younger brother, Lewis was sent to the local schools. But soon the family decided that Flushing High School was not quite ready to prep another Thomas for Princeton. After three semesters in Queens, Lewis Thomas transferred to the McBurney School, a less than exclusive prep school in Manhattan. He graduated in 1929 in the top quarter of his class. Medical practice was to protect the Thomas family against the worst of the Great Depression, which began on Black Tuesday, exactly one month after 15-year-old Lewis left for Princeton in September 1929.

At Princeton he "turned into a moult of dullness and laziness, average or below in the courses requiring real work." He took little interest in physics or inorganic chemistry and dismissed athletics as a general waste of effort. By reason of youth and family standing, he ranked low in the eating club hierarchy of prewar Princeton and was grateful to find safe haven at Key and Seal, a club that was literally the furthest out on Prospect Avenue. But high spirits and natural wit brought him to the offices of the Princeton Tiger, where Thomas soon published satires, poems, and parodies under the nom de plume of ELTIE. "After the crash of '29, we were in thrall to Michael Arlen; we slouched around in Oxford bags and drank bootleg gin from the tub like Scott and Zelda," Thomas recalled. "They told us we'd go out like a light from that stuff. Out like a light. I think I did a piece on bootleg gin for the Tiger about that." He had: it's unreadable. Then on one winter weekend visit to Vassar in 1932, Lewis Thomas met a young freshman from Forest Hills. Her father was a diplomat, her name was Beryl Dawson, and after years of separation for one or another reason they were married a decade later. By then the moult had spread its wings.

Years later his editor, Elisabeth Sifton, asked me, "When was it that Thomas became so wise?" Thomas attributed his metamorphosis to his senior year at Princeton and a biology course with Professor Wilbur Swingle. Swingle's discovery of a life-saving adrenal cortical extract—a crude version of deoxycorticosterone—had won wide acclaim. Thomas recalled that Swingle sparked his lifelong interest in the adrenals. Swingle also introduced him to Jacques Loeb's literary/ philosophical speculations on ions and cell "irritability" in *The Mechanistic Conception of Life* (1916). Five years out of Princeton, young Thomas would sign up to work with Jacques Loeb's son.

In his senior year the Depression hit home and Thomas knew that getting into medical school was one solution to the unemployment problem. He also confessed he had a leg up on other applicants: "I got into Harvard . . . by luck and also, I suspect, by pull. Hans Zinsser, the professor of bacteriology, had interned with my father at Roosevelt and had admired my mother, and when I went to Boston to be interviewed in the winter of 1933 [Zinsser] informed me that my father and mother were good friends of his, and if I wanted to come to Harvard he would try to help."

Help he did and Thomas entered Harvard at the age of 19 in the fall of 1933. Thomas's career at the Harvard Medical School turned out just fine; he received grades far better than at Princeton. When asked in 1983 which member of the Harvard faculty had the greatest influence on his medical education, Thomas replied, "I no longer grope for a name on that distinguished roster. What I remember now, from this distance, is the influence of my classmates." Nevertheless, some on that roster made a lasting impression. Hans Zinsser in bacteriology showed that it was possible to function both as a laboratory scientist and a respected writer; Walter B. Cannon in physiology taught him that the details of homeostasis held the keys to "*The Wisdom of the Body*"; David Rioch in neuroanatomy had him build a wire and plasticene model of the brain, which Thomas trekked about for 15 years; and in Tracy Mallory's office Lewis Thomas came across a pickled specimen that "like King Charles's head" would haunt his investigative career for decades to come.

At one of Mallory's weekly pathology seminars in the depths of Massachusetts General Hospital, Thomas leaned back in his chair and by accident knocked over a sealed glass jar containing the kidneys of a woman who had died of eclampsia. Replacing the jug, he noted that both organs were symmetrically scarred by the deep, black, telltale marks of bilateral renal cortical necrosis. Thomas remembered having seen something like those pockmarked kidneys before. They had been provoked in rabbits by two appropriately spaced intravenous injections of endotoxin: It was called the generalized Shwartzman phenomenon, and he would tussle with it for the rest of scientific career.

Thomas graduated cum laude from the Harvard Medical School in 1937 and began an internship at the Harvard Medical Service of the Boston City Hospital. A history of the Harvard Medical Unit at Boston City Hospital documents that of the 71 young physicians who trained there between 1936 and 1940, 52 became professors of medicine, while 6 went on to the deanships of medical schools. Thomas waxed eloquent on those days: "I am remembering the internship through a haze of time, cluttered by all sorts of memories of other jobs, but I haven't got it wrong nor am I romanticizing the experience. It was, simply, the best of times."

He remained at Boston City until 1939, when the confluence of his interests in neurology, adrenal hormones, and the Loeb mystique brought him to New York. Halfway through his internship in Boston, Thomas heard that Dr. Robert F. Loeb was becoming director of the Neurological Institute in New York and resolved to study with him because "Loeb was a youngish and already famous member of the medical faculty in the Department of Medicine at P&S, recognized internationally for his work on Addison's disease [and] the metabolic functions of the adrenal cortex and the new field of salt and water control in physiology."

He served as a neurology resident (his only specialty training) and research fellow at P&S from 1939 to 1941, with time out to marry Beryl at Grace Church in New York in January 1941. Robert Loeb abruptly moved to the chairmanship of medicine, but Thomas found that there was a fellowship with John Dingle awaiting him back at the Thorndike and jumped at the chance.

Almost as soon Lew and Beryl had established themselves back in Boston, Thomas was sent by Dingle on a month-long medical mission to Halifax, where an outbreak of meningococcal meningitis had struck the wartime port. Beryl served as lab assistant. Those four weeks in the field, a publication of the effects of sulfadiazine in meningitis, and a thorough analysis of the prozone phenomenon in Dingle's lab were a prelude to a naval commission after Pearl Harbor. Thomas reported in March 1942 to the Naval Research Unit at the Hospital of the Rockefeller Institute and on January 12, 1945, landed with a detachment of that unit headquartered on Guam. Thomas and Horace Hodes were put to work on Japanese B encephalitis on Okinawa and quickly identified horse blood as a reservoir for the virus.

At war's end, August 1945, Thomas was left with no further official tasks. The unit had unused research equipment, an ample supply of laboratory animals, culture media, and stock microbes. So Thomas went to work on a problem of major interest to him and the Navy, the pathogenesis of rheumatic fever. He tried to reproduce rheumatic myocarditis by injecting rabbits with streptococci plus or minus groundup heart tissue. These experiments continued until he was demobilized in January 1946 and led directly to his most stunning observation.

LEWIS THOMAS THE SCIENTIST

Most scientists have one discovery that is dearest to their heart; for Thomas it was the use of the floppy-eared rabbits. He first put it all together in 1955 on the fifth floor of the Medical Science Building of New York University. As NYU's new professor of pathology, Lewis Thomas (age 42) pulled an albino rabbit out of the cage, turned to the group of second-year medical students perched on stools around the bench, and asked them, "Notice anything?"

They didn't, immediately. "It's a healthy bunny, if that's what you mean," one of students volunteered.

The professor smiled in reply, "You know, I didn't notice anything either when I first did this a few years ago. But last night, I gave this little fellow some papain by vein. Let's sit him next to one that hasn't been injected with papain. Here. Look."

He pulled out another rabbit. "Here's the control." Finally, he reached for the third. "And here's another rabbit I also injected with papain."

The students looked at the two papain bunnies side by side with the control. Now came the burst of recognition.

"Of course. Gosh! The papain bunnies' ears are droopy!"

"I'll be darned. They look like dachshunds!"

"No, spaniels."

"What is papain?"

"What made you inject the animals with papain?"

"Is it cartilage that's wilting?"

Lewis Thomas did his best to answer the questions. He'd done this many times before and it happened like clockwork. Sure, the rabbits will be fine. In a day or so the droopy ears will become erect again. Three days later, you won't be able to tell the papain bunnies from the controls. No. He's found no other ill effects of any kind in rabbits given papain. He has looked at sections of ears from the injected animals for days on end under the microscope and found nothing of interest. Nothing. Papain? It's a proteolytic enzyme from the papaya plant. A protease best known as a meat tenderizer. Only cartilage? He didn't know. He guessed that cartilage is a "quiet, inactive tissue." But why inject rabbits with papain in the first place? Well, he told the students, it's a long story, but it's still the most reproducible phenomenon he's ever seen in the lab. He told them that he "couldn't really explain what the hell was going on." But the students' questions led to him to the answer. "I was in irons on my other experiments. I was not being brilliant on my other problems. . . . Well, this time I did what I didn't do before. I simultaneously cut sections of the ears of the rabbits after I'd given them papain and sections of normal ears. This is the part of the story I'm most ashamed of. It still makes me writhe to think of it."¹

He didn't know what the hell was going on because he hadn't done the controls! Doing it right took quite an effort. Two hundred and fifty rabbits were sacrificed, hundreds of sections were taken, but in the end the differences under the microscope were clear and striking. Although sections from the ears of papain-treated rabbits showed perfectly normal cells, the basophilic, metachromatic matrix between cells seemed to have melted away. But papain had no effect on the cells themselves and there was no evidence of cellular infiltration. Thomas correctly deduced that the dramatic ear droop was a direct attack by papain on cartilage matrix, "the chondroitin sulfate or component to which it is bound."

On the morning after the rabbits had received papain, most of the matrix had been leached out. Happily, when the ears snapped back to normal in a few days, the bluestaining material was back in force. Thomas figured out that cartilage, far from being a dead or inert tissue, could survive a withering attack and make new matrix by the earful. Thomas immediately understood the implications of this finding. Perhaps, he reasoned, tissue injury in general was due to the uncontrolled release of the body's own papainlike proteases, whether released from cells of the tissue itself or from white cells escaping from the circulation. He was ready to go to press. In 1956 the work appeared in the *Journal of Experimental Medicine,* and its opening lines became an instant classic of scientific description.

For reasons not relevant to the present discussion rabbits were injected intravenously with a solution of crude papain, and the following reactions occurred with unfailing regularity: Within 4 hours after injection, both ears were observed to be curled over at their tips. After 18 hours they had lost all of their normal rigidity and were collapsed limply at either side of the head, rather like the ears of spaniels. After 3 or 4 days, the ears became straightened and erect again. . . . Apart from the unusual cosmetic effect, the animals exhibited no evidences of systemic illness or discomfiture, and continued to move about after the fashion of normal animals of the species.

Thomas also noted that cortisone, given after papain, kept the animals' ears limp: strong proof that cortisone inhibited resynthesis of what we now call "proteoglycans." When cortisone inhibits the synthesis of proteoglycans and/ or collagen in humans, osteoporosis results. Thomas's rabbits taught us why.

The "unusual cosmetic effect" was pictured in newspapers countrywide: "An accidental sidelight of one research project had the startling effect of wilting the ears of rabbits," wrote the *New York Times.* The droopy-eared rabbits became a Picture of the Week in *Life* magazine and reporters flocked to NYU wanting to know what the research project was that these bunnies were the sidelight of. Why was that research "not relevant to the present discussion?" Why papain? The papain story began at Guam. Thomas found that rabbits receiving a mixture of streptococci and heart tissue became ill and died within two weeks; histologic sections of their hearts showed lesions that frankly resembled the myocarditis of rheumatic fever. Control rabbits injected with streptococci alone or with heart tissue alone remained healthy and showed no cardiac lesions. Thomas was entirely confident that he had solved the whole problem of rheumatic fever. He hadn't. On his return to the Rockefeller Institute in New York, he couldn't repeat those experiments, sacrificing "hundreds of rabbits, varying the dose of streptococci and heart tissue in every way possible." He was vastly relieved that he hadn't rushed into print on the basis of those rabbits on Guam.

Thomas's first faculty position after discharge from the Navy in 1946 was as an assistant professor of pediatrics at the Harriet Lane Home for Invalid Children of Johns Hopkins. Thomas tried once more to repeat those rabbit experiments, mixing streptococci and heart tissue with Freund's adjuvants. Bad news for Assistant Professor Thomas: The rheumatic fever experiments failed once again. But Thomas could not shake off those experiments that had worked so well on Guam. Perhaps the host—the rabbits in Guam, for example, but not those in New York or Baltimore had been "prepared" by an earlier insult as by that endotoxin prep in the Shwartzman phenomenon.

He tackled the problem with Chandler ("Al") Stetson, a lifelong friend who was to become his colleague in Minnesota and his successor as the professor of pathology at NYU. Thomas and Stetson "prepared" rabbits with endotoxin from meningococci. The prepared skin had an excess of lactic acid, and they reasoned that lactic acid might activate tissue proteases, the cathepsins. But they were neither able to measure cathepsin activity nor obtain purified cathepsins, so they injected rabbits with off-the-shelf trypsin or papain from papaya pulp. Trypsin was ineffective, but papain produced lesions in the skin that looked very much like the local Shwartzman reaction.

When Thomas left Hopkins, he took the problem with him. He served a brief stint at Tulane, where he became a professor of medicine and the director of the Division of Infectious Disease. He was diverted for a while by studies of humoral antibodies in allergic encephalomyelitis but returned to rheumatic fever when he was appointed as American Legion Professor of Pediatrics and Medicine at the University of Minnesota in 1951. In quick time he put together a team of young investigators, most of whom were soon at work on the Shwartzman phenomenon and the streptococcus: Robert Good, Floyd Denny, Lewis Wannamaker, Richard Smith, and Joel Brunson. Al Stetson came on board as well.

He reverted to the notion that proteases, either secreted by the streptococcus or released from the victims' own cells, caused damage in a "prepared" heart or joint. With a young Minnesota pediatrician, Robert A. Good ("the smartest investigator I ever met," he once told me), he found out that if one removed white cells from the Shwartzman equation (e.g., by nitrogen mustard), kidney injury would be prevented. The kidneys were also spared if one gave heparin, which prevented blood vessels from becoming plugged by fibrin, platelets, and white cells. Good and Thomas suggested that "a combination of humoral and cellular factors made by the host caused the tissue injury." Nowadays we invoke anaphylatoxins, Toll receptors, signal transduction, apoptosis, caspases, and cytokines to explain the Shwartzman phenomenon. But in the 1950s Good and Thomas had provided a satisfactory explanation and the flow of satisfying, explanatory papers followed Thomas from Minnesota as he moved to NYU in 1954.

Thomas was recruited to NYU by Colin McLeod to become professor and chairman of the Department of Pathology. He was delighted to return to the metropolis with Beryl and his three daughters, Abigail (b. 1941), Judith (b. 1944), and Elizabeth (b. 1948), and to set up his household at Sneden's Landing, a small town up the Hudson from the city. He remained at NYU for 15 years and proceeded to turn it into a world center of immunology, first in pathology (1954-1958), then as professor and chairman of the Department of Medicine at NYU-Bellevue Medical Center; director of III and IV medical divisions, Bellevue Hospital (1958-1966); and finally as dean of the New York University School of Medicine and deputy director of NYU Medical Center (1966-1969). Over those years he attracted and/or trained a legion of scientific stars and superstars at NYU: Frederick Becker, Baruj Benacerraf, John David, Edward Franklin, Emil Gottschlich, Howard Green, H. Sherwood Lawrence, Robert T. McCluskey, Peter Miescher, Victor and Ruth Nussenzweig, Zoltan Ovary, Jeanette Thorbecke, Stuart Schlossman, Chandler Stetson, Jonathan Uhr, and Dorothea Zucker-Franklin. Thomas's international colleagues were frequent visitors: Sir Macfarlane Burnett, Dame Honor Fell, Philip Gell, James Gowans, Sir Peter Medawar, Thomas Sterzl, and Guy Voisin.

Early on in his NYU days Thomas hit a rough patch. Whereas cortisone, the miracle drug, clearly stopped inflammation in the clinic, Thomas was astonished to find that cortisone not only proved ineffective against the Shwartzman phenomenon but also actually provoked it. This puzzle took the wind out of his sails. He was indeed "in irons on his other experiments" and "not being brilliant." Then came the floppy-eared bunnies, as he later explained: "I was able to justify working on so seemingly frivolous a problem by the possibility that one might figure out how cortisone might work. But, I was obliged to confess, despite this, that the work had been done because it was amusing."

After papain, new discoveries proceeded apace. If an exogenous protease caused connective tissue damage, where might endogenous proteases reside? Thomas spent a summer with Dame Honor Fell, director of the Strangeways Research Laboratory in Cambridge. Fell had been studying vitamin A and had found that it produced depletion of cartilage matrix in mouse bone rudiments growing in a dish. Fell and Thomas decided to trade experimental systems. They first added papain to the little bone cultures in the dish and were able to produce vitamin A-like lesions in mouse cartilage. Thomas then returned to NYU to do the reciprocal experiment. With Jack Potter and R. T McCluskey, Thomas and I stoked rabbits full of vitamin A and sure enough: twenty-four to forty-eight hours later, their ears drooped as if they had been given papain. We were convinced then that Vitamin A in some fashion released an endogenous papain-like enzyme from cartilage cells and that this enzyme proceeded to break down the extracellular matrix. At the time we supposed that the enzyme was present in lysosomes, recently described by Christian de Duve. We suggested that vitamin A had ruptured the walls around these organelles, and that cortisone and its analogues must therefore stabilize the lysosomes.

These days the answer is more complicated. Nowadays we believe that metalloproteinases are released from cells and that synthesis of these proteases is under opposing transcriptional control by vitamin A and cortisone acting via well-defined cytoplasmic and nuclear receptors. Cortisol receptors recognize palindromes of DNA, vitamin A receptors see tandem response elements of DNA, there are at least two types of glucocorticoid receptors, these antagonize fos/jun transcription factors, and so on and so on in abundant detail. It all seemed simpler a generation ago. But these experiments, the last in which Thomas played a handson role, pointed the way for Thomas's students and their students to elucidate the roles of anaphylatoxins in neutrophil activation, of oxygen-derived free radicals in tissue injury, of lymphokines (now cytokines) such as MIF and IL-1 in cartilage catabolism, of glucocorticoid action in inflammation via NFkB, and, as a follow-up of the cortisone/lysosome experiments, the description and clinical development of liposomes.

LEWIS THOMAS THE STATESMAN

Thomas had a broad interest in how medical science shapes, and is shaped by, society. Wit, candor, and attention to principle rather than politics made him a valuable spokesman for medical science. While still at NYU, Thomas served as a member of the New York City Board of Health (1957-1969), was instrumental in the construction of the new Bellevue Hospital, and set up the Health Research Council, a sort of local National Institutes of Health. As chairman of the Narcotics Advisory Committee of the New York City Health Research Council, he guided Vincent P. Dole into methadone research and pointed Eric Simon to endorphins (1961-1963). After a stint in New Haven as a professor of pathology and dean (1969-1973) at Yale University School of Medicine, he became president and chief executive officer of the Memorial Sloan-Kettering Cancer Research Center (1973-1980). At MSK he launched a major attack on tumor immunology, recruiting Robert Good as director; Thomas became chancellor of MSK from 1980 to 1983. In retirement, his summer home in the Hamptons made a University Professorship at SUNY-Stony Brook (in 1984) convenient; his Manhattan apartment let him serve as writer in residence at the Cornell University Medical School.

His honors were legion. Lewis Thomas was a member of the National Academy of Sciences, the American Academy and Institute of Arts and Letters, and the American Academy of Arts and Sciences. He served as a Phi Beta Kappa scholar at Harvard, won the Woodrow Wilson Award at Princeton, an award in literature from the American Academy and Institute of Arts and Letters, and the National Book Award in 1973. He was president of the New York Academy of Sciences, received the Kober Medal of the Association of American Physicians, the Britannica Award from the encyclopedia itself, and a Lasker Award for Public Service to Science. His last accolade, before a stoic death of macroglobulinemia, was the first Lewis Thomas Prize from Rockefeller University, "honoring the scientist as poet."

LEWIS THOMAS THE WRITER

Thomas was for several decades the most widely read interlocutor between the older literary culture and the new world of medical science, preceded in this role by such other American physician-writers as Oliver Wendell Holmes, William James, Walter B. Cannon, and Hans Zinsser. Thomas's literary career began modestly enough in 1970 as the result of an after-dinner speech for an inflammation symposium at Brook Lodge. After the usual fawning tribute from the chairman, Lew mounted the podium, murmured, "Thank you, I think," and proceeded to knock the somnolent inflammation boffins out of their seats. Accustomed to the passive voice of dreary fact, they heard instead Thomas making more sense of inflammation in 50 minutes of elegant prose than had prolix lecturers on endotoxin or macrophages in the preceding 16 hours. The talk was printed; someone brought it to the attention of Franz Ingelfinger, editor of the New England Journal of Medicine; and Thomas began his career as author of the bimonthly "Notes of a Biology Watcher." Thanks to Elisabeth Sifton, then an editor at Viking Press, those marvelous essays were soon collected into *Lives of a Cell;* the volume became a best seller and won a National Book Award—and the rest is history. Here, for example, is Thomas's suggestion for signals we might send from Earth to announce ourselves to whatever life there might be in outer space.

Perhaps the safest thing to do at the outset, if technology permits, is to send music. This language may be the best we have for explaining what we are like to others in space, with least ambiguity. I would vote for Bach, all of Bach, streamed out into space, over and over again. We would be bragging, of course, but it is surely excusable for us to put the best possible face on at the beginning of such an acquaintance. We can tell the harder truths later.

That sort of writing was the product of a unique period in American culture. Thomas and his colleagues were educated in colleges at which the liberal arts were still firmly in place, and John Dewey's learning by doing had moved from primary schools into the universities. It was an era when those who did medical science were expected to make only modest claims for their success. "I was lucky," Thomas quipped after he received a gold medal at Bologna in 1978. "Chance favored the prepared grind." He believed that one could do serious work without taking oneself too seriously.

Thomas's chosen means of expression was the informal essay, a literary form that accommodates many topics but always has the mind of its author as the subject. Thomas was as likely in print as on the wards to pair epiphany (à la James Joyce) with entropy (à la the second law of thermodynamics, or $\Delta S > q/T$). In Thomas's prose, epiphany seemed to be having it out with entropy on every page. He would point out that the *Oxford English Dictionary* defines grammar as a body of statements of fact, a science if you will. But a larger portion of grammar spells out the *rules* of practice

and therefore ought to be considered an "art." Thomas was convinced that medicine was like grammar, a hybrid of science and art united by syntax.

He was sparing of words when fewer spoke louder. When he received that last award at Rockefeller University, he was confined to a wheelchair. He declined to go to the podium and apologized to the audience for "not rising to the occasion." About the same time, I had reached him on the telephone. "How are you doing?" I asked. He knew what I was asking.

"So," he replied.

"What do you mean by 'so'?"

"Well," said Thomas, "in my family, there were only three ways of answering that question of yours. If things were going along splendidly, you'd answer 'fine.' If there were a bit of trouble around, you'd say 'so-so.' Right now, I'm 'so.'"

When more words were required, they flowed like wine. Thomas understood the very human need to turn the strands of fact into a fabric of belief. Fact marched hand in hand with solace; he assured us that a meningococcus with the bad luck to catch a human was in more trouble than a human who catches a meningococcus. His years in the lab served him well on the page. His sense of trial and error at the bench and in the clinic, of how cells divide, microbes hurt, and creatures die gave an edge to his writing.

When injected into the bloodstream, endotoxin conveys propaganda, announcing that typhoid bacilli (or other related bacteria) are on the scene and a number of defense mechanisms are automatically switched on, all at once, including fever, malaise, hemorrhage, shock, coma, and death. It is something like an explosion in a munitions factory.

Prose of this rough measure supports the argument that Lewis Thomas has a shot at permanence in the world of letters. A number of his compositions stand up to essays by such other modern masters of the genre as E. B. White,

BIOGRAPHICAL MEMOIRS

A. J. Liebling, and John Updike. In a select few Thomas reaches back to touch the mantle of Montaigne.

NOTE

1. B. Barber and R. Fox. The case of the floppy-eared rabbits: An instance of serendipity gained and serendipity lost. *Am. J. Sociol.* 64(1958):128-136.

ALL OTHER quotations by Lewis Thomas and other biographic details are taken from his memoir *The Youngest Science* (1983). They are also based on personal notes, as well as interviews with George Mirick, H. S. Lawrence, Beryl Thomas, and material generously forwarded by Baruj Benacerraf, P. Y Patterson, Jonathan Uhr, Paul Marks, and others.

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