THE BULLETIN

Mount Desert Island Biological Laboratory



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THE MOUNT DESERT ISLAND BIOLOGICAL LABORATORY

SERVING HUMANITY THROUGH RESEARCH AND TEACHING IN MARINE BIOMEDICINE

INTRODUCTION

The Mount Desert Island Biological Laboratory (MDIBL) is an independent non-profit biological station. It is located on the north shore of Mount Desert Island, overlooking the Gulf of Maine about 120 miles northeast of Portland near the mouth of the Bay of Fundy. The island, well known for Acadia National Park, provides a variety of habitats including shallow and deep saltwater, a broad intertidal zone, saltwater and freshwater marshes, freshwater lakes and streams, forests and meadows.

The Laboratory is the largest cold water research facility in the Eastern United States, and its unique site provides an outstanding environment for studying the physiology of marine and freshwater flora and fauna. During 1993, the scientific personnel included 50 principal investigators, 17 associates and 56 assistants/technicians, representing 62 institutions in 29 states and 3 European countries.

HISTORY AND ORGANIZATION

MDIBL was founded in 1898 at South Harpswell, Maine by J.S. Kingsley of Tufts University. Its present site at Salsbury Cove was donated by the Wild Gardens of Acadia and relocation was completed in 1921. The Wild Gardens of Acadia, a land-holding group headed by George B. Dorr and John D. Rockefeller, Jr., was instrumental in the founding of Acadia National Park.

The Laboratory was incorporated in 1914 under the laws of the State of Maine as a non-profit scientific and educational institution. Founded as a teaching laboratory, MDIBL is now a center for marine biomedical research and teaching that attracts investigators and students from across the U.S. and around the world. Since the pioneering work of H.W. Smith, E.K. Marshall, and Roy P. Forster on various aspects of renal and osmoregulatory physiology of local fauna, the Laboratory has become known worldwide as a center for investigations in electrolyte and transport physiology, developmental biology and electrophysiology.

The Mount Desert Island Biological Laboratory is owned and operated by the Board of Trustees and Members of the Corporation; at present, there are 444 members. Officers of the Corporation - Chair, Vice-Chair, Director, Secretary, Treasurer, Clerk - and an Executive Committee are elected from among the Trustees. The Chair and Executive Committee oversee the general administration and long range goals of the Laboratory. The Director, with the aid of a full-time Administrative Director and staff, is responsible for implementing the scientific, educational and public service activities of the Laboratory.

NIEHS TOXICOLOGY CENTER

In 1985, with the support of the National Institute of Environmental Health Sciences (NIEHS), MDIBL established a center dedicated to the study of the toxic effects of heavy metals and other environmental pollutants that pose an increasing health risk to humans and a threat to the marine environment. The focus of The Center for Membrane Toxicity Studies (CMTS), is the use of marine animals like the shark, the flounder and the skate to define sites of action for metals such as mercury and cadmium that enter the environment due to improper disposal of industrial waste and as a component of some pesticides. The effects of these pollutants are wide-spread in the human body, with affected organs including the brain, the kidney, the liver, the gastrointestinal tract and the reproductive system. The goal of the CMTS is to identify the molecular targets for toxic substances and to provide the scientific basis for the development of treatments for heavy-metal intoxication. Inquiries concerning the center are welcome.

APPLICATIONS & FELLOWSHIPS

Research space is available for the entire summer season (June 1 - September 30) or a half-season (June 1 - July 31 or August 1 - September 30). Applications for the coming summer must be submitted by February 1st each year. Investigators are invited to use the year-round facilities at other times of the year, but such plans should include prior consultation with the MDIBL Office concerning available facilities and specimen supply.

A number of fellowships and scholarships are available to research scientists, undergraduate faculty and students, as well as high school students. These funds may be used to cover the cost of laboratory rent, housing and supplies. Stipends are granted with many of the student awards. Applications for fellowships for the coming summer research period are generally due in January.

For further information on applications and fellowships/scholarships, please contact:

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The Mount Desert Island Biological Laboratory is indebted to the National Science Foundation and National Institutes of Health for substantial support. Funds for building renovations and new construction permitted the Laboratory to expand and upgrade its research and teaching facilities. Individual research projects served by the Laboratory are funded by private and government agencies, and all of these projects have benefited from the NSF and NIH grants to the Laboratory. For supporting our educational initiative, MDIBL acknowledges the Lucille P. Markey Charitable Trust, Pew Charitable Trusts, Burroughs Wellcome Fund, Hearst Foundation, Grass Foundation, Milbury Fellowship Fund, American Heart Association - Maine Affiliate, State of Maine EPSCoR funds, Mr. Robert E. Blum and the Maine Community Foundation.

AN HISTORICAL ACCOUNT OF THE MOUNT DESERT ISLAND BIOLOGICAL LABORATORY: 1898-1993

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As we approach the 100th year of this Laboratory, it seems appropriate to put forth a short history, particularly for the younger people and all those who aspire to that definition. There are rich lodes of material, some not readily accessible except in the main office of the Laboratory. I have drawn on accounts by the following and these are documented in the bibliography: Mary Frances Williams and Max Morse (Harpswell days), E. K. Marshall, Roy P. Forster, J. Wendell Burger, Bodil Schmidt-Nielsen, Marty McManus and, most importantly, THE BULLETINS available from 1921 to the present.

My introduction to MDIBL was by Homer Smith. He had encountered a problem close to my own research: why sea-going fish did not have a renal response to a carbonic anhydrase inhibitor while all other vertebrates (except <u>Crocodilia</u>) respond with typical HCO_3^- diuresis. I made a preliminary solution to the problem and have been here for the ensuing 40 years. I had a double affiliation to the Laboratory since a major part of my training was in the Pharmacology Department of E. K. Marshall at The Johns Hopkins School of Medicine. Thus I grew up with the remarkable advantage of twin loyalties and friendships to these heroic figures of our past.

This essay is divided into seven segments covering in each case some 10 to 20 years and attempting to give, in addition to the social and academic picture, a brief but necessarily superficial account of the types of research done through these many decades. My account of our first 60 years inevitably has perspectives lacking in the recent history. In the earlier time this institution was the shadow of a few great men; now there are many players and their lasting influence is not always clear. I hope that some future historian will record in more critical detail the manifold accomplishments in all of these times.

I. Beginnings, Harpswell Laboratory, 1898 - 1921

This Laboratory was founded by John Sterling Kingsley (Fig. 1), a professor of biology at Tufts who visualized in the small town of South Harpswell, Maine, a summer school for undergraduates in biology at Tufts and elsewhere, and also a research laboratory. He was a man of remarkably affable character and fine scholarship and to some degree the Harpswell Laboratory was a reflection of his personality. He was born in 1854 in upper New York State, graduated from Williams College in 1875, and acquired an Sc.D. degree from Princeton in 1885. He went to Tufts in 1892. At South Harpswell which was a few miles from Bowdoin College and one and one half hours by boat from Portland, he built the small laboratory that you see in the background of Fig. 2, and in Fig. 3 a characteristic picture of Kingsley gathering specimens on the beach. He also built a small cottage for himself near the Laboratory, and for many years served as director, business manager, host for scientific visitors, and editor of many of the journal articles destined for publication. As he put it, "This biological station is one of the most unpretentious structures one could imagine as readily will be understood when it is said that the whole plant---land, building and permanent equipment--cost within one thousand dollars."

The permanent equipment was two rowboats, assorted dredges, abundant glassware, several microscopes and a nucleus of a library on morphology and marine biology. There were no pumps, no running water, no electricity. Warmhearted Mrs. Kingsley hosted women scientists with the help of her daughter Mary. Social occasions comprised Dr. Kingsley and the

ladies of his family and staff who entertained guests in the Laboratory's big room which smelled of lemonade, cookies and formaldehyde (Fig. 4). There were no automobiles, and the local stable rented horse and buggy for those who wished to ride about or visit friends. Simplicity and congeniality abounded. Many of the families lived in tents. The shop talk was lively, especially with visiting scientists. Kingsley's personality welded the Laboratory together into a close and congenial community. His energy seemed inexhaustible as was his capacity for friendship. After some seven or eight years, however, they abandoned the teaching program, and the Harpswell Laboratory became entirely a research facility. Undergraduate instruction, he said, was a drawback to the investigators. Interestingly, this pattern was repeated many years later and several times after the move to Salsbury Cove.



Figure 1. John Sterling Kingsley. See text.

However, they were not isolated. A boat from Portland left every two hours, making libraries in Portland available, and equipment could readily be brought back every day. During the 23-year period a hundred papers were published. Most unfortunately, the abstracts of publications from the Harpswell Laboratory, which is Volume I in our own series, are missing (but the titles of papers have survived) so that our bibliography begins in Vol. II after the move to Salsbury Cove. Representative papers from Harpswell included the followcatalog of marine invertebrates of ing: Casco Bay, basic work on the anatomy of the skull in Squalus acanthias, morphology and development of eye muscles and nerves, essays on sexual plants, and most importantly, early pioneering work on the cleavage of eggs in Cerebratulus by the noted Japanese morphologist, Yatsu. Kingsley also wrote a widely-used textbook on the comparative anatomy of vertebrates.

At the end of World War I, matters changed at Harpswell. Kingsley departed to the west coast; Ulrich Dahlgren and Herbert V. Neal became the dominant figures who were to play vital roles in establishing the Laboratory at Salsbury Cove. Their lives will be briefly outlined now.

Dahlgren (Fig. 5), despite his foreign-sounding name, was a classic American patrician, an ancestor having fought with George Washington and a grandfather who served as an admiral in the Civil War who invented a gun which brought fame and money to the family. Dahlgren was born in Brooklyn in 1870 and entered Princeton in the autumn of 1890, graduating with the Class of 1894 and getting a master's degree in biology two years later. He never went on for the Ph.D. but stayed at Princeton as a stalwart of the Biology Department until his death in 1948. He was a biologist of the old type, interested in speciation and specimen collections. He came to Harpswell in about 1908, had a home there and published a classic text called <u>Principles of Animal Histology</u>, built up largely from his own observations. When Kingsley left the

Harpswell Laboratory in 1919, Dahlgren became Director and, as we shall see, was a vital engineer in the move to Salsbury Cove.



Figure 2. Harpswell Laboratories and living quarters.

The other moving spirit in those latter days at Harpswell and then Salsbury Cove was Herbert V. Neal. He was born in Lewiston, Maine, in 1869, the only native in our cast. He was graduated from Bates and in 1896 received Ph.D. from the Harvard where he began work on the vertebrate skull. After a year in Munich he went to Knox College in Illinois and stayed until 1913 when he moved to Tufts for the rest of his life;

there he was greatly admired as a teacher. His research was chiefly in embryology, particularly development of eye and head muscles and nerves, and the skull of elasmobranchs. He came to Harpswell early in its history and was Associate Director from 1908 - 1915. He was a prime factor in the move to Salsbury Cove, and the first building was named for him. He became Director in 1927. As described by Wendell Burger, "His wife, Helen, was an energetic Yankee, self rightaous

self-righteous. able, and considered herself the Oueen Mother of the Laboratory, as though she and Herbert had given it birth. As faculty without resources but with competitive aspirations, they were thrust into an environment of affluence." Their patroness, the wealthy and socially impeccable Louise de Koven Bowen, had helped to 70-acre buv the McCagg tract (the land east of the post office on both sides of the road and extending to the Bay) and stip-



Figure 3. Kingsley (right) collecting.

ulated that the house, barn and four acres of land (Bow-End) belong to the Neals for life and the Laboratory was to keep it up. Mrs. Bowen believed that professors (at least professor-directors)

should live in style; Neal had a car and chauffeur as well as a motor boat, appropriately named The Dahlgren. We shall never know what Ulrich thought of this.

In later years Neal(with H.W.Rand) published a famous text on Comparative Anatomy of the Vertebrates. To his own research he brought both scientific and artistic skills and questions of the place of man in nature. He died in 1940; Helen Neal lived on for many years in Bow-End, then in a nursing home in Bar Harbor. She kept keen interest in MDIBL and visits from younger scientists.



Figure 4. Interior view, Harpswell.



Figure 5. Ulrich Dahlgren. See text.

II. <u>The Move to Salsbury Cove and</u> Establishment There

A new major player now appears on the scene-George B. Dorr, a wealthy Boston aristocrat and bachelor who had been raised summers on Mount Desert Island. He devoted a large part of his life to the maintenance of the island in its natural state and the acquisition of land to protect it against the depredations of civilization. Importantly, he had the ear of John D. Rockefeller, of Charles William Elliot and virtually all of the distinguished summer inhabitants of the island which was flourishing as a resort for the rich and wellsocieties of New York. established Philadelphia, Boston and Washington. The record is not completely clear, but it is likely that it was Dorr's idea to move the Harpswell Laboratory to Mount Desert. In the name of his corporation, the Wild attractive land in Gardens of Acadia, Salsbury Cove was acquired, which he called the Weir Mitchell Station. This was named for his friend, the distinguished neurologist from Philadelphia who was practicing cures on the wealthy and neurotic elite women of his time by making them virtual prisoners in their homes while they

were forbidden to work or think. Mitchell had no connection to the Laboratory. At a meeting in Princeton in the Fall of 1920 with Dahlgren, Dorr and Henry Lane Eno (a long-term summer resident and philanthropist), the basis for a land transfer from the Wild Gardens of Acadia was laid down, and the so-called Weir Mitchell tract, 14 acres comprising the Leland house and the present dining room and surrounding area was leased for 99 years to the Laboratory. In 1949 this was changed to perpetual ownership after conference with Wendell Burger, E. K. Marshall and the remaining member of the Wild Gardens, S. Rodick.

In June 1921 the laboratory at Harpswell was packed up, loaded on a ship and the exodus took place (Fig. 6). The trip lasted 11 hours, and the Salsbury Cove site was established. From the sale of the laboratory at Harpswell, they were able to build a new one, to be called Neal, for some thousand dollars, which was a virtual replica of the one they left behind. (It is on this site that the shell was used to build a new laboratory in 1991.) Dahlgren was the first Director at Salsbury Cove. They wasted no time in



Figure 6. The Great Migration.

establishing in the summer of 1921 an extremely rigorous course in biology that lasted six

THE MOONT DESERT ISLAND BIG	LOGICAL LABORATO	RY	
Statement			
January lat to December	24th, (inc.) 19	25	
	••		
	1 Beceipte	1	Expenditures
Balance from 1924	1 587.31	1	
Contributions	1735.00		
Contributions to boat maintenance	100.00		
7001	t 250.00		
Dues	1 75.00		
Supplies	1 324.33		
Rent of tent	10.00		
Dining Hell	1 1303.44		
CADCAILED VOUCABLE NOS. 75 6 00	38.13		
Interest	1 10	- 1	
Net UDO		-	
		- i	
	i	i.	
		i.	
Mainistration	i		332.75
Laboratory Current			1017.43
Laboratory Equipment			148.73
Supply Department	1		849.90
Dining Hell			1423.38
Insurance			32.50
McCagg Trect			137.25
Library			100.00
Building Repairs	1	1	10.07
To lance	4853 77	:	4052 03
B&1 ence	1	÷	800.76
Total	4852.77	-	4852.77

Figure 7. Budget, 1925.

weeks, with students working every morning and afternoon collecting, dredging, listening to lectures on animal embryology and reproduction and physiology. Dahlgren loved to dredge. He ran the course with the assistance of Dr. J. L. Connel of New York University. Tents on the Laboratory grounds could be rented for two dollars a week, and board was furnished to all personnel, including students, for seven dollars a week. Examinations were given at the end and credit was obtained for college work. For the first few years the Laboratory was still called Harpswell, Weir Mitchell Station. The Harpswell designation was abandoned by 1924, but the "Mitchell Station" persisted well into the '30s. Figure 7 shows the economy of that time; Fig. 8 shows Neal Laboratory without the steps, the old photography shed (now Union Station) and, most importantly, the director's car.

In 1923 another player major appeared. William Proctor, who leased two additional parcels of land to the west of Wild the Gardens tract and built what is now known as the Forster Cottage and the Kidney Shed as his laboratory. He was an amateur collector and made substantial contributions to the Laboratory in the early days. There was continuing accumulation of land from the Rockefellers and other contributors such as Mrs.Maxfield,



Figure 8. Laboratory (Lewis), Darkroom and Director's car, 1928.

Wasgat and Mrs. Bowen. This is all documented in the manuscript of Dr. Wendell Burger.



Dr. Warren Lewis (Fig. 9) and his wife, Dr. Margaret Reed Lewis, were principal actors at Harpswell and were part of the move to Salsbury Cove. The Lewises were great pioneers in cell culture and made enormous contributions to the field. Other early investigators and contributors to the organization and politics of the Laboratory were Harold D. Senior, Professor of Anatomy at NYU, and Milton J. Greenman, Director, Wistar Insitute in Philadelphia. The trustees present at a critical meeting in 1927 were Mrs. Bowen, A. C. Bumpus, Dahlgren, Milton Greenman, Neal and Proctor. It was at this meeting that Proctor was defeated in a vote for president; thereupon he left the Laboratory in a rage and became an enemy for the rest of his life.

I shall now describe briefly the work of E. K. Marshall and of Homer Smith and their interrelations.

Eli Kennerly Marshall (Fig. 10, at age 64 with Bodil Schmidt-Nielsen at age 35) was born in Charleston, South Carolina,

Figure 9. Warren Lewis (1870-1964) and Margaret Reed Lewis (1881-1970). W.L., M.D., Johns Hopkins, 1900. Professor, Anatomy, Johns Hopkins. M.L., B.S. and D.Sc Goucher. Research Associate, Anatomy, Johns Hopkins. Picture taken in 1960, when they were still at work at the Wistar Institute.



Figure 10. E. K. Marshall (see text) and Bodil Schmidt-Nielsen in 1952. B.S-N., born Copenhagen, 1918. D.D.S., 1941, Ph.D. (Copenhagen) 1946. Professor, Biology, Case Western Reserve 1964-1971. MDIBL President 1982-1985.

in 1889 and grew up in that genteel city in classic southern tradition. He attended the small excellent private Charleston College where there were eight in his graduating class, and was the only he chemist. His professor suggested that he go to Johns Hopkins for graduate work, and so at the age of 19, this shy, inexperiuntravelled enced, young man went to Baltimore. After several years of an excellent life, socially and scientifically, he received the Ph.D. in Chemistry in 1912. He went for a brief

time to Abderhalden's laboratory in Germany where he accomplished little, but quite on his own got the idea for the determination of urea using urease. Upon returning to Baltimore, he applied to the Department of Biochemistry at The Johns Hopkins Medical School. However, the professor, Jones, assured Marshall that there was nothing more to be done in biochemistry and suggested some other occupation. Marshall walked upstairs where he found the professor of pharmacology, John J. Abel, already a world-class figure. Abel gave him the opposite advice from Jones, said he would take him into the department with one small condition, that Marshall attend medical school. This came about, and Marshall received the M.D. from Hopkins in 1917. Meanwhile, he had made a major strike, discovering a quantitative method for the determination of urea using the enzyme urease. He became a captain in the Medical Corps in 1917 stationed in Washington, and there he discovered one night working in a lonely back room on some chemical experiments another shy, skinny young man named Smith enlisted from Cripple Creek, in Colorado where he had been selling vacuum cleaners. The two became friends, and Marshall vowed that when the war was over, he would see that Homer Smith got an advanced degree, possibly in medicine, from Johns Hopkins. Somehow this did not work out, and instead Smith got the Sc.D. from the Hopkins School of Hygiene and Public Health. We shall return to his story in a moment. At the end of the war Marshall, virtually just out of medical school, was appointed Chairman of the Pharmacology Department at Washington University in Saint Louis. He stayed there only two years and returned to Hopkins in 1921 as Professor of Physiology and began work on the vitally important issue of active transport of dyes and other substances by the kidney. In 1923 he discovered that phenol red was actively secreted by the mammalian kidney. It was the first clear demonstration of active transport in any organ and was opposed by essentially all the leaders in the field, particularly Cushny in Edinburgh and Richards at the University of Pennsylvania. He was undaunted by all of this. He did not belong to the fraternity of renal physiologists anyway, and he was never one to walk away from a good fight.

In 1925, reading the literature he discovered aglomerular fish and, after conversations with his friend Alan Chesney (later to become dean of the medical school at Hopkins and a summer visitor to Maine), Marshall decided to come to Mount Desert Island in search of aglomerular fish, notably, the goosefish (Fig. 11). He came in 1926 with a student, Allen Grafflin, and with his wife participated in the rough and ready living conditions at the Laboratory. They had bad luck with obtaining live goosefish, but he returned in 1927 with Grafflin



and did the crucial experiments showing renal excretion in the complete absence of glomeruli which, in addition to his impeccable work on the mammalian kidney. made it certain that urine could be formed by tubular secretion as well as glomerular filtration. A finding of the greatest importance was that the aglomerular fish did not excrete glucose, i.e. it was not handled by the tubules. This led to the development of xylose and inulin as the markers

Figure 11. The aglomerular goosefish, Lophius piscatorius.

for glomerular filtration rate, in the hands of Smith, Shannon and the NYU school. Marshall's great contributions in this decade were reviewed in <u>Physiological Reviews</u> in 1934. At MDIBL in 1926, to his surprise, he once again found Homer Smith who had been a Fellow at Harvard and was now studying the diffusion of acids and bases into arbacia eggs and their effect on cell division. Alas, it is not clear what brought Smith to MDIBL.

Marshall and Smith were very different personalities, and perhaps it is not surprising that they did not become more intimate. Marshall was rather austere, reserved, had fairly limited interests, did not delve very much into literature or music or art and had no taste for outdoor sports. His great strength was original and imaginative investigation. He was totally honest, outspoken and selectively profane. He had the old-fashioned habit of addressing colleagues of all ages by their last names; at least he did in Baltimore. In Maine he was considerably more relaxed and did use first names in addressing us.

Smith, on the other hand, had universal interests in music, literature, theology as well as science. His books Komongo and Man and His Gods were required reading for new arrivals at the Laboratory. Marshall brought few students here and only worked at the Laboratory from about 1927 to 1934. Smith, however, had a major stake in the Laboratory and occupied the Kidney Shed for some 30 years, extending well into the '60s. He brought dozens of young men and a few women, mostly physicians, into his laboratory where he had a profound effect on their future lives. Three of them are shown with Smith in Fig. 12. Another is Stanley Bradley who became Chairman of Medicine at Columbia. Smith's major work was the magisterial monograph, The Kidney (1951), singly written and encompassing the entire world literature. There have been few books in the history of science with this scope and critical acumen.

Although Marshall's home in Salsbury Cove was chiefly for vacation after 1934 when he succeeded Abel as Chairman of Pharmacology at Hopkins, he still exerted tremendous influence in the Laboratory by visiting the young people at work and pointing out to them that much of what they were doing had been in the literature for several decades. Marshall's particular favorite was Roy Forster of whom we shall speak later. Roy had once introduced Marshall with a line from Carlyle, "Genius is the transcendental capacity for taking trouble," which he emended to fit Marshall, "... for making trouble."

It must have been Marshall who got Smith interested in the kidney, although there are no extant records on that point. But by 1928 Smith was interested in water equilibrium in various fish and published a very important paper on the body electrolytes in elasmobranchs. In 1930 he and Marshall collaborated on а monograph. (Biol. Bulletin. 1930) in which they related the evolution of vertebrates to the evolution of the kidney in fish, that presumably arose in fresh water. There the glomerulus was needed as a filter; fish then migrated to the sea where the glomerulus became either lost or degenerated. This theory had very wide appeal. The power of Smith's reasoning, his grasp of biology, evolution and paleontology and masterful prose is best



Figure 12. On dock, 1953. Right to left: Homer Smith (see text), Henry Heinemann, Julius Cohen, Al Fishman.

seen in his 1932 paper in <u>Quarterly Review of Physiology</u>. His strength in thinking and exposition appears in the "perfect matching between the large and small scales of his subject" (see Homer Smith Dedicatory issue of <u>THE BULLETIN</u>, Supplement, Vol. 28). Smith used the Laboratory for war research in 1942, and when work was reestablished, he resumed high activity, becoming president from 1950 - 1960. Smith established musicales, dances, expeditions around the island and was generally interested in younger people, speaking readily to all of us, particularly those who had sense enough to penetrate a rather rough facade. He became Chairman of Physiology at New York University in 1928, where he remained until his death in 1962. The brief partnership of Marshall and Smith in those years in Maine (they lived but 200 yards apart) was admirable scientifically; Marshall handled secretion, Smith water balance.

Returning to the state of the Laboratory in this decade, it was certainly thriving on an unpretentious scale and low budget. Dahlgren was Director from 1921 to 1926 and President from 1937 to 1946. He had contact with the wealthy and influential visitors to the island and instituted weekly seminars by distinguished professors, many from Harvard. In this era some 43 papers were published on plant and invertebrate biology, still with an emphasis on morphology. These are listed in the 1929 announcement. There was only one paper on the kidney, that of Marshall reporting the discovery of aglomerular function in the goosefish. The most prolific workers in this period were Warren and Margaret Lewis, already mentioned as pioneers in cell culture, who developed time-lapse photography showing previously unappreciated aspects of cell division.

Unfortunately, there are no abstracts in Vol. II (1921 - 1930). In this period there was an attempt to publish Communications of the Laboratory (1926 and 1927), but this proved expensive and difficult. In its place, and beginning with Vol. III (1931 - 1950) the present system of annual abstracts was adopted. The budget for each of the years, 1925 and 1926, was about five

thousand dollars. Some of these details are seen in Fig. 7. By the end of this decade, in addition to the Neal Building, the Kidney Shed, which was originally Proctor's collecting station, was activated as the laboratory of Marshall and Smith, and a bit later the Lewis, Halsey and Hegner laboratories were built. There was a small director's office, dark room and our crowning disgrace in disorganization and age, the tool shed. On the Old Route 3 was the Emery House Dining Room and the old schoolhouse, now the lecture and meeting room, Dahlgren Hall. All of this was unchanged until the early '70s.

III. <u>1931 - 1952</u>

There are <u>BULLETINS</u> for the years 1931 to 1941 with no further publication until 1950. The 1950 number, the last of Vol. III (12 numbers), summarizes the work between 1942 and 1949. The 1950 <u>BULLETIN</u> contains the all-important bibliography of the Laboratory for the period 1929 to 1949. Vol. IV, No. 1, gives abstracts for 1950, 1951, 1952.

The 1950 <u>BULLETIN</u> lists 217 papers (including abstracts) of which 69 (30%) are concerned with kidney, heart and electrolytes. Of these, two thirds came from the heavy hitters, Forster, Marshall-Grafflin, Smith-Shannon. Although MDIBL was gaining a formidable reputation in the renal field, the large majority of workers—about 20 senior investigators in 1946 - 1950 (the same as in 1930)—were in other fields. These include invertebrate behavior, ecology, anatomy, cell culture, growth of cancer cells, reproduction. Philip White, Lankenau Hospital, Philadelphia, in these years had an important research and teaching program in tissue culture, housed in the Hegner laboratory. He was the first to grow cells (plant) in wholly synthetic media.

THE BULLETIN for 1950 reflects only dimly the heroic and successful efforts of Dr. Roy to restore the Laboratory after its neglect during the war years when the dock was blown away, the buildings somewhat damaged and no funds were available for reconstruction. A remarkably lucid account, however, is given in a pamphlet dated 1946, of the war years, reconstruction, plans for the future, and gentle appeals for money. Due in part to the friendship of Mr. Amory Thorndike who had roots in Maine on both sides of his family and who was now a year-round resident, Roy was put in touch with influential people on the eastern seaboard who contributed to the rebuilding of the Laboratory. Dahlgren was succeeded as president by Dwight Minnich from 1946 - 1950. During all this time Roy Forster was Director.

The bibliography for these 20 years shows work on renal and cardiac function in fish. We see the beginning of attention to isolated tubules in various species, continued work by Marshall in the relation between glomerular and aglomerular fish, Robert Pitts' careful analysis of phosphate excretion in fish, and further comparative studies by Smith and his group among the elasmobranchs, teleosts and seals. A major theme was the methodology for measuring glomerular filtration rate here and at home (for the Smith group at NYU). The Lewises continued to be fabulously productive with work on cell culture, the growth of cancer cells in vitro. Marshall left his long shadow in the Laboratory in the person of Allen Grafflin, who contributed greatly to the knowledge of the fish anatomy and electrolyte excretion.

A main player during the '30s was James A. Shannon (Fig. 13), later to become most notable as the first director of the National Institutes of Health and in large part responsible for the growth of this unique and marvelous organization. Shannon was a protege of Smith, and the record shows some 10 papers on the renal excretion of metabolites and markers in the teleost and elasmobranch fishes, some by himself and some in association with Smith. Roy Forster tells the story about his own introduction to Shannon and to MDIBL. In 1936, Roy was completing his thesis at the University of Wisconsin when Shannon came to Chicago to lecture at the Federation. Roy found, to his chagrin, that Shannon had done virtually all of the experiments he had done or was planning, and he approached the visitor after the lecture wanting some conversation. Shannon suggested that he could talk better back in the hotel room fortified with some whiskey, and so the 25-year old graduate student and the young assistant professor from New York spent the rest of the evening swapping anecdotes about phosphate secretion, whereupon Shannon suggested that Roy come to Maine the following summer and work in his laboratory. Roy had never been East, but he took the risk, and arrived at Salsbury Cove, came down to the Kidney Shed where Shannon was washing glassware, and he pitched in a hand. A few minutes later a vigorous-appearing man came in the laboratory, and Shannon said, "I want you to meet Dr. Homer Smith." Roy thought it was a joke, but a few minutes later another man, a rather dark saturnine young fellow, came in and Shannon said, "Roy, I want you to meet Dr. Robert Pitts." Roy was finally beginning to catch on when a few minutes later a tall austere man walked in and Shannon said, "Roy, I want you to meet Dr. E. K. Marshall." Roy was certain that it all was a dream and that he had ascended finally into a renal heaven.



Figure 13. James Shannon (1904 -), M.D., Ph.D., NYU. Professor NYU and the Rockefeller Institute. Director, NIH 1952-1968.

Forster's engaging personality and impeccable scientific tastes were important assets when he was made Director a few years later and piloted the Laboratory through the evil days of World War II and its later recovery. A little-known chapter in MDIBL history is the "plague of the red feed" in herring in 1939 - 1940 and Forster's brilliant analysis of its cause. For the only time in its history, MDIBL was engaged by the Maine State Fisheries to investigate the red tide in local sea waters and the destructive skin and organ lesions in the fish. Forster, with no experience or training in mycology, working with two medical students, found that these were separate events: the color was a food metabolite in the intestine, the organ lesions were due to parasitic fungus. His work drew great praise from professors of mycology and the herring industry; I wonder if they knew they were dealing with a talented amateur.

Roy went to Dartmouth in 1938, where he has been ever since. His great love and genius was teaching, and he was honored many times by his college. Virtually all of his research was done at MDIBL, where he was the pioneer, among other things, in <u>in</u> <u>vitro</u> techniques for study of metabolism in renal tissue and their transport properties (Fig. 14). He had major influence on dozens of young people here. As Humphrey Davy

called Michael Faraday, "my major discovery," Roy could have said (and perhaps did say) the same of Leon Goldstein who has given admirable scientific and administrative leadership here for 37 years.

The Laboratory was open in 1941, but only a modest amount of work was done. No <u>BULLETIN</u> appeared for this year (which would have been 1942 issue), but the titles of work are recorded in the 1950 <u>BULLETIN</u>, pages 15-16. In 1942 the Laboratory was leased to New York University for pharmacologic study of mustard gases, under Homer Smith and David Karnofsky (1950 <u>BULLETIN</u>, page 17). The Laboratory was closed in 1943 and 1944; in 1945 Director

Forster was in residence, perhaps alone, working on diuresis in aglomerular fish and planning for the future.



(Fig. 15), Professor of Biology at Trinity College (Connecticut) succeeded Roy as director in 1947 and Smith became President in 1950. By that time Marshall had retired from work at MDIBL but continued summers here until his death in 1966. His research in Baltimore was very compelling. As he had done many times before, he abandoned research that the drove him to Maine which was so and productive, for an en-

Wendell

Burger

Figure 14. Roy Forster (right) ready for deep-sea fishing, circa 1960. See text.

different type of work, first in the chemotherapy of bacterial diseases, then in World War II on malaria, later on on drugs that affected the endocrine system, and finally on the pharmacology of alcohol. I have written elsewhere a biography of the life of this remarkably productive and interesting man (see Bibliography).

The 1953 BULLETIN covering the years 1950 -1952 contains but 22 abstracts, some quite long, reflecting to three two summers' work. Thirteen (59%)were on renalcardiovascular topics. Inspection of these, particularly the 1952 section, shows that indeed things were heating up to what Forster called the "summer mecca of the kidney world." Figure shows 16 the during Laboratory this period (and the next 20 years). Figure 17 gives the seminar program for 1952, showing the remarkable richness of the current science.



Figure 15. J. Wendell Burger (1910-1987). A.B. Haverford, Ph.D., Princeton. Professor of Biology, Trinity College, 1936-1975.

IV. <u>1953 - 1961</u>

My family and I arrived in the middle of the night on July 20, 1953. Early the next morning there was a knock on the door, and there was Homer Smith, whom I had only seen once before, carrying in one arm his little son Houdi and in the other arm a bundle of wood, which he proceeded to put in our fireplace and start the fire for us on that cold, but now very friendly,

morning. I was then working at the American Cyanamid Company in Stamford, Connecticut, where we were developing the carbonic anhydrase inhibitors. The company had generously given me one week to come to Maine which. added to my two weeks vacation, gave me a little time to work with Smith. Henry Heinemann, Al Fishman and Jurg Hodler where we showed the absence of carbonic anhydrase in elasmobranch kidney. I was regarded with some suspicion because I was an outsider in academia.



Figure 16. MDIBL aerial view, 1952.

working then in industry. But there was some aura of respectability from my five years with Marshall at Hopkins, where I also received my medical training. In that era the Laboratory had one telephone in the dining room and one in the secretary's office. The entire secretarial staff was Sally Murdaugh who worked half time. The other employee was Nelson Mitchell, the

> Reymond Represent. "Uptake of Water During Development of Amphibing Tissues"

> Margaret H D Smath, "Some Bacteria which are Pathogenic to both Animals and Plants"

> William D. Blahn. "Neural Control of Ranal Functions in the Dog".

> John V. Yaggart "Some Aspects of the Energetics of Transport".

Solomon A. Keplan. "Control of Renal Excretion Solutes by the Autonomic Nervous System".

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redoubtable Mainer who was at home at sea (but could not swim) and land and did every chore with equal skill and cheerfulness, including his annual ritual of kissing all the Laboratory wives when they returned in June. The total budget had then increased to fourteen thousand dollars.

Work on the kidney had continued, on acidification and transport with Smith and Forster as leading spirits. Also studied were the uptake of drugs and methods for measuring glomerular filtration rate. Most importantly, two major discoveries were made this decade, the nasal salt gland in birds (1956) by Knut Schmidt-Nielsen (Fig. 18) and the rectal gland in the intestine of elasmobranchs by Wendell Burger in 1959 (Fig. 15). Smith's agreeable habit of inviting new people to the Laboratory to work on key problems resulted in the bringing of Knut and Bodil Schmidt-Nielsen here as well as John Boylan to work on a basic problem of why urea, a readily diffusible small molecule, was locked into the shark and impermeable at the gill. Smith was as interested in structure as in function and brought Johannes Rhodin, of the new breed of electron microscopists, to MDIBL.

Smith and Marshall, despite their many intellectual differences, had in common a very strong background and orientation in chemistry, and this lent a precision and attitudes toward the physiological work that had far-reaching consequences.



Figure 18. Knut Schmidt-Niclsen (left) (1915-). Born Norway. Ph.D. Copenhagen 1946. Professor of Zoology, Duke 1952-

The Laboratory developed over the years the most important tradition of bringing students (undergraduates through postdoctoral fellows) who stayed or later returned to become senior investigators and leaders of MDIBL. These include R. Rappaport, L. Goldstein, J. Claiborne, G. Conrad, G. Kormanik, D. Miller, E. Swenson, K. Karnaky, R. Solomon, J. Forrest.

A significant generation of talent was made by John Boylan, from his keen interest in German physiology. After World War II there was a remarkable growth of German renal research sparked by Kurt Kramer and Karl Ullrich, close friends of Boylan. This resulted in visits or work at MDIBL by these and younger colleagues, all to become leaders in the field: P. Deetjen, H. Stolte, E. Frömter, R. Greger, S. Silbernagl, R. Kinne, E. Kinne-Saffran. The Kinnes have become permanent, with a great influence scientifically and administratively.

During these years there was an admirable selection of directors, Warner Sheldon from 1950 - 1956, Alvin Rieck from 1958 - 1963. As President, succeeding Smith, in 1960 was Marshall, and then Forster from 1964 - 1970. William Doyle, a noted anatomist and electron microscopist had an important influence on policy, Director 1954 - 1967 and President 1970 - 1975.

Most investigators came for the entire summer. The split season was virtually unknown. The tradition of bringing students, both medical and graduate, came into prominence. The group at the dining hall was cheerful and companionable. Lifelong friends and sometime marriages were made. There were important annual traditions such as the trip to Mount Katahdin, the band concert and dance on the streets of Salsbury Cove early in August and Sunday baseball. The tradition began of having the children of laboratory workers act as technicians and assistants. The four parts of Vol. IV (1953, 1956, 1959 and 1962), with their attractive layout, photographs, descriptive material, histories, and seminar schedules, tell the tale of those halcyon days. From 1930 - 1951 (excluding war years) the investigations numbered 20 - 30. In 1954 - 1961 it jumps to about 45; most significantly the number of students grew from about five to 23 in this period.

Vol. IV, Part 4 (dated 1962) reflects an explosion of activity in the years 1959, 1960 and 1961. There were 115 abstracts; half were concerned with some aspect of renal, cardiac or transport function. Eleven of these (!) came from the fertile mind, hands and pen of Eugene D. Robin, a talented pulmonary physician-scientist from the University of Pittsburgh, utilizing not only dogfish but seals, turtles and tunicates.

V. <u>1962 - 1973</u> Vol. 5 (2 parts) - Vol. 13. The Year-Round Programs

The work and spirit described in the previous section continued through the '60s. The Robin group, now including H. V. Murdaugh, continued to be active and imaginative in studies of metabolic and acid-base chemistry. Forster and new colleagues Leon Goldstein and Fred Berglund studied nitrogen metabolism in teleost and elasmobranch. Interest continued high in the avian nasal salt gland. In these years Dr. Franklin Epstein studied the relation of activity and inhibition of Na⁺K⁺ATPase to salt transport in the euryhaline eel. He then went on (with Patricio Silva, Richard Solomon and peripatetic groups largely from Harvard) to establish a comprehensive program on the physiology and biochemistry of rectal gland secretion in the dogfish, using largely <u>in vitro</u> techniques. Electrolyte and drug transport in the alkaline gland, gill, aqueous humor, cerebrospinal fluid and brain was studied in the elasmobranch by the writer and his students. Investigators used many species: seals, turtles, sculpin, goosefish (Fig. 11), dogfish, flounder, eel and killifish. Chemical work came into more prominence; an exotic finding was the bromination of aniline derivatives by the dogfish uterus, analogous to the ancient discovery of Tyrian purple in sea animals.

Charles Wilde, a distinguished chemical embryologist, was a leader in Laboratory affairs, Director 1967 - 1970 and President 1978 - 1979. David Rall (later to become director of the National Institute of Environmental Health) and his colleagues pioneered studies of the isolated choroid plexus, distribution of drugs, and fluid compartments in brain. Dr. David Karnofsky, a world leader in cancer research, used sand dollar embryos to study mechanisms of anti-tumor activity of metabolite antagonists used in chemotherapy. Adrian Hogben took advantage of the absence of transmucosal potential differences in dogfish stomach (unlike the mammal) to study relation between electrical activity and H⁺ and Cl⁻ secretion. This is one of many examples throughout, of the virtues of comparative physiology, in elucidating general mechanisms.

1971 brought a radical change, the "winter operation". Two of the country's leading physiologists in summer residence at MDIBL for many years and both connected to the transport field (in different ways) decided to work year-round: Bodil Schmidt-Nielsen and William B. Kinter. Fortunately, the Karnofsky laboratory had been so well built that it could be used in winter; later Marshall was built to be a year-round facility. Including two or three young Ph.D.s and assistants, there were 10 in the group: they are listed in THE BULLETIN as a separate entity starting in 1975. Research seminars were held through the year at Bowen, in front of a blazing fire and with proper internal warming. The 1978-80 BULLETINS (Vol. 18 - 20) gives a good account: visitors came not only from the Jackson Laboratory, but from Harvard, Bowdoin, Brown and far away Georgia and Stanford. Kinter's first work was on uptake and transport of dyes, reflecting earlier work with Forster, but he then turned to ecology and environmental problems, particularly the effect of oils on sea-bird and teleost physiology. His most able associate was David Miller. Schmidt-Nielsen and her group studied ion and fluid fluxes in elasmobranch and eel, including the urinary bladder of the skate. They showed that the kidney of euryhaline eel, in fresh water, secreted water. In these different species they measured for the first time intracellular ion concentrations. They studied the structure and function of the renal pelvis in several species, showing how its movement "milked" the collecting duct.

Kinter died at a tragically young age (52) in October 1978; his group gradually dissipated. Bodil continued until she retired in 1986. In 1982-85 she was active and effective as President of the Laboratory, beginning a new sense of awareness and participation from the community. The winter program brought much needed overhead to the Laboratory. When it disappeared in 1984, the advent of the toxicology program brought a new source of support. Winter work was resumed in 1989 by a single but most important scientist, Raymond Rappaport, who began in MDIBL in 1948 and built a world-class reputation in studies of the physical mechanism of cell division in animals. He had been Director and President and, now retired from Union College, works year round at MDIBL.

Although much fewer than the renal and transport scientists, those in developmental biology (P. White, R. Rappaport, C. Wilde) were a notable intellectual force; the latter two were prominent in Laboratory affairs. It may be argued that the "transporters" did not sufficiently appreciate the implications of the findings in cell biology.

VI. <u>1974 - 1983 (Vol. 14 - 23)</u>

During this period the Laboratory continued with new emphasis on brain and CSF in the work of Helen Cserr. There was keen interest also in the electrophysiology of the intestinal tract (M. Field, R. Frizzell, G. Kidder), gill (K. Karnaky, J. Zadunaisky), and heart of the "sea potato" (M. Morad). The rectal gland continued in a leading role. Cell volume regulation was imaginatively explored by Arnost Kleinzeller. The gill and red cell transport of carbon dioxide and its role in formation of various body fluids were pursued by Erik Swenson and the writer.

Volume 20 (covering 1980) is illustrative of the vitality at that time. Surprisingly, 27 years after Watson and Crick, there was still no genetics. There were about 110 people on the site, 38 ipal investigators, the rest students or technicians. The fashion continued of having atory "children" as assistants. At least five marriages resulted from this mix. Six or seven families left at least one child to live permanently in Maine. These hostages are now raising their own families. The summer season closed with a poster session and demonstrations. That year there were 39 research reports. Only five were on kidney; 13 on rectal gland, 3 in cell biology. The remainder, in one way or another, were connected to ion or fluid transport or metabolism. The same proportions obtained in 1983. Again the Laboratory had excellent directors, Richard Hays (1975 - 1979) and Leon Goldstein (1979 - 1983).

The Laboratory still held firm against formal classes, but there were (in summer) seminars on Tuesday evening, noon Thursday, and 8:00 A.M. Friday. The winter program had 19 seminars between late October and April, again transport dominated, but the heritage from Kinter was plain in the several ecological sessions.

VII. <u>1984 - Present (Vols. 24 - 33)</u>

The general pattern continued in the first years of this decade. Transport still dominated, with a strong few in cytokinesis and development. In 1986 the Laboratory was established as a toxicology research center under the domain of the National Institute for Environmental Health Sciences. Its main thrust was the toxic effects of "heavy" metals and other environmental contaminants on membrane transport. The program was unique in the experience and sophistication of the local investigators in various physiological systems; much remained to be learned about the complex chemistry of the metal ions. Fourteen of the 43 principal investigators at MDIBL became part of the program; in later years this was reduced to 10. Dr. David Evans became its Director. This grant provided intellectual stimulation, produced some unexpected and remarkable results (particularly concerning cadmium) and generated important support for the Laboratory (it should be noted that before the "winter operation" the Laboratory had very little overhead since grants were made to principal investigators through their home institutions). By the end of 1993 the compounds of the following metals had been studied in one

way or other: As, Hg, Sn, Cu, Zn, Cd. In the first year (1986), eight abstracts were generated, and this rose to 11 in 1990. There have been two renewals of this grant which will run until 1998. The Program Director is now James L. Boyer.

In 1990 - 1992 the rectal gland continued to lead: 13 - 14 abstracts/year compared to 5 - 8 for kidney and bladder. Transport topics included volume regulation at differing salinities, gill and liver function, localization and effect of neuropeptides, regulation of urine pH in teleosts, work on ion channels and Cl⁻ currents. Developmental studies continued at the level of cell cleavage in invertebrates (Gary and Abigail Conrad), and the uterus in elasmobranchs (Ian and Gloria Callard).

1991 and 1992 saw the impact of the genetic revolution. John Forrest and his talented group worked on cloning and sequencing of natriuretic peptide from shark heart. DNA sequencing of Na⁺K⁺ATPase isoforms from shark rectal gland was begun. Gene sequencing was also done on the muscarinic receptor in aortic rings and cerebellum. Studies began on the gene expression of the yolk protein in turtles and construction of cDNA libraries from flounder gill and kidney, and alkaline and rectal gland of shark.

Franklin Epstein became president in 1985 and David Evans was director from 1983 -1992. The present director is David Dawson. There has continued an effective participation of the winter and summer residents of Mount Desert Island and the neighboring mainland, notably Ellsworth and Hancock Point. David Opdyke, who for many years studied cardiovascular reflexes in the dogfish, inaugurated and runs afternoon tours of the Laboratory. Particularly welcome are children of island natives and visitors. MDIBL is no longer "the best kept secret in Maine."

Hopefully, the character of MDIBL is reflected in this essay. We have been greatly fortunate in living in a cosmopolitan mix of research physicians, biologists, chemists, physiologists, and pharmacologists from many countries and of different ages. We are ringed by sea and mountain with changing light and temper—all inspiring. The future continues to challenge.

I acknowledge with pleasure and affection the participation of Heidi Beal and Joyce Hearn.

BIBLIOGRAPHY

- BULLETINS of The Mount Desert Island Biological Laboratory, 1921 1993, Volumes II (2) 32. The ordering of these volumes was complicated until Volume 6 and will be listed as follows:
- Vol. I. Harpswell years to 1920. Missing; see text. Titles have been preserved, in MDIBL Archives.
- Vol. II. Yearly, 1923 1930, 8 numbers. These are not numbered. Not abstracts but accounts of the Laboratory program. The 1929 issue gives a bibliography for years 1925 - 1929; the 1930 issue gives the seminar programs.
- Vol. III. Yearly, 1931 1941: 1950, 12 numbers. Abstracts begin. The 1950 number contains accounts of the war years and bibliography for 1929 - 1949. In 1946 an account of the Laboratory was printed entitled "Instruction and Research." Written by Roy Forster, it is also a gentle appeal for funds.
- Vol. IV. Four numbers, each covering the three years preceding: #1 (1953), #2 (1956), #3 (1959), #4 (1962).

- Vol. V. #1 covering 1962 1964 and #2 covering 1965.
- Vol. 6 32. 1966 1992. Includes Index to Volumes 2 6 in Vol. 6. Beginning here there is a volume each year. Initially the year issued gave the abstracts for the preceding year, and the volume was given that date. This was changed in 1987 - 1988 so that now, for example, the work done in 1992 has the publication date of 1993 (Vol. 32).
- These volumes, as well as the unpublished manuscripts listed below, are all available in The MDIBL Archives.
- Amos, William. Life after Summer. Mount Desert Island Biological Laboratory Fifty Years Ago. Unpublished Manuscript, April 1989.
- Bowen, Louise de Koven. Baymeath. 1945. (This fine book, now out of print, is available also at the Jesup Library in Bar Harbor.)
- Burger, J. Wendell. The Mount Desert Island Biological Laboratory. The Pioneer Days. 1898 -1951. Unpublished manuscript, West Hartford, CT, 1982. (Transcribed and edited by Marty McManus, 1989).
- Forster, Roy P. My Forty Years at the The Mount Desert Island Biological Laboratory. J. Exp. Zool. 199:299-308, 1977.
- Maren, Thomas H. Eli Kennerly Marshall, Jr. May 2, 1889 January 10, 1966. Biographical Memoirs of the National Academy of Sciences, 56:313-352, 1987.
- Marshall, E. K., Jr. A History of The Mount Desert Island Biological Laboratory. Unpublished manuscript. August 1, 1962 (incorporates an account of the early history of the Harpswell Laboratory, written in 1921 by J. S. Kingsley).
- McManus, Marty. An Historical Deck Chair Tour of The Mount Desert Island Biological Laboratory, October 17, 1991.
- Morse, Max. The Harpswell Laboratory. Popular Science Monthly, May 1909 (in MDIBL Archives).
- Pitts, R. F. Homer W. Smith. Biographical Memoirs of the National Academy of Sciences, 39:445-470, 1967.
- Schmidt-Nielsen, Bodil. A History of Renal Physiology at The Mount Desert Island Biological Laboratory. The Physiologist, 26:261-266, 1983.
- Williams, Mary Frances. The Harpswell Laboratory 1898 1920. A Marine Biological Station. Maine Historical Society Quarterly, 27:82-99, 1987.

REPORT TITLES

Rappaport, R. Furrow establishment by the moving mitotic apparatus in sand dollar (<u>Echinarachnius parma</u>) eggs1
Trotter, J.A. and T.J. Koob. Evidence that Ca ²⁺ -modulation of the stiff- ness of <u>Cucumaria</u> <u>frondosa</u> dermis is a result of Ca ²⁺ -dependent cellular processes
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Xiao, Y-F. and M. Morad. A new enzymatic technique provides isolated fresh cells for electrophysiological studies on rectal gland of <u>Squalus</u> <u>acanthias</u>
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Xiao, Y-F. and M. Morad. Inhibitory effects of cAMP on inwardly rectifying K ⁺ currents in freshly isolated cells from rectal gland of <u>Squalus</u> <u>acanthias</u> gland
Devor, D.C., W. K. Suggs, J.N. Forrest and R.A. Frizzell. Characteriza- tion of a cAMP-mediated Cl ⁻ current in primary rectal gland cultures of the spiny dogfish (<u>Squalus</u> <u>acanthias</u>)43
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Preston, R.L., P.R. Zimmermann, M.T. Kaleta and K.A. Simokat. Evidence for HgCl ₃ as the form of mercury that inhibits taurine transport in coelomocytes of the marine polychaete, <u>Glycera</u> <u>dibranchiata</u>
r, D.S., J. Clark, N. Bianchi and D.M. Barnes. Nocodazole inhibition of organic anion secretion in teleost (winter flounder, <u>Pseudopleuronectes americanus</u> and killifish, <u>Fundulus heteroclitus</u> renal proximal tubules56
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