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## RESEARCH TREND OF MEDICAL BACTERIOLOGY

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DURING the last three years, conservative bacteriology has shown increasing discontent with nineteenth century theories of microbial infection and bodily resistance, a receptive attitude toward newly suggested hypotheses and alternative interpretations.

The suggested theories would offer plausible explanations for clinical non-success in the past and renewed hope of ultimate clinical victory.

### I

Fifty years ago, clinicians were introduced to a new biological world. Mid-Victorian microscopists intuitively pictured the newly discovered disease germs as miniature animals or midget plants. Thus pictured, it was perhaps inevitable that they should have read into these minute pathogenic specks many of the laws and generalizations of higher biological science.

Centuries of dwindling superstition had taught modern man that, from generation to generation, each

higher plant and animal species is almost static in anatomical structure and physiological peculiarities. Minor variations, of course, were known to occur. Since the Middle Ages, however, rats had never been known to transmute into lizards, to fractionate into locusts, nor to evaporate into corrosive miasmas. It seemed logical to assume that this stability is in obedience to a general law of nature, equally applicable to microbial life. Obeying this static law a tubercle bacillus could never arise except from a pre-existent bacillus of approximately the same morphology and chemical composition. A diphtheria bacillus could never transmute into a gonococcus, nor fractionate into ultramicroscopic poliomyelitis colloids.

This static purpose of nature became a major premise for subsequent epidemiologic, diagnostic and therapeutic deductions. Tuberculosis, gonorrhoea and poliomyelitis were wholly unrelated infectious diseases, because of the postulated microbial invariability.

Test-tube vaccines were logical therapies because artificial cultures were assumed to be biochemically identical with the corresponding natural infections. Antiserums prepared by immunizing horses against such vaccines were also logical and for the same reason.

A quite different infectious logic might have developed if the early microscopists had turned to the known facts of histology for their basic analogies, to tissue cells which like bacteria multiply by simple cell-division. From a single fertilized ovum a hundred different cell types were known to develop. Atypical mitoses, asymmetrical cell-divisions, cellular fusions, embryonic reversions, hetero-regenerations, dwarfisms, giantisms and functional metaplasias were the commonplace of cellular pathology. Morphological, functional and chemical transmutability of microbes rather than their invariability might have been the assumed law of clinical medicine. An artificial culture of the tubercle bacillus would have been tested as a hoped-for specific vaccine. This test, however, would not have been made with the preconception that this bacillus must necessarily possess the qualitative biochemical invariability necessary for vaccine success.

The static bacteriology of Pasteur, Ehrlich and Koch led to diphtheria antitoxin, the most spectacular therapeutic victory of all ages. Each victory of this type, however, was eventually paralleled by a half dozen diagnostic paradoxes and therapeutic failures. Tetanus partially surrendered, but tuberculosis and streptococcus mocked at nineteenth century infectious logic.

In spite of accumulating disappointments of this type, however, the static microbiology of the 1880's was not seriously questioned for nearly forty years. A few impatient Löhnises<sup>1</sup> dared report evidence in favor of limited microbial transmutability. Such reports, however, were not taken seriously.

Two years ago, however, Hadley<sup>2</sup> dared champion the "Löhnis phenomenon," and was, in his own language, "sufficiently foolhardy" to summarize previous "pleomorphic" data and supplement it by his own laboratory evidence. Hadley's paper released a flood of confirmatory reports. Orderly or disorderly pleomorphism rather than morphological invariability became an accepted possibility of microbial life, though bacteriologists were and still are far from agreement in their interpretations of the reported "mutations" or "involution." The "dissociation" of a score or more pure bacterial strains into two or more morphological, tinctorial or cultural "variants" is now well

confirmed. Bacterial "dwarfism," "fragmentation" or even complete "disintegration" into almost invisible, viable micromidgots is no longer seriously questioned. "Life cycles," "hibernating phases," "conjugations," "primordial revisions" and "free gonidial units" are suggested terms now asking official endorsement.

That the bacterial colony and not the individual bacillus is the essential physiological unit or microbial growth is probably the most radical of these suggestions, the colony pictured as a primordial multicellular plant. Purposeful differentiations, orderly life cycles, resting stages, nutritional and hormonal integrations and even conjugations would thus become logical, convenient explanations for reported pleomorphic data. Another extremist hypothesis of more than passing interest is the current suggestion that many highly parasitic micro-organisms have lost their primordial autonomy, and can now multiply only under the influence of certain extraneous plant hormones, equivalent zoological enzymes or other growth-stimulating factors.<sup>3</sup>

## II

If, as progressive bacteriologists allege, many bacilli can masquerade as pseudo-spirochetes or transmute into quasi-streptococci, if tuberculosis and gonorrhoea can disguise their infectious habits under new or altered staining reactions, and dysentery and typhoid fever pass hygienic filters as invisible micromidgots, then marked changes must be made in conventional clinical logics. It is apparently well confirmed that many of the "dwarf phases" of even the most hardy pathogenic bacteria do not grow, or grow only after prolonged "maturation" or "regeneration" periods when placed on routine culture media. Doubts are thus cast on many previously assumed sterilities of serums, bloods, organs, tissues, exudates and filtrates.

Special techniques are now being perfected to meet this clinical emergency, variants of the apparently inconstant Kendall's medium,<sup>4</sup> for example, and suggested reinforcements of routine culture media by the addition of bacteria-growth-stimulating plant hormones.<sup>5</sup> By one of these techniques, Miller<sup>6</sup> reports the successful test-tube cultivation for many generations of non-acid-fast midgots of the tubercle bacillus. Mellon's<sup>6</sup> description of his cultivatable *B. tuberculosis* dwarfs as non-acid-fast granules microscopically identical with the well-known diphtheroids of certain benign tumors is perhaps prophetic of pleomorphic data pathologists soon may be called upon to interpret.

<sup>3</sup> "Plant Hormones and Bacterial Growth," *J. A. M. A.*, 98, 1307, 1932.

<sup>4</sup> A. I. Kendall, *Northwestern University Bulletin*, 32, No. 8, 1931.

<sup>5</sup> F. R. Miller, *SCIENCE*, 74, 343, 1931.

<sup>6</sup> R. R. Mellon, *Proc. Soc. Exper. Biol. and Med.*, 29, 206, 1931.

<sup>1</sup> F. Löhnis, *Jour. Agric. Research*, 18, 675, 1916; *Nat. Acad. Sci.*, 16, 1, 1921.

<sup>2</sup> P. Hadley, E. Delves and J. Klimik, *Jour. Infect. Dis.*, 48, 1, 1931.

There is rapidly accumulating evidence that departures from classical test-tube morphology are almost invariably accompanied by equally marked changes in chemical composition. Whether this is due to the acquisition of new chemical specificities or to asymmetrical atrophies or hypertrophies of pre-existing specificities is still in doubt. "Chemovariation" also may occur without demonstrable morphological or tinctorial changes.

The clinical significance of such "chemomutations" arises from the qualitatively altered antigenicity or vaccination potential. Two test-tube "dissociates" of the same pure culture of *B. typhosus*, for example, might not be recognized as belonging to the same bacterial species by routine specific agglutination tests. Animals immunized against one *B. typhosus* "mutant" may show little or no demonstrable specific immunity against its sister "dissociate," nor will serums drawn from such immunized animals necessarily protect normal animals against the original "undissociated" culture. Many inadvertent "involution vaccines" have undoubtedly been used in the past.

"Chemomutations," "chemadaptations" or "chemodegenerations" may also take place on or within the infected animal body. The same filterable virus, for example, injected into two different animal species is reported to transmute into two different vaccination specificities.<sup>7</sup> The alternate generations of the spirochetes of relapsing fever have long been known to be of different immunological specificities, each wave of fever stimulating little or no specific immunity against the immediately preceding or immediately succeeding wave. Equally marked antigenic differences are now apparently well confirmed between primary and tertiary *T. pallidum*.<sup>8</sup> Staphylococci of different antigenicities have been isolated from different organs at the same human autopsy. Rosenow's<sup>9</sup> much-debated organotropic variants in focal infections are no longer isolated phenomena. Test-tube simulations of the "Rosenow variants" are currently reported by growing routine cultures of pneumococci and *T. pallidum*, for example, in certain organ-emulsions. These microbe-transmuting organ-emulsions contain organ-specific lipoids.<sup>10</sup>

### III

There is a growing tendency among progressive bacteriologists to picture the bacterial cell, not as a

<sup>7</sup> P. P. Laidlaw and G. W. Dunkin, *Jour. Comp. Path. and Therap.*, 41, 1, 209, 1928.

<sup>8</sup> "Artificial Neurotrophic Syphilis," *J. A. M. A.*, 96, 119, 1931.

<sup>9</sup> E. O. Jordan and I. S. Falk, "The Newer Knowledge of Bacteriology and Immunology," University of Chicago Press, Chap. 43, p. 576, 1928.

<sup>10</sup> "Organ-Specific Lipoids," *J. A. M. A.*, 97, 1628, 1931.

final indivisible infectious unit, but as an organized aggregate of vital colloids, or vital potentials, in much the same way that the animal body was divided about a century ago into an organized aggregate of histological units. Progressive bacteriologists allege that they must take this step, if they are to avoid postulating a supermaterial vital force or somatic spirit in the bacterial cell.

Apparently two distinct "morphons," or "vital colloids" are tentatively pictured in the bacterial cell.<sup>11</sup> The first, or "autonomous bion," is a single colloidal molecule, or "monomolecular amoeba," with a complete armament of crystalloid, hereditary genes and crystalloid, nutritional enzymes (see "Landsteiner phenomenon," section V). The second, or "nonautonomous bion," is a colloidal molecule deficient in one or more of the necessary hereditary or enzymic crystalloids. Such a "sub-bionic colloid" can show orderly synthetic increases in size and subsequent depolymerization into two or more daughter "sub-bions" only with the cooperation of intrabacillary hormones, enzymes or other integrating factors.

Bionic metaphors admittedly furnish convenient explanations for most of the alleged facts of the new dynamic microbiology. The "transmissible lysin" of Twort,<sup>12</sup> for example, may be pictured as a "non-autonomous bion" of no greater size or complexity than the ordinary protein molecule. This species-specific, non-autonomous colloid is incapable of self-proliferation, but proliferates or is proliferated in symbiosis with the homologous bacterial cell. Under certain conditions the resulting bion-bacterium-complex functions as a bacillus of exalted physiological functions.<sup>13</sup> *B. typhosus*, for example, homoplastically ingrafted with the corresponding Twort "sub-gonidial colloid," becomes the *B. typhi-hemolyticum* of recent nomenclature. This "hyper-gonidiate" has been repeatedly isolated from typhoid bloods and is regarded by certain radicals as the probable etiologic factor of typhoid septicemia. The natural or artificially synthesized *B. typhi-hemolyticum* is alleged to breed true for several test-tube generations, but eventually to "dissociate," one of its "mutants" or "degenerates" being the primordial non-hemolytic saprophytic *B. typhosus* of routine laboratory study.

Under certain other conditions<sup>14</sup> the homoplastic ingrafted Twort sub-bion may overgrow and eventually dominate the 'phage-bacterium-complex. This dominance conceivably forces the transmutation of the bacillus into the filterable, dormant or free gonidial

<sup>11</sup> J. Alexander, *Protoplasma*, 14, 296, 1931.

<sup>12</sup> "Limitations of Bacteriophage Therapy," *J. A. M. A.*, 96, 693, 1931.

<sup>13</sup> "Further Limitations of Bacteriophage Therapy," *J. A. M. A.*, 98, 1190, 1932.

<sup>14</sup> J. H. Northrop and A. P. Krueger, *Jour. Gen. Physiol.*, 15, 329, 1932.

phase, or causes autolysis, depending upon the ultimate interpretation of the word "lysis." Why a similar bionic overgrowth or resulting "lysis" does not take place with the "phage-resistant" *B. typhi-hemolyticum*, however, will necessitate further elaboration of the Alexandrian bionic metaphor.

Bionic metaphors are not wholly foreign to clinical medicine, though usually disguised in much more conventional nomenclature. During the last few years, for example, and in spite of prompt and heroic doses of diphtheria antitoxin, diphtheria has reasserted its ancient 25 per cent. mortality in Europe.<sup>15</sup> European clinicians, have not been forced to postulate an Asiatic importation of a superdiphtheria to account for this apparently new toxin specificity. Almost without exception they have turned to bionic hypertrophies, bionic metaplasias or Alexander's bionic modifications to account for the new specificity, forced bionic mutations conceivably due to the wide-spread use of the Schick test and diphtheria toxin immunization. A few visionaries have even gone further than this and have postulated a heteroplastic ingrafting of alien bions onto pre-war *B. diphtheriae*. This fantasy finds some support in the recently alleged artificial ingrafting of streptococcus bions onto the diphtheria bacillus to form "hybrid" or synthetic *B. streptodiphtheriae*, which allegedly breed true for a dozen test-tube generations.<sup>16</sup> Bacterial-bionic symbiosis has also been postulated to explain the relationship of streptococcus to scarlet fever and of proteus X to certain animal diseases. The recent well-confirmed serological conjugation of virulent, type-specific pneumococcus bions with degenerated pneumococci with a resulting synthesis of a new type-specificity which breed true for innumerable test-tube generations,<sup>17</sup> is probably the most spectacular colloidal wizardry to which conservative bacteriologists are now trying to avoid applying the bionic metaphor.

#### IV

During the last three years, there has been awakened interest in hitherto ignored biochemical identities or cross-reactions between pathogenic bacteria, environmental saprophytes and certain higher plant and animal tissues. The characteristic polysaccharide of the meningococcus, for example, is currently reported to be present in such apparently non-related bacteria as *B. anthracis*, *B. proteus*, *B. subtilis* and *B. mesentericus*.<sup>18</sup> Since the pneumococcus polysaccharides are known to function as successful fractional oral

vaccines, cross-reactions of this type are not without suggestive clinical interest. Sub-antigenic (see: "Landsteiner phenomenon," section V) porphyrin compounds are allegedly present in numerous shellfish and in diphtheria toxin. The characteristic lipid of certain strains of the Shiga bacillus is antigenically identical with a lipid fraction of sheep erythrocytes and guinea-pig kidneys.<sup>19</sup> A *T. pallidum* lipid is currently reported to be antigenically indistinguishable from the organ-specific lipid of the human brain.<sup>10</sup>

A bacterial enzyme hydrolyzing one of the typed pneumococcus polysaccharides has recently been found by Avery and Dubos.<sup>20</sup> This enzyme not only de-capsulates the corresponding type pneumococcus *in vitro*, but protects laboratory animals against multiple lethal doses of the homologous pneumococcus culture.

One of the extractable lipids of the Shiga bacillus is antigenic for certain animal species,<sup>18</sup> but stimulates the production of no demonstrable antilipoid antibodies in other animal species. The Shiga antiserum from the second animal species is, therefore, deficient in an antilipoidal fraction conceivably needed by the first species. Physiological interchangeability of homologous antisera was one of the basic tenets of the older immunology.

The anti-Shiga serum from the first animal species contains an antilipoidal factor not only superfluous for the second species, but potentially toxic for its tissues. Guinea-pigs, for example, injected intravenously with anti-Shiga rabbit serum may be killed in from two to four minutes with symptoms resembling acute anaphylactic shock. Accessory cytotoxins of this type have not yet been demonstrated in human medicine, although the clinical toxicity of certain discarded antisera suggests similar relationships.<sup>21</sup>

Since *T. pallidum* allegedly contains a lipid antigenically identical with a normal lipid of the human brain, speculative immunology is beginning to wonder if convalescent immunity to syphilis may not be accompanied by the development of a human serum factor cytotoxic for human brain tissues. Such a conceivable but still unproved "immunological vicious circle" finds some support in the recently described "myalinolysin" in the serum of patients with multiple sclerosis. The injection of *B. welchii* toxin into a single bone marrow of a rabbit is reported to result in explosive degenerations of all bone marrows of its body, with a resulting circulatory deficiency resembling human pernicious anemia.<sup>22</sup>

<sup>15</sup> J. S. Anderson *et al.*, *Jour. Path. and Bact.*, 34, 667, 1931.

<sup>16</sup> "Upsetting Immunologic Tenets," *J. A. M. A.*, 96, 1232, 1931.

<sup>17</sup> J. L. Alloway, *Jour. Exper. Med.*, 55, 91, 1932.

<sup>18</sup> "Polio-myelitis Immunity," *J. A. M. A.*, 98, 1307, 1932.

<sup>19</sup> E. O. Jordan and I. S. Falk, *loc. cit.*, Chap. 53, p. 733, 1928.

<sup>20</sup> "Enzyme Therapy," *J. A. M. A.*, 91, 1540, 1931.

<sup>21</sup> "Serological Hazard," *J. A. M. A.*, 97, 710, 1931.

<sup>22</sup> J. C. Torrey and M. C. Kahn, *Amer. Jour. Path.*, 5, 117, 1929.

## V

It is conceivable that future medical historians may regard the "Landsteiner phenomenon"<sup>23</sup> as the most important basic advance in infectious theory since the discovery of the phenomenon of anaphylaxis. Stripped of its chemical hieroglyphics, the Rockefeller Institute chemists demonstrated that conjugation of a relatively simple non-antigenic crystalloid with a specific protein often confers upon that protein a new immunological specificity. Injected into laboratory animals the protein-crystalloid-complex leads to the development of what may be described as a "duplex antiserum." One part or function of this antiserum is a crystalloid-specific "fractional antibody." With this "fraction" the crystalloid can be identified, either in its free state,<sup>24</sup> or when combined with a protein "carrier." The identification is allegedly made with the same ease and certainty with which *B. typhosus*, for example, can be differentiated from the colon bacillus.

It is, of course, too early to predict the numerous possible clinical applications of this new "duplex serology" or "crystalloid immunology." Any crystalloidal bacterial toxin, however, or any gastrointestinal putrefactive crystalloid that can be conjugated with or semi-permanently absorbed onto a protein "carrier," becomes a theoretically feasible antigen for attempted diagnostic and therapeutic research. Alkaloids and other non-colloidal pharmacodynamic agents may be conceivably studied by this conjugation technique, with specific immunizations of drug addicts and the serological verification of the basic tenets of homeopathy as legitimate research goals. A cancer-specific crystalloid<sup>10</sup> has already been reported, which can be raised to full fractional antigenicity by the Landsteiner conjugation technique, suggesting a future successful diagnostic test for malignancy.

Two facts of broad biological interest, however, are already well confirmed by the new crystalloid technique. First, a single crystalloid conjugated with animal, plant or microbial proteins may so completely dominate or homologize these proteins that they might readily be mistaken as belonging to the same biological group. Second, the fractional antigenic properties of a conjugated crystalloid depend, in part at least, on its type of union with the protein "carrier." Avery,<sup>25</sup> for example, found it necessary to guard against "burying" his sub-antigenic pneumococcus polysaccharide in the protein "carrier," if he wished to preserve its specific vaccination potential.

<sup>23</sup> "Non-protein Allergy," *J. A. M. A.*, 98, 1564, 1932.

<sup>24</sup> K. Landsteiner and J. van der Scheer, *Jour. Exper. Med.*, 54, 295, 1931.

<sup>25</sup> O. T. Avery and W. F. Goebel, *Jour. Exper. Med.*, 54, 437, 1931.

Facts of this type strongly suggest that future immunologists may find it advisable to recast the entire nomenclature of protein immunity and protein allergy in terms of unit sub-protein crystalloids. Certain European extremists are already postulating that the protein molecule in itself is nothing more than an immunologically inert colloidal "carrier" of superficial "determinants," "characteristics," "coefficients" or "quotients." This intuitively suggests that enzymes and heredity genes may be of no greater complexity than one of the Landsteiner crystalloids, a single protein molecule being the carrier of a score or more of unit hereditary, synthetic and lytic factors.<sup>11</sup> A single protein molecule thus becomes a conceivable "monomolecular amoeba" (see Alexander's "bions," section III).

## VI

One of the theoretical surprises of the past three years has been the fairly conclusive evidence that properties simulating specific serum "antibodies" appear apparently spontaneously in the circulating blood of both man and laboratory animals at the approach of sexual maturity.<sup>26</sup> Jungeblut and Engle, of Columbia University,<sup>27</sup> have been bold enough to apply this "pubescent immunity," "serological ripening," "maturation panimmunity" or "phylogenetic recapitulation of ancestral immunity"<sup>26</sup> to a study of adult immunity to poliomyelitis. The sexually immature, poliomyelitis-susceptible monkeys of routine laboratory research were forced by them to a precocious maturity by ovarian transplants or by repeated injections with pituitary extract. Thus artificially ripened, the monkeys became insusceptible to routine intracerebral inoculations with poliomyelitis virus, and their serums neutralized poliomyelitis virus *in vitro*.

## VII

To those who have dreamed of the early test-tube syntheses of therapeutically useful "antibodies," the most discouraging surprise, however, is the recently alleged experimental evidence that there is a specific "immunity center" in the brain.<sup>28</sup> Without this "integrating center" specific somatic antibodies are alleged not to be formed in the body or liberated into the blood stream. Specific immunological conditioned reflexes are seriously proposed to account for certain specific immunological phenomena.

The mere suggestion of a conceivable "neurological integration" of specific antibody formation is so for-

<sup>26</sup> "Phylogenetic Immunologic Recapitulation," *J. A. M. A.*, 96, 775, 950, 1931.

<sup>27</sup> C. W. Jungeblut and E. T. Engle, *J. A. M. A.* (in press).

<sup>28</sup> "Tissue Autonomy and Antibody Formation," *J. A. M. A.*, 98, 484, 1932.

eign to the classical immunological autonomy of organs and tissues as to be almost insulting in its implications. One must admit, however, that this Ehrlich autonomy is not in harmony with modern theories of protein, carbohydrate and lipid metabolism.

#### SUMMARY AND CONCLUSIONS

The last three years of theoretical bacteriology and immunology have been characterized by four major movements:

(a) A tentative acceptance of a new dynamic concept of the infectious unit.

(b) A growing interest in the possible epidemiological importance of minor cross-reactions between pathogenic bacteria, environmental saprophytes and certain higher plant and animal tissues.

(c) An increasing skepticism of the classical belief that the protein molecule functions as a single antigenic unit.

(d) The beginning of serious interest in the basic genetic, enzymic, hormonal and neurological factors operative in specific immunity.

Professional bacteriologists and immunologists are divided into two schools in their acceptance or rejection of the newly suggested theories or plausibilities. The conservative school emphasizes the "intellectual recklessness"<sup>29</sup> that has led to futuristic theorizing before accumulation of absolutely conclusive experimental and observational evidence. The progressive school alleges that conservative theories are largely ancestral traditions, originally drawn from equally inconclusive data. If there is an element of truth in this allegation, the burden of proof rests equally on both schools.

Until the radical and conservative schools are harmonized, clinicians must apply the infectious logic of either school with an open mind,<sup>30</sup> depending for predictable clinical effects solely upon previous, adequately controlled clinical evidence.

## OBITUARY

### GEORGE KIMBALL BURGESS

On July second, Dr. George K. Burgess, director of the National Bureau of Standards, was stricken with a cerebral hemorrhage while in his office at the bureau and died on the way to the hospital.

Dr. Burgess was born in Newton, Massachusetts, January 4, 1874, and was a direct descendant of Thomas Burgess, of England, who settled in Sandwich, Massachusetts, in 1638. He was educated in the public schools of Newton and later entered the Massachusetts Institute of Technology, where he graduated in 1896. Most graduate students of that period who were able to continue their studies abroad went either to Germany or England, but Burgess decided to study at the Sorbonne. This decision had a profound influence upon his later work. In Paris he became deeply interested in high temperature measurements under the guidance of Le Chatelier, and later translated Le Chatelier's book on this subject. Here he acquired a fluent use of the French language, which later was to prove of great service to him in important international conferences. Here also he met Mlle. Suzanne Babut, whom he married in 1902, and who survives him.

Following the award of his doctorate from the Sorbonne in 1901 with highest honors, Dr. Burgess joined the physics staff of the University of Michigan, and the following year was called to the University of California. In 1903 he entered the service of the Bureau of Standards, two years after its organization, and began a series of notable researches

in the field of pyrometry, in large part in collaboration with Dr. C. W. Waidner. These investigations included an extended study of optical pyrometry, platinum resistance thermometry at high temperatures, the determination of the melting points of pure metals, and the study of the selective radiation from incandescent bodies.

It was during this period (1908) that Waidner and Burgess proposed as an absolute standard of brightness the radiation from the interior of a black body immersed in a bath of pure platinum at its freezing point. Lack of suitable refractories made it impossible to carry out the experimental procedure at that time, but twenty years later as director of the Bureau of Standards, Dr. Burgess had the keen satisfaction of seeing the Waidner-Burgess standard experimentally realized by members of the bureau staff.

His interest in the properties of materials at high temperatures led him into the field of physical metallurgy, and in 1913 he was made chief of the newly organized metallurgical division of the bureau. This marks the second stage of his career. He took up this work with characteristic energy and enthusiasm, and in the course of its development he demonstrated his marked ability as a technical executive. While directing this work, he still found time for his own researches on the causes of dangerous defects in railway materials. He demonstrated the practicability of measuring the temperature of steel rails as they pass

<sup>29</sup> H. Zinsser, *SCIENCE*, 75, 256, 1932.

<sup>30</sup> "Recommendations of the Allergic Research Council," *J. A. M. A.*, 94, 654, 1930.