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Comparative Dermatology

Cultivated Mammalian Cells

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Staff Meeting Report

A Comparative Study of Human and Canine Dermatology*†

Milton Orkin, M.D.‡

"Between animal and human medicine there is no dividing line—nor should there be. The object is different, but the experience obtained constitutes the basis of all medicine."

RUDOLF VIRCHOW (1821-1902)

Animals have often been used for experimental production of disease but seldom for observation of spontaneous disorders. The broad purpose of the present study is to define and characterize spontaneous skin diseases of the dog and to correlate these with human counterparts, when they exist. No such systematic comparison of skin diseases of man and another species has been made previously. The more specific purposes are: (1) to accumulate fundamental knowledge of canine dermatoses and tumors, both for the intrinsic value of this information and for its usefulness in future research; (2) to compare canine and human dermatoses and tumors and to experiment on analogous canine lesions so as to permit application of the information to both species; and (3) to seek for common patterns of disease behavior despite species differences.[1]

Milton Orkin

This delineation of canine diseases is based upon intensive study of 292 dogs spontaneously afflicted with cutaneous tumors or dermatoses or both. The initial phase of the project consisted of review and study of comparative (dog and man) cutaneous anatomy, biochemistry, and physiology.[2] This information is not included in the present com-

*Presented at the Staff Meeting of the University of Minnesota Hospitals on October 20, 1961

†The study which forms the basis of this report was undertaken in conjunction with Dr. Robert M. Schwartzman, formerly Instructor, College of Veterinary Medicine, University of Minnesota; presently Assistant Professor, School of Veterinary Medicine, University of Pennsylvania.

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munication; emphasis here is placed on interesting clinical and histologic aspects of comparative dermatology.

A. Cutaneous Tumors

Spontaneous tumors are more common in dogs than in any other animal species. Approximately one-third of canine neoplasms originate from skin and subcutaneous tissue,[3] visceral carcinomas being relatively uncommon.

Our initial series consisted of 100 cutaneous tumors collected from 90 dogs. There was slight preponderance of ectodermal over mesodermal neoplasms. In addition, the incidence of sarcoma approximated that of carcinoma, while in human beings a higher proportion of carcinoma is noted among skin tumors.

In order to assess the age, breed, and sex distribution among dogs in the original tumor series, we found it necessary to correlate the observed cases with a general canine population. The "sample normal population" consisted of the first 1,000 dogs examined for any condition at the University of Minnesota Veterinary Clinic during 1956.

Age Distribution. Age distribution of the affected dogs differed grossly from that of the sample normal population. In this tumor-bearing population very few animals under one year of age were affected (human equivalent—15 years). The vast majority of *malignant* conditions occurred in animals nine years of age and older (H. E.—52 years). The marked proclivity toward malignant disease among older dogs has been widely reported.

Breed Distribution. There was no tendency for cutaneous neoplasia in general to be associated with any major breed of dog in the sample normal population. There is, however, an apparent tendency for breeds to be afflicted by *specific* types of tumors and dermatoses, and these will be mentioned under specific entities.

Sex Distribution. The incidence of cutaneous tumors was independent of the sex of the canines of the sample normal population.

Specific Entities

1) *Transmissible Reticulum-Cell Tumor.* This unique, and fairly common neoplasm (17 per cent of original series) is characterized by the ease with which it can be transmitted to other dogs, by natural or artificial means.[4] Despite their sometimes sarcomatous appearance clinically, and its malignant aspect histologically, the vast majority of these tumors spontaneously regress. The cellular appearance and total architecture of the

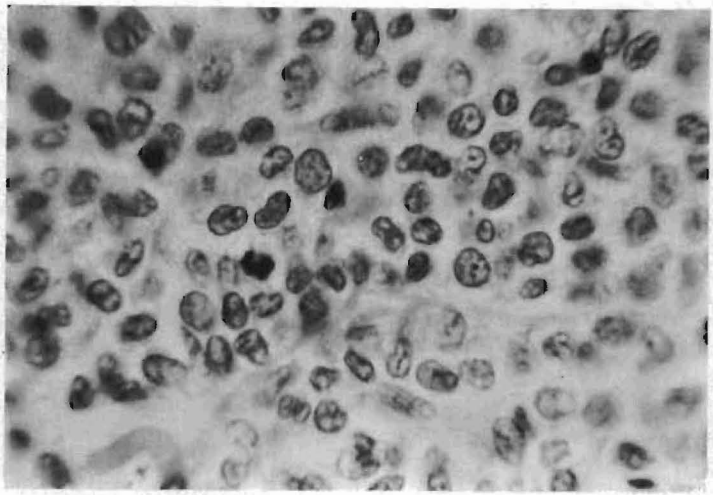

Fig. 1. Transmissible Reticulum-Cell Tumor—reticulum cells with several mitotic figures indistinguishable from human reticulum-cell lymphoma. Hematoxylin and eosin; × 242.5

tumor are microscopically indistinguishable from those of reticulum-cell lymphoma of man (Fig. 1). Clinical and experimental data suggest the presence of a specific tumor cell antibody in animals recovering from this neoplasm.

No specifically comparable tumor exists in man, although human keratoacanthoma shares the following facets of host response: (1) Both are essentially benign conditions in which malignancy is simulated histologically, i.e., reticulum-cell sarcoma simulated in transmissible reticulum-cell tumor, and squamous-cell carcinoma in keratoacanthoma; (2) frequent spontaneous healing occurs in both; and (3) relative immunity is achieved in both conditions after involution of the tumor.

2) *Mastocytoma.* This entity accounts for 13 per cent of cutaneous canine tumors,[5] a predilection for mastocytoma being evident in Boston terriers and boxers. It is not clear whether the condition represents a sarcoma, systemic hyperplasia, reticuloendotheliosis, or systemic inflammatory process. Clinical involvement of regional lymph nodes, spleen, and liver, is fairly common. Whether or not this implies metastases or autochthonous involvement of normally present mast cells cannot be stated. Canine mastocytoma and human urticaria pigmentosa (systemic form) yield very similar autopsy findings.

Pathologic diagnosis of atypical cases requires the use of a metachromatic stain. Such cases tend to simulate reticulum-cell lymphoma or Hodgkin's disease in humans.

3) *Pigmented Nevus and Malignant Melanoma.* Pigmented nevi and malignant cutaneous melanomas are relatively common in man and dog.[6] Although in the dog the clinical evolution of pigmented nevi is incompletely delineated, the disorder appears comparable to its human counterpart. Malignant melanoma is clinically comparable in both species, and is often associated with widespread metastases and poor prognosis (Fig. 2). Darkly pigmented dogs are more susceptible to malignant melanoma, while lightly pigmented humans are more likely to exhibit this disorder.

Histopathologically, canine benign and malignant melanocytic tumors have rare junctional nests (with the exception of oral lesions) as compared to many human lesions, which have frequent junctional nests.

Interestingly, malignant melanoma has been produced experimentally in the dog with the use of tar, even though dogs are refractory to induction of the usual tar cancer (spinocellular).[7,8]

4) *Senile Sebaceous Hyperplasia (Adenoma).* These cutane-

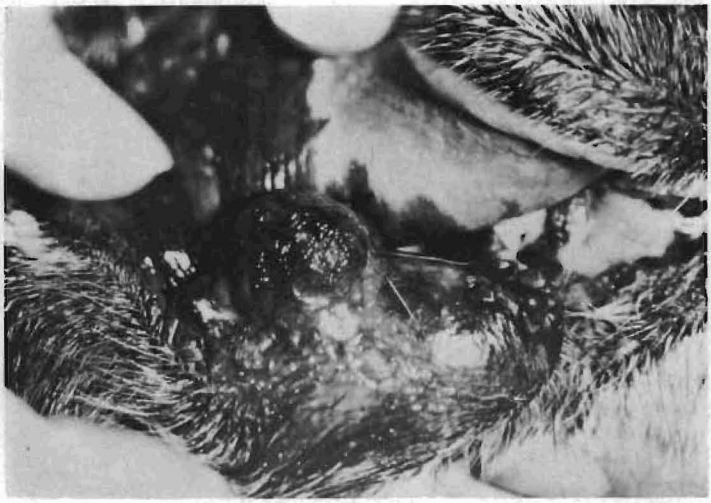

Fig. 2. Canine Malignant Melanoma—ulcerated, black, nodular lesion of lower lip

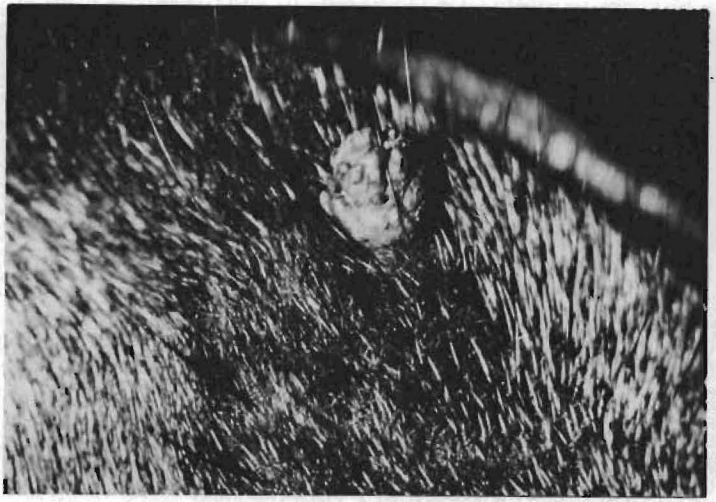

Fig. 3. Canine Verruca—digitate, rough growth

ous tumors are common in both species and appear to be comparable in morphology and topography, and in age at which they occur. The condition usually affects male dogs. Canine and human lesions are indistinguishable histopathologically; both show dermal hyperplasia of mature sebaceous glands.

5) *Epidermal Cysts.* These tumors are common in man and dog. Sebaceous cysts, however, are uncommon in both species.

6) *Verruca Vulgaris.* This condition occurs in all species. The tumors are common in dogs under two years of age (H. E.—24 years) or less. They tend to predominate on the mucous membranes of the mouth, tongue, and lips, then being referred to as *Canine Oral Papillomatosis.* Warts are clinically and histologically comparable in dog and man (Fig. 3). The virus of each is apparently species-specific; interspecies transmission has not been satisfactorily accomplished.[9]

7) *Dermatofibroma.* These lesions are clinically and histopathologically comparable in dog and man. In both species the tumors are common and benign, usually consisting of single lesions composed microscopically of mature fibroblasts (with spindle-shaped nuclei) admixed with young collagenous fibrils and bundles.

8) *Fibrosarcoma.* Canine fibrosarcomas appear to be analogous, histologically and clinically, to the poorly differentiated

group of human fibrosarcomas. Both species show a remarkable capacity for invasion (by the tumor) of contiguous structures. Visceral metastases usually occur late after repeated local recurrences.

9) *Neurofibroma.* Individual canine neurofibromas are clinically comparable to, and histologically indistinguishable from, their human counterparts. The complex syndrome of human multiple neurofibromatosis (von Recklinghausen's disease) has not been described fully in the dog.

B. Canine Dermatoses

These disorders are common, accounting for approximately 25 per cent of small animal practice.

1) *Seborrheic Dermatitis.* In both species seborrheic dermatitis occurs with characteristic yellow lesions, having greasy scales and crusts (Fig. 4). The disease tends to affect patients—both human and canine—from puberty onward. Sites of predilection, morphology of individual lesions, and potentiality for an exfoliative phase are observed in both species. Also common to both is the tendency to secondary infection (same organisms), eczematization, and lichenification. In both species seborrheic determatitis involves endocrine activity in complex ways.

2) *Cutaneous Pollinosis.* The canine condition has many fea-

Fig. 4. Canine Seborrheic Dermatitis—yellow patches with greasy scales and alopecia

tures in common with human ragweed contact dermatitis, which has been related to sensitivity to the oleoresin fraction of the plant. In both species the recurrence of the pruritic disease parallels the season of ragweed pollination, namely, from early August until shortly after the first frost. No definite statement of comparability can be made until more intensive skin testing of afflicted dogs is accomplished with ragweed oleoresin (patch tests) and protein (scratch and and intradermal) fractions.

3) *Localized Neurodermatitis.*

a. *Acral Pruritic Nodule.* This appears comparable to the hypertrophic or nodular variant of localized neurodermatitis of man. The absence of lichenification in the canine lesions is probably a manifestation of terrain, since similar traumata (prolonged licking, rubbing, or scratching) in the lateral flank, axilla, thigh, or abdomen, often result in lichenification microscopically and macroscopically similar to that of man. Similarly, in man localized neurodermatitis may present eczematization rather than lichenification in areas of thin skin, and may be seen in sharply demarcated plaques on the palms and soles.[10] In both species, patients (usually adults) frequently confine self-inflicted trauma to relatively small segments of the body surface. Many of the "emotional" facets of this disorder in human patients have their counterparts in similarly afflicted canines: pruritus is out of proportion to the presenting dermatitis, symptoms are likely to develop when the patient is inactive, and certain accessible scratch sites are often utilized (ankle and lower third of the leg commonly).

b. *Axillary Intertrigo.* In the dog one form of this condition appears comparable to localized neurodermatitis in man. In both species lichenified, thickened, pigmented patches are observed in adults.

c. *Lichenification of the Flanks.* Lichenified plaques in dogs are morphologically and histologically comparable to those in the human condition (Fig. 5).

4) *Hypothyroidism.* Facets shared by both species include: similar relative age of patients, elevated cholesterol, decreased basal metabolic rate, and some clinical signs, e.g., lethargy, irregular menses, and frequent weight gain. Dermatologic changes shared include coarseness, dryness, and scaliness of skin (seborrhea-like at times), and varying degrees of alopecia. Non-pitting edema significant in some human cases is not prominent in the dog.

5) *Demodectic Mange.* The causal organism, *Demodex fol-*

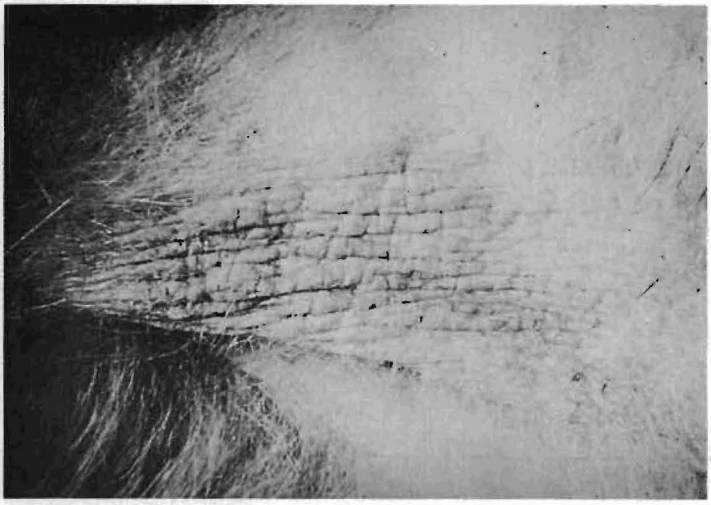

Fig. 5. Canine Lichenification of the Flanks—
lichenified pigmented plaque

liculorum, may inhabit hair follicles in many species: man, dog, cat, cow, horse, mouse, etc. The mite of one animal is virtually indistinguishable from that of another. In canines, the condition occurs as a localized or generalized, subacute or chronic, non-pruritic dermatosis of young animals. It is characterized by patchy alopecia or pyoderma or both. The hair follicle may undergo destruction and thus allow the entrance of mites and bacteria into the corium. The canine mite has been isolated in blood, viscera, lymph glands, and feces; it tends to flourish in seborrheic tissue.

In man, as opposed to the dog, the entire life cycle of the mite occurs within the pilosebaceous apparatus. No convincing evidence exists that *Demodex folliculorum* contributes, either directly or indirectly, to the pathogenesis of any human disease.

6) *North American Blastomycosis.* The dog is the domestic animal most commonly afflicted with this condition. As in man, canines with this disorder are characterized clinically by fever and debility, cough, dyspnea, and cutaneous lesions (e.g., cutaneous ulcers, furuncles, and subcutaneous abcesses). The organisms which infect dog and man are apparently identical; neither has been isolated from the soil. The condition does not spread from man to man, and no instance has been reported involving transmission from dog to man. Little is known about

the epidemiology of this condition. We have reported on a canine and a human case of Northern American blastomycosis which appeared to be related epidemiologically.[11] Both cases occurred in a small community in northern Minnesota, where the dog was owned by friends of the patient. The canine infection preceded the human infection by three months, and both ended fatally. The possibility of dog-to-man transmission of this disease was suggested but not proved.

Conclusion

Dermatoses and tumors discussed in the preceding sections may not be biologically identical in dog and man, because of obvious species dissimilarities. Nevertheless, a number of the dermatoses and tumors discussed can be considered analogous—i.e., they are similar in function and appearance, if not in origin or development. Such conditions offer a unique opportunity for study of disease biology as it occurs spontaneously in an available mammal.

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Staff Meeting Report

Species-Specificity and "Transformation" Phenomenon of Cultivated Mammalian Cells*†

K. Gerhard Brand, M.D.‡

For a number of years we have been interested in immunologic studies on cultivated mammalian cells. In fact, the experimental work underlying this report was begun in 1957, under the guidance of the late Dr. J. T. Syverton.

The purpose of the present report is to relate those of our findings that appear to have some theoretical as well as practical importance. We have been concerned with the following problems:

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1) Mammalian cells when cultivated *in vitro* lose or change progressively many of their original *in vivo* characteristics such as morphologic appearance, functional capacities, virus susceptibilities, chromosomal composition, and even certain antigenic specificities. Availability of well defined reference cell strains is, therefore, highly desirable.§ Accordingly, we sought to determine whether or not cell strains can be effectively characterized immunologically with special reference to species, individual, or organ of cell strain origin.

2) A striking feature of established cell strains is their capacity for continuous and indefinite propagation. The obvious analogy to the growth of malignant tumors had occasioned speculation as to whether or not established cell cultures have

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†Aided by grants from the National Foundation, National Cancer Institute, and American Cancer Society.

‡Associate Professor, Department of Microbiology

§A national "Cell Culture Collection" is presently being established for those purposes.

Acknowledgments: I acknowledge gratefully many opportunities for discussion with the late Dr. J. T. Syverton—discussions that never failed to produce valuable suggestions. I also wish to thank Mrs. Josephine Brumbaugh, Senior Technician, Department of Microbiology, for her technical help.

malignant properties or potentialities. This possibility precludes the use of established human cell strains for the production of viral vaccines such as Salk's polio vaccine. It is obvious that cancer-biological studies, including immunologic investigations, on tissue and cell cultures of normal and malignant origin may furnish theoretically and practically valuable information, especially regarding cellular indices of malignancy.

3) Since 1957, observations of cell transformation or alteration have attracted much interest. This phenomenon may best be explained by a description of what had happened with the prototype of one class of cell strains. The ERK-1 strain[1] was derived from embryonic rabbit kidney. The primary culture, as usually happens, faded away after five passages. In one culture bottle, however, there appeared a single colony of cells which looked morphologically different, grew very rapidly, and could easily and continuously be subcultivated. These particular cells were found—amazingly—to be fully susceptible to poliovirus infection, although rabbit cells do not normally have such susceptibility. This discovery was considered to have utmost practical importance, since mass cultivation of poliovirus for vaccine production in a non-primate established cell strain now appeared feasible. But was ERK-1 still a real rabbit cell strain? Genetic hypotheses adduced to explain the phenomenon[3] were challenged by the assumption of either cell contamination or "mix-up" of cell cultures. In view of the history of ERK-1 and other strains, it was thought that the primary cultures, while slowly dying away, were outgrown after contamination with cells of an established laboratory cell strain. Clarification of this controversial matter was considered an urgent necessity. Immunologic identification or at least classification of cell strains appeared to be a promising approach.

Experimental Approach

1) We decided to concentrate our main efforts on the demonstration of species-specific antigens in cells. Such a method, we felt, would facilitate cell characterization. Moreover, it promised to help clarify the cell transformation phenomenon: If cell "transformation" did indeed result from cell contamination, then contaminating cells appeared to belong to established cell strains predominantly employed in tissue culture laboratories, *e. g.*, the human HeLa or the mouse "L" cell strains. It was to be expected, therefore, that most "transformed" cell strains independent of their original species could be of either human or mouse species.

2) Detection of species changes in transformed cell strains would not necessarily disprove the genetic hypothesis. If this concept was true, however, lability and variability of cellular species-specificity should be demonstrable under controlled experimental conditions. Findings to the contrary, proving species-specificity to be a stable and permanent characteristic of cells, would strongly favor the contamination hypothesis. With regard to general classification purposes, stability of cellular species-specificity would be the prerequisite for a permanent species label of cell strains. Investigations in this direction, therefore, were considered essential.

Development of a Species-Specific Hemagglutination Test[4,5]

It soon became clear from our work as well as from publications of other authors that conventional serologic procedures such as precipitation, agglutination, and complement fixation, were difficult to apply to immunologic studies on cultured cells. The multiplicity of cellular antigens was so great that direct reactions between cellular material and corresponding antisera were too complex to yield sufficiently specific results for satisfactory evaluation. Not even species-specificity expressed itself unequivocally. Moreover, latent microbial contaminants of cells or culture media, such as pleuro-pneumonia-like organisms,[6] were found to overlap cell-specific reactions considerably. We realized that it would be essential to develop a method able to match specifically those various obstacles in cell-immunology. Among several methodological possibilities, an application of the hemagglutination technique appeared to be promising. Accordingly, cultured cells under investigation were injected into guinea pigs or other laboratory animals. Anti-cell sera were tested for the presence of hemagglutinins against erythrocytes of various species. The species of erythrocytes positively agglutinated were found to correspond to the species of the cultured cells as used for immunization. The main feature of this method was the nonidentity of immunizing antigen (cultured cells) and indicator test antigen (erythrocytes). Furthermore, the antigenic composition of the erythrocyte membrane was assumed to be much simpler than that of a complex cell. Therefore, we expected that it might be possible to define precisely the specificity of this type of hemagglutination reaction.

Study of the literature revealed several reports on incidental findings of hemagglutinins in anti-cell sera, and others. No attempts had been made, however, to determine the exact specificity.

Tests of Specificity[5,8]

After the technique was basically established, optimal test conditions were worked out by trying various modifications. In order to prove the species-specificity of the reaction several experiments were designed:

1) Blood group substances may be present in cultured cells to evoke blood group antibodies. Since certain blood groups are known to overlap species, the possibility of interference had to be excluded:

a) Antisera against various human cell strains were checked in agglutination tests against human erythrocytes of every possible blood group or blood group combination, including Rh-factor. No significant differences in titers were observed.

b) The same antisera were absorbed with blood group O, Rh negative erythrocytes. This resulted in elimination of hemagglutinins for erythrocytes of any blood group.

We concluded that hemagglutinins in anti-cell sera were definitely not blood group antibodies.

2) Pre-immunization sera usually contained low-titered "natural" heterophile hemagglutinins. It therefore appeared advisable not to rely on absolute titers of post-immunization sera in order to evaluate immunization effects, but rather to calculate increase of hemagglutinins by comparing pre- and post-immunization sera in simultaneous titrations.

The following experiment was undertaken to differentiate natural heterophile from cell-induced hemagglutinins: Pre- and postimmunization sera were absorbed a) with homologous erythrocytes, and b) with cultured cells. Erythrocytes were observed to remove hemagglutinins from both pre- and postimmunization sera. Cells, however, removed only cell-induced hemagglutinins from their homologous postimmunization sera. From this observation the following conclusions were drawn: a) Cell-induced hemagglutinins were distinguishable from natural heterophile hemagglutinins; b) Cultured cells did not contain demonstrable heterophile components related to heterophile antigens of erythrocyte membranes; c) Post-immunization sera contained mainly cell-induced hemagglutinins with the pre-immunization level of heterophile antibodies unchanged.

3) Crucial experiments to verify positively the species-specificity of the reaction were performed as follows: Antisera against cells of various species such as man, monkey, rabbit, mouse, hamster, swine, and calf were titrated in hemagglutination tests against erythrocytes from man, monkey, rabbit, mouse, hamster,

swine, calf, sheep, horse, cat, dog, chicken, duck, and other species. Results obtained were clearly species-specific, with only one exception: species-overlapping reactions were regularly recorded between man and monkey, but only occasionally (and almost never in high titers) among the other species tested.

4) In order to distinguish human and monkey species, cross absorption procedures had to be carried out: antisera against human and monkey cells were absorbed with a) human and b) monkey cells. The species-specific antibody fractions were observed to be removed only by cells of the same species. In other words, human cells did not reduce significantly the hemagglutination titer in anti-monkey serum for monkey erythrocytes, and vice versa. The strict species-specificity of this absorption method was thought to be a valuable (in certain instances, even necessary) addition to a routine procedure of species-determination on cultivated cells. Therefore, in comparative studies the technique was improved and simplified.

Species Determination on Transformed and Non-Transformed Cell Strains[8,9]

The problem of cell transformation was investigated by determining the actual species of 17 transformed and 14 nontransformed established cell strains besides numerous primary cell cultures of various species to serve as controls. The method included: a) demonstration of species-specific hemagglutinins in sera of animals after injection of cells under investigation, and b) absorption of species-specific hemagglutinins from anti-cell sera by control cells of known species. The following results were obtained: Twelve transformed cell strains which reportedly were derived from monkey, rabbit, swine, calf, hamster, or duck definitely belonged to human species. The remaining five transformed cell strains, reportedly derived from man or monkey, definitely were mouse cells. As for the 14 nontransformed cell strains, no discrepancy was found between species diagnosis and species of stated origin.

The interpretation of these results, therefore, favored the cell contamination hypothesis rather than the genetic concepts of cell transformation, i.e.: 1) Though transformed cell strains had originated from many different species they were found to be related to only two species, human or mouse; 2) established human and mouse cell strains are the most probable sources of possible contaminations; 3) in individual laboratories multiple cell transformation occurred either to mouse or to human species; 4) there was no indication of possible inductive mechanisms

which might explain these changes. In particular, culture media reportedly did not contain human or mouse specific substances before or during phases of transformation. However, as discussed earlier, the significance of our results largely depended on two factors: a) the stability and permanence of the species-specific hemagglutinogen in cultured cells; b) the sensitivity of our method. The following experiments were concerned with these factors.

Stability of Cellular Species-Specificity[10]

Various approaches were taken in investigating the stability of species-specific antigens:

1) Comparative species determinations were made on original tissues and primary cultures, as well as on established "parent" cell strains and their clonal variants. In addition, sublines of the HeLa strain were kept through some one hundred passages on media containing various heterologous serum supplements such as calf or horse serum. In no instance was the original species-specificity influenced, lost, overlapped, or changed.

2) Similar results were obtained with the mouse L strain. This strain was originated as early as in 1943 from normal mouse skin.[11] After treatment with carcinogens, cells resulted which produced malignancies in mice. This alteration was reflected by marked chromosomal changes to an extent that the L cell-specific idiogram was readily distinguishable from a normal mouse cell idiogram. Nevertheless, parent and clonal L cell strains were still found to carry their mouse-specific antigen labels.

3) HeLa cells were subjected to various treatments, such as X-irradiation, heating up to 80° C., repeated freezing and thawing, and partial trypsinization. Species-specific antigenicity remained qualitatively unchanged.

We concluded that species-specific hemagglutinins in cultured cells are remarkably stable. It appeared highly unlikely that under controlled natural conditions the species label of cells can easily be lost or changed. Cell contamination was therefore declared the most convincing explanation of the cell transformation phenomenon.

Sensitivity of Method[5,9]

In order to determine the sensitivity of this method, the following experiments were performed:

1) An artificial mixture of less than 10 rabbit cells per 10,000 human cells was used for immunization of guinea pigs. The

sera were found to contain both human and rabbit hemagglutinins, suggesting that the method possessed a high degree of sensitivity.

2) Animals were pre-immunized with the transformed rabbit ERK-1 cell strain which actually had been diagnosed as of human species. After about four weeks the animals were divided into two groups and hyperimmunized with a) known human cells or b) known rabbit cells. In animals hyperimmunized with human cells, a secondary type of antibody response occurred as the titer of human hemagglutinins rose rapidly within a few days. In animals hyperimmunized with rabbit cells, a primary type of response with slow increase of rabbit hemagglutinins at the end of the second week was observed, indicating no presensitization to rabbit antigens. Control animals showed convincingly that presensitization with minute amounts of rabbit cell antigen would have been detected in this type of "cross-hyperimmunization" experiment.

Work of Others

Results and conclusions described in the foregoing account have been supported by several authors.[12] Their work was based in part on immunologic techniques as well as transplantation experiments, mixed cell agglutination, and application of fluorescent antibodies. Strong support has come from chromosomal studies. Clausen[13] in our department and other authors have been able to obtain unequivocal species-specific results which are in agreement with those obtained by immunologic techniques. Identification of cell strains by determination of the spectrum of viral susceptibilities has been used by several investigators. However, these characteristics are biologically too variable to justify decisive conclusions.[14]

The Present Problem: Cell Contamination Within Species

Undoubtedly, contaminations of cell cultures with established cells of a different species have occurred with remarkable ease and frequency. This observation would seem to justify the expectation that certain "transformed" cell strains, though unchanged in species, might nevertheless stem from contamination with established cells of the same species. This possibility can be suspected especially for some transformed human cell strains, since established human cells evidently represent the most likely source of contamination. Examples of contamination of mouse cell cultures with mouse L-cells have already been demonstrated,[15] based on strain-specific chromosome markers of L-cell lines.

Preliminary studies designed to attack the problem by immunologic means are reportedly under way in several laboratories,[15] as well as in this department.

The Nature of Species-Specific Hemagglutinogens in Cells[10,17]

Investigations to be described in the concluding part of this report were concerned with problems of theoretical interest. The first series of experiments aimed at investigating the chemical nature of species-specific hemagglutinogens in cells. Whereas a direct analysis appeared difficult, an indirect approach involving investigation of species-specific erythrocyte receptors turned out to be fruitful. Erythrocytes were treated with trypsin, papain, or periodate. Treated and untreated erythrocytes were comparatively evaluated in agglutination and absorption tests with anti-cell, blood-group specific, and heterophile hemagglutinating sera. The following results were obtained:

a) Hemagglutination titers of anti-cell sera decreased when erythrocytes were treated with trypsin or papain, but remained unaffected when erythrocytes were treated with periodate. With anti-A control sera and heterophile pre-immunization sera, the pattern was reversed: erythrocyte treatment with trypsin or papain caused increase, and use of periodate caused decrease of hemagglutination titers.

b) Absorption of anti-cell sera with untreated or periodate-treated erythrocytes eliminated species-specific hemagglutinins, while absorption with trypsin- or papain-treated erythrocytes was relatively ineffective. Again, opposite results were observed with anti-A and heterophile sera.

It was concluded that heterophile and blood group reactions take place on receptor components of carbohydrate nature. Species-specific antibodies in anti-cell sera, however, appeared to be directed against proteinaceous receptor substances of erythrocytes. Hence, it was inferred that the evocative cellular antigens also are proteins. Detailed analyses of our results suggested further that the species-specific erythrocyte receptor substance consists of at least two antigenetically distinct components with differing susceptibilities to enzymatic treatment.

The Location of Species-Specific Hemagglutinogens in Cells[10]

Attempts to locate species-specific hemagglutinogens in cells were carried out in the following way: Cells were mechanically disrupted, and the nuclear, mitochondrial, microsomal, and sol-

uble fractions were separated. The cell fractions were completely homogenized and then examined for their capacity to inhibit homologous species-specific hemagglutination, and for their protein content. (The principle of the species-specific hemagglutination inhibition test is that cellular fractions are admixed in various dilutions to the reaction between anti-cell serum and homologous erythrocytes. The highest dilution of cellular material preventing species-specific hemagglutination represents the "titer.") It was found that every cell fraction was capable of inhibiting species-specific hemagglutination. Inhibition titers and protein contents appeared to have a close quantitative correlation. Nuclear fractions possessed the weakest inhibiting power, corresponding to their low protein content. It was concluded that proteins throughout the cell may be carriers of species-specific hemagglutinogenic activity.

Comparative experiments have been carried out with cells which were pre-treated with papain in order to remove peripheral parts of cellular cytoplasm. It was clearly demonstrated that cellular species-specific hemagglutinogens are equally distributed throughout the cytoplasm without accumulation in the cell surface region.

Summary

1) An immunologic method was developed for species determination of cultivated mammalian cells.

2) The method was proved to possess high degrees of sensitivity and specificity.

3) Species-specificity was demonstrated to be a stable characteristic of cells.

4) Classification of cell cultures according to species is, therefore, considered a valuable aid for "Cell Bank" purposes.

5) Cell "transformation" with resultant species change is postulated as being caused by cell contamination rather than by a genetic process.

6) Species-specific receptors of erythrocytes as well as hemagglutinogens in cells are proteins.

7) Proteins located throughout the cell, including the nucleus, carry species-specific hemagglutinogenic activity.

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Medical School News

$8 MILLION IN RESEARCH GRANTS AWARDED

A dozen major grants for medical research have been received recently by the Medical School and its individual faculty members, underlining again the national reputation enjoyed by the University of Minnesota in the field of medical research and experimentation.

In recent months more than $8,100,000 was awarded to finance the following projects:

ROBERT A. GOOD

• A U. S. Public Health Service grant of more than $3.1 million was committed to establish a seven year program in heart disease research. Major part of the program will be the establishment of a cardiovascular clinical research center, with new equipment and up to two dozen new professors, assistant professors, research professors, and technicians. The "center" will be integrated within existing departments of the Medical School already engaged in heart research. Dr. Robert A. Good, Professor of Pediatrics, will be scientific director.

• A seven-year U.S.P.H.S. grant for $200,000 for continued research in rheumatic fever and rheumatic heart disease. Dr. Lewis W. Wannamaker, American Heart Association career investigator and Professor of Pediatrics, is directing the project.

• A National Science Foundation grant of $20,000 to cover two years' research on "Ion Fluxes in Heart Muscle" by Dr. Victor Lorber, American Heart Association career investigator and Professor of Physiology.

• A $20,786 U.S.P.H.S. grant to Dr. Lloyd D. MacLean, Associate Professor of Surgery, for study of "Distribution of Blood Flow to the Heart."

• A $16,170 U.S.P.H.S. grant to Dr. Naip Tuna, Assistant Professor of Medicine, for "Fatty Acid Metabolism and Atherosclerosis" studies.

• A $15,907 U.S.P.H.S. grant for "Electron Microscopy of Human Skin and Cutaneous Tumors" by Dr. Alvin S. Zelickson, Instructor in Medicine.

• Dr. William G. Kubicek, Professor of Physical Medicine and a University colleague received a $75,869 research contract from the U.S. Air Force for a medical electronic project aimed at developing a rapid, convenient method of measuring cardiac output.

• A U.S.P.H.S. grant of $438,071 to help build and equip psychiatric, neurologic, and pediatric research facilities in Diehl Hall, the University's new bio-medical library.

• A seven-year grant totaling $418,950 from U.S.P.H.S. for long range basic research into oxidative phosphorylation. Dr. Paul D. Boyer, Professor of Physiological Chemistry, will conduct a study of the production by the body cells of a new substance called adenosine triphosphate, used within the body for many vital cellular functions.

• Establishment of a major rehabilitation-research-training center by the Office of Vocational Rehabilitation at the University of Minnesota under a $2.5 million grant covering five years. Director of the center will be Dr. Frederic J. Kottke, Professor and Head of the Department of Physical Medicine. Much of the research will be conducted at the Sister Elizabeth Kenny Rehabilitation Institute.

F. J. KOTTKE

• A U.S.P.H.S. grant of $1.2 million for five years to establish a neurological research center for the study of cerebrovascular disease. Dr. Maynard M. Cohen, Professor of Neurology and director of the center, said the grant will enable the University to nearly triple the amount of neurological studies previously done in basic research into strokes, mental deterioration, and involvements of the nervous system.

MAYNARD M. COHEN

• Research grants totalling $129,651 were received from the American Cancer Society. Recipients were Dr. Norman B. Ackerman, Dr. John J. Bittner, Dr. Edgar L. Makowski, Dr. Carlos Martinez, and Dr. Samuel Schwartz.

Medical Foundation News

N. L. GAULT ELECTED SECRETARY-TREASURER OF MEDICAL FOUNDATION

Trustees of the Minnesota Medical Foundation have elected Dr. N. L. Gault, Jr., to the post of Secretary-Treasurer. An Assistant Dean of the Medical School, Dr. Gault will serve a one-year term succeeding Dr. John A. Anderson, now on sabbatical leave in Sweden. Dr. Gault formerly served in the same capacity for the Foundation.

N. L. GAULT, JR.

Meeting October 25, the Trustees also accepted the trusteeship and administration of a fund to be raised by the Minneapolis Society of Internal Medicine. Using funds contributed by members and friends, the Society will sponsor an annual research award of $500.00 to be given for the most outstanding research achievement by a physician in graduate clinical training in any clinical department of the Medical School, including the departments of Pathology and Laboratory Medicine.

The award will be designated as the "Watson Award," in honor of Dr. Cecil J. Watson, Professor and Head of the Department of Internal Medicine at the University, and selection of the recipient will be a function of the Medical School administration, in cooperation with the Society.

The Society will sponsor the award from current funds each year, with the objective of ultimately endowing the award, according to Dr. Alvin Schultz, president. The award is aimed at strengthening the research program of the Medical School by recognizing and rewarding physicians in graduate clinical training who actively pursue medical research as part of their medical education.

Dr. Arnold Lazarow, president of the Foundation, said the Foundation was pleased to serve as Trustee of the Watson Award fund, as part of its objective of advancing medical education and research at the University of Minnesota.

HERMAN E. DRILL RECEIVES OUTSTANDING ACHIEVEMENT AWARD

"Don't forfeit what you stand for in Medicine, out of Apathy or by Default!"

With those words, Dr. Herman E. Drill, Hopkins, Minn., accepted the University of Minnesota's Outstanding Achievement Award at special ceremonies held Oct. 27, 1961. The 58-year-old physician, cited for "noted professional attainment," became the 30th Medical School graduate to receive the honor. The gold medal and citation were presented by Dr. Charles W. Mayo, Rochester, Minn., who has since been elected chairman of the University's Board of Regents. Only 350 of the University's 160,000 degree-holders have been named recipients of the Outstanding Achievement Award.

HERMAN E. DRILL

Before a Medical Alumni Association homecoming reunion throng which included Mrs. Drill and sons Frederick (Med. '56), and David (Med. '59), Dr. Drill declared it a privilege to be counted as an alumnus of the Medical School. "I have been proud of my preceptors and peers for the many, and often great, contributions they have made to the advancement of medicine and science," he said. "From the day I graduated I always have felt an obligation and sense of duty to the University, and especially to the Medical School. Medicine has been good to me; the community I have lived in has been good to me; and my friends in the Medical Alumni Association and the Medical School have been good to me. I am happy to share this honor with them."

Dr. Drill, a graduate of the Class of 1928, is a past president of the Minnesota Medical Alumni Association and the Minnesota Medical Foundation. He has served for several years as president of the Hennepin County Tuberculosis Association, and Hopkins city health officer. He is especially recognized for his concern for all aspects of medical education and practice in Minnesota, and in the nation.

GEORGE E. FAHR PROGRAM ANNOUNCED

HOWARD SPRAGUE

Dr. Howard B. Sprague, Brookline, Mass., one of America's leading cardiologists, will be the main speaker at the banquet climaxing Dr. George Fahr's 80th Birthday Testimonial January 27th.

Dr. Sprague's address, titled "Dr. George E. Fahr and His Era," will highlight a formal dinner at the Minneapolis Club, and will follow the presentation of an oil portrait of Dr. Fahr, commissioned and painted for the observance. Dr. Robert B. Howard, Dean of Medical Sciences, will accept the portrait for the University. It will be hung at the Medical School in recognition of Dr. Fahr's 40-year teaching career at the institution.

GEORGE E. FAHR

Hundreds of his friends, former students, and colleagues are participating in the observance. A committee headed by Dr. A. C. Kerkhof has planned the event, which includes a full day of scientific sessions at the Mayo Auditorium, featuring fifteen papers written and presented by former students of Dr. Fahr.

Contributions are still welcome and may be made payable and sent to the Minnesota Medical Foundation, 1342 Mayo Memorial Building, University of Minnesota, Minneapolis 14, Minn. Donors of $30.00 or more will receive a hard-cover *festschrift* containing all papers presented at the meeting, as well as Dr. Fahr's life story, and a full color reproduction of the painting. Dinner reservations should be made with Dr. Kerkhof, 601 Medical Arts Building, Minneapolis 2, Minn.

A. C. KERKHOF

Dr. Sprague is a past president of the Massachusetts and American Heart Association. He is a former lecturer in medicine at Harvard Medical School, from which he graduated in 1922.

SCIENTIFIC PROGRAM

Mayo Memorial Auditorium
University of Minnesota

MORNING SESSION – 9:00 a.m.

O. L. NORMAN NELSON, M.D., *Chairman*

1. *Hypothyroid Heart Disease*
   DAVID L. FINGERMAN, M.D. Minneapolis, Minn.
2. *Relative Hypoglycemia (A Clinical Review of 350 Cases)*
   MARTIN C. BUEHLER, M.D., Dallas, Texas
3. *Colorado Tick Fever: A Study of the Natural History of the Virus*
   CARL M. EKLUND, M.D., Hamilton, Montana
4. *Life Insurance and Medical Research*
   HARRY E. UNGERLEIDER, M.D., New York, N. Y.
5. *Clinical Value of Left Axis Deviation in the Electrocardiogram: A Renaissance*
   HOWARD B. BURCHELL, M.D., Rochester, Minn.
6. *Surgical Treatment of Stokes-Adams Syndrome by Pacemaker Implantation*
   C. WALTON LILLEHEI, M.D., Minneapolis, Minn.
7. *The Urobilin Problem – A Semi-historical Survey*
   CECIL J. WATSON, M.D., Minneapolis, Minn.

AFTERNOON SESSION – 2:00 p.m.

REUBEN BERMAN, M.D., *Chairman*

8. *The Problem of Immunological Deficiency*
   ROBERT A. GOOD, M.D., Minneapolis, Minn.
9. *The Effect of Fibrinolytic Agents on Experimental Myocardial Infarction*
   JOHN S. LaDUE, M.D., New York, N. Y.
10. *Simultaneous Measurements of Work, Heart Production, and Oxygen Consumption by the Working Mammalian Heart*
    MAURICE B. VISSCHER, M.D., Minneapolis, Minn.
11. *Our Teachers*
    OWEN H. WANGENSTEEN, M.D., Minneapolis, Minn.
12. *Surgically Correctible Hypertension of Renal Origin, with Case Reports*
    RICHARD L. VARCO, M.D., Minneapolis, Minn.
13. *The Correlations of Dermatology and Cardiology*
    ROBERT R. KIERLAND, M.D., Rochester, Minn.
14. *The Dilemma of the Full-Time Instructor in Medicine*
    GEORGE N. AAGAARD, M.D., Seattle, Wash.
15. *A Wonderful Year*
    CHARLES E. REA, M.D., St. Paul, Minn.

Medical Alumni News

Dr. Virgil J. P. Lundquist, (second from right) showed guests at the Medical Alumni Association Homecoming Reunion the slide pictures of the Medical Student Center Project scheduled to be built next year at the University of Minnesota Medical School. Dr. Lundquist is chairman of the project. Onlookers (left to right) include Dr. H. E. Drill (Med. '28), Dr. Robert B. Howard (Med. '43), Dean of the College of Medical Sciences, Dr. Charles W. Mayo, Choirman, Boord of Regents, University of Minnesota, Mr. Eivind Hoff, Jr., Executive Secretary, Minnesota Medical Foundation, Dr. Lundquist, and Dr. Sheldon M. Lagaard, President, Minnesota Medical Alumni Association.

MEDICAL ALUMNI IN HOMECOMING FETE

Members of the Minnesota Medical Alumni Association held their Annual Meeting, Dinner-Dance and Homecoming Reunion Oct. 27, 1961, at the Radisson Hotel, Minneapolis. One hundred fifty one alumni and guests attended, including two dozen members of Class of 1936, University of Minnesota Medical School, who were honored on the 25th anniversary of their graduation.

Dr. Charles J. Beck (Med. '40), St. Paul, and Dr. Charles Haberle (Med. '45), Dr. John W. LaBree (Med. '40), and Dr. James C. Mankey (Med. '43), all of Minneapolis, were elected to three year terms on the Board of Trustees.

At a subsequent meeting of the Board on Nov. 21, Dr. Charles J. Beck was elected President of the Minnesota Medical Alumni Association. Other new officers are Dr. Neil Palm, St. Paul, (Med. '50), 1st Vice President; Dr. James C. Mankey, Minneapolis, (Med. '43), 2nd Vice President; Dr. Robert Hugh Monahan, St. Paul (Med. '42), Secretary; and Dr. Duane C. Olson, Minneapolis, (Med. '37), Treasurer.

The Silver Aniversary observance for the Class of 1937 will be held Friday, October 19, 1962, at the Radisson Hotel, Minneapolis. Co-chairmen of the event are Dr. Lyle Hay and Dr. Lloyd F. Sherman, Minneapolis.

The annual Senior-Alumnus luncheon will be held May 3, 1962, in Coffman Memorial Union at the University.

MEDICAL SCHOOL ENROLLMENT

A total of 527 students were enrolled at the Medical School of the University of Minnesota during the Fall Quarter, 1961, including a full quota of 145 freshmen. In only one other year in the Medical School's 73-year history have there been this many freshmen students.

There were 125 sophomores, 135 juniors, and 122 seniors included in the student body, which is exceeded in size by only seven of the 86 U.S. medical schools. Relatively fewer of the nation's college graduates have gone into medical training since World War II. Minnesota, however, has counted an increase in applications for its freshman class each year since 1958, and plans to accommodate a freshman class of 150 students in the near future.

Student News

The Medical School Student Council has been organized for 1961-62. Thomas Crowley, a senior, is president, Quentin Anderson, a senior, is vice president, and Allen Larson, a junior, is Secretary-Treasurer. Members-at-Large include Keith Burnes, senior; James H. Quakenbush and Bruce Jensen, juniors; William B. Torp, Eugene Bagley, Donald Oines, Dick Siebert, Ralph Bergstrom, and Robert Van Tassel, sophomores; and John Barry, Alexander Janes, and James Good, freshmen.

DR. JONAS SALK GIVES A.O.A. LECTURE

Dr. Jonas Salk, discoverer of the polio vaccine which bears his name, was guest lecturer of Alpha Omega Alpha, honorary medical fraternity, at the University of Minnesota Nov. 16. The distinguished University of Pittsburgh researcher and professor is shown (center) with Charles Drage, president, and Margaret Grunnet, secretary, of the Minnesota Chapter, A.O.A. He lectured on "Humanities from the Viewpoint of a Biologist," before a capacity audience at the Mayo Auditorium, and was an honored guest at the A.O.A. initiation banquet that evening. Dr. W. Albert Sullivan, Jr., Associate Professor of Surgery, was elected a faculty member of A.O.A., and twenty medical students were initiated as members. They are: Joseph S. Emond, Jr., Paul F. Engstrom, Stanley A. Gall, Bruce D. Howard, Roger J. Jackman, Woldemar G. Johanson, Eugene S. LaPlante, Ronald L. Logemann, Douglas Mair, Paul E. Mertens, Lawrence B. Pearson, Laurence S. Rivkin, Albert H. Roth, Barbara Williamson Goksen, Richard A. Willson, Robert C. Wood, Charles W. Decker, Dennis D. Jacobsen, H. Thomas Hobday, and James H. House.

Alumni Notes

◆ 1912

Ralph T. Knight received the Distinguished Service Award of the American Society of Anesthesiologists on Oct. 26th in Los Angeles, Calif. He headed the University of Minnesota's Department of Anesthesiology from its inception in 1920 until his retirement in 1954. The Ralph T. Knight Anesthesiology Research Laboratories in Diehl Hall at the University of Minnesota Medical Center were dedicated in his honor last February.

◆ 1918

Lester D. Powell has been promoted to the rank of full professor in the Department of Medicine at the State University of Iowa, Iowa City, Iowa.

◆ 1925

Ejvind P. Fenger was appointed Minnesota state director of tuberculosis services. Dr. Fenger, 64, has been associated with the Glen Lake (Minn.) sanatorium for the past 35 years, and is a clinical assistant professor of medicine at the Medical School.

SUMNER S. COHEN

◆ 1927

Sumner S. Cohen, veteran tuberculosis fighter, was appointed medical director of the nursing home and tuberculosis treatment center, which is being transferred from Walker, Minn. to Glen Lake, Minn. Dr. Cohen will also continue the private practice of medicine in Minneapolis.

◆ 1928

Herman E. Drill, Hopkins, Minn. general practitioner, was reelected president of the Hennepin County (Minneapolis) Tuberculosis Association.

◆ 1929

E. G. Hubin was elected president of the Medical Staff of Pine County Memorial Hospital, Sandstone, Minn.

◆ 1935

Clifford O. Erickson of Minneapolis was elected president of the Minnesota Psychiatric Society.

◆ 1936

GEORGE N. AAGAARD

George N. Aagaard, Dean and Professor of Medicine at the University of Washington School of Medicine, Seattle, Wash., has been appointed a member of the National Advisory Heart Council by Dr. Luther L. Terry, surgeon general of U. S. P. H. S. He will serve a four year term. He is current president of the Association of American Medical Colleges.

◆ 1937

Lyle J. Hay is serving as president of the Minnesota Division, American Cancer Society. Newly elected Directors of the Division include Dr. W. F. Nordman, Mora (Med. '29), Dr. Melvin B. Sinykin, Minneapolis (Med. '35), Dr. N. Logan Leven, St. Paul (Med. '27), and Dr. Frederick Owens, Jr., St. Paul.

JOHN B. MOYER

◆ 1943

John B. Moyer, Duluth cardiologist, was elected president of the Minnesota Heart Association. He will serve until September, 1962.

Col. John P. Stapp, associated with the Aerospace Medicine program at Brooks Air Force Base, Texas, was a main speaker at the fifth Stapp Automotive Crash and Field Demonstration conference held Sept. 14-16 at the University of Minnesota. The annual conference, originated by and named after Col. Stapp, is designed to study means of reducing automobile deaths and injuries through improved safety engineering. Col. Stapp is a holder of the University of Minnesota's Outstanding Achievement Award.

◆ 1944

John I. Coe, chief of pathology at Minneapolis General Hospital, was named a diplomate in forensic pathology by the American Board of Pathology. He is the first pathologist in Minnesota to pass the tests in legal pathology recently instituted by the Board. He became a diplomate in general pathology in 1950.

◆ **1946**

Harold O. Perry, a member of the Mayo Clinic staff since 1953, was awarded the bronze medal of the Southern Minnesota Medical Association on Sept. 11. His report on "Ichthyosis and Loss of Hair Following the Administration of Triparonal (MER-29), was judged best given at the Association's 1961 annual meeting.

◆ **1953**

Arnold M. Berg of Roseau, Minn. announces his association in practice at the Roseau Clinic with Dr. John J. Gisvold.

◆ **1954**

Richard H. Meyer is now associated at Faribault, Minn. with his father, Dr. Paul F. Meyer (Med. '22), and brother, Dr. Robert F. Meyer (Med. '47) in the practice of medicine and surgery.

◆ **1956**

Jack E. Wall is now associated with Dr. R. T. Seashore and Dr. K. W. Teich at Duluth, Minn. in the practice of Obstetrics and Gynecology. He completed a three-year residency at University Hospitals and the Fargo, N.D. Clinic before moving to Duluth.

Lt. Abel R. Ellingson is now in duty as a medical officer at the Naval Hospital, National Naval Medical Center, Bethesda, Md.

◆ **1957**

John E. Mulvahill has begun the private practice of psychiatry at 824 Marquette Bank Building, Minneapolis, Minn. He is also on the clinical teaching staff in psychiatry at Minneapolis General Hospital, and is serving as a consultant at Hastings (Minn.) State Hospital.

◆ **1958**

Lt. Roger A. Meyer has received his discharge from the Medical Corps of the U. S. Navy.

Floyd J. Swenson will begin a residency in orthopedic surgery on Jan. 1, 1962 at the Mayo Clinic. He has been associated with the Lenont-Peterson Clinic in Cook, Minn.

◆ **1960**

Richard G. Rowe has entered into practice in Littlefork, Minn., in association with Dr. R. A. MacDonald (Med. '46).

Roger D. Morse has joined his father in practice at LeRoy, Minn.

James Knapp has become associated with the Detroit Lakes, (Minn.) Clinic.

Louis A. Vontver is now with the U. S. Air Force Medical Corps in the Pacific area. His address is Capt. Louis A. Vontver, U. S. A. F. Hospital, Detachment 5, A.P.O. 99, San Francisco, Calif.

Memorial Gifts

Memorial gifts to the Minnesota Medical Foundation have been received recently in memory of:

Mr. Ray J. Quinlivan
St. Cloud, Minn.

Mr. Isaac Moskowitz
Los Angeles, Calif.

Dr. Ben Sommers
St. Paul, Minn.

Mrs. Clinton T. Johnson
St. Paul, Minn.

Memorial contributions are a practical means of honoring the memory of a friend or loved one, while helping the Minnesota Medical Foundation in the advancement of medical education and research. Appropriate acknowledgements are promptly sent to both donor and family of the deceased.

ALUMNI DEATHS

◆ **1903**

Dr. Frederick C. Schuldt, St. Paul, died August 17, 1961 at the age of 85. He had retired in 1945 after practicing thirty years, and was a past president of the Ramsey County (St. Paul) Medical Society.

◆ **1905**

Dr. Joseph Patrick Kane died June 16, 1961 at the VA Hospital in Palo Alto, Calif. He formerly practiced in Tacoma, Wash., where he was a past president of the Pierce County Medical Society. A veteran of World War I, Dr. Kane died of cancer at the age of 88 years.

◆ **1923**

Dr. Richard Stanley Ahrens, Hot Springs, Ark., died July 1, 1961 of a cerebro-vascular accident. He was 67 years old, and a practicing psychiatrist.

◆ **1925**

Dr. John Dordal, Sacred Heart, Minn., died July 20, 1961 after an illness of six months. He was 71 years old. Dr. Dordal was a member of many medical societies and active in community affairs in Sacred Heart.

◆ **1937**

Dr. Ben Sommers, widely known St. Paul, Minn. cardiologist, collapsed and died of a heart attack on October 18, 1961. At the time of his death he was teaching a Medical School class in cardiology at Ancker Hospital. Dr. Sommers was 51 years old, and a diplomate of the American Board of Internal Medicine.

◆ **1939**

Dr. Russell George Barnes, Jr., Medford, Ore., died July 13, 1961 of cancer at the age of 46 years. He was a member of the American Academy of General Practice, and veteran of World War II.

◆ **1942**

Dr. Max Marcus Tenen of Downey, Calif. died May 11, 1961 at the age of 45 years. He had interned at Minneapolis General Hospital, and was a resident physician there and at the University Hospitals.

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The Medical Student Center Project is a special account of the Minnesota Medical Alumni Association, Inc. Gifts to the project are designated wholly to use by the University of Minnesota and are deductible for tax purposes.

Coming Events

University of Minnesota Medical School

List of Continuation Courses for Physicians

University of Minnesota
Center for Continuation Study

1962

All Year	Cancer Detection for General Physicians
January 2-6 . . .	Intermediate Electrocardiography for General Physicians and Specialists
February 12-14 . .	Pediatric Neurology
March 5-7 . . .	Anesthesia for General Physicians
March 16-17 . . .	Treatment of Traumatic Injuries
April 12-14 . . .	Otolaryngology for General Physicians
April 16-18 . . .	Internal Medicine for Internists
April 26-28 . . .	Surgery for Surgeons
April 30-May 2 . .	Gynecology for General Physicians
May 7-9	Ophthalmology for Specialists
May 14-18 . . .	Proctology for General Physicians
May 31-June 2 . .	Psychiatry for General Physicians

The University of Minnesota reserves the right to change this schedule without notification.

Courses are held at the Center for Continuation Study or the Mayo Memorial Auditorium on the campus of the University of Minnesota. Usual tuition fees are $30 for a two-day course, $50 for a three-day course, and $75 for a one-week course.

Specific announcements are sent out about two months prior to each course to all members of the Minnesota State Medical Association and to any physicians who request information for a specific course. For further information write to:

DIRECTOR
DEPT. OF CONTINUATION MEDICAL EDUCATION
THE MEDICAL CENTER
UNIVERSITY OF MINNESOTA
MINNEAPOLIS 14, MINNESOTA

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A Word About

Memorial Gifts

The Minnesota Medical Foundation welcomes your memorial contributions when an appropriate occasion arises. Memorial gifts serve the living and pay thoughtful tribute to the memory of a friend or relative.

The Foundation will promptly acknowledge your gifts to both the donor and the family of the deceased. The gift will help finance the Foundation's program for the advancement of medical education and research. The Medical School at the University of Minnesota will be the direct beneficiary.

Gifts should be sent to the **Minnesota Medical Foundation, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14, Minn.**