

UNIVERSITY OF MINNESOTA

# Medical Bulletin

OFFICIAL PUBLICATION OF THE

UNIVERSITY OF MINNESOTA HOSPITALS

THE MINNESOTA MEDICAL FOUNDATION

AND THE MINNESOTA MEDICAL ALUMNI

ASSOCIATION

IN THIS ISSUE:

*Studies on Experimental  
Shock*

*Modern Bronchology*

*Problems of Illegitimacy*

MAY 1951

NUMBER 13

VOLUME XXX

# University of Minnesota Medical Bulletin

## *Editor*

W. ALBERT SULLIVAN, JR., M.D.

## *Associate Editors*

E. B. BROWN, Ph.D.

VIRGIL J. P. LUNDQUIST, M. D.

WILLIAM F. SCHERER, M.D.

WESLEY W. SPINK, M.D.

EUGENE L. STAPLES

ALAN THAL, M.D.

ROBERT A. ULSTROM, M.D.

LEE WATTENBERG, M.D.

## *Copy Editor*

ELLEN Y. SIEGELMAN

---

## ***University of Minnesota Medical School***

J. L. MORRILL, *President, University of Minnesota*

ROBERT B. HOWARD, M.D., *Dean, College of Medical Sciences*

N. L. GAULT, JR., M.D., *Assistant Dean*

H. MEAD CAVERT, M.D., *Assistant Dean*

## ***University Hospitals***

RAY M. AMBERG, *Director*

## ***Minnesota Medical Foundation***

HERMAN E. DRILL, M.D., *President*

ARNOLD LAZAROW, M.D., *Vice-President*

N. L. GAULT, JR., M.D., *Secretary-Treasurer*

## ***Minnesota Medical Alumni Association***

VIRGIL J. P. LUNDQUIST, M.D., *President*

SHELDON M. LAGAARD, M.D., *First Vice-President*

CHARLES J. BECK, M.D., *Second Vice-President*

NEIL M. PALM, M.D., *Secretary*

JAMES C. MANKEY, M.D., *Treasurer*

---

UNIVERSITY OF MINNESOTA

# Medical Bulletin

OFFICIAL PUBLICATION OF THE UNIVERSITY OF MINNESOTA HOSPITALS, MINNESOTA MEDICAL FOUNDATION, AND MINNESOTA MEDICAL ALUMNI ASSOCIATION

---

VOLUME XXX

May 1, 1959

NUMBER 13

---

## CONTENTS

### STAFF MEETING REPORTS

*Studies on Experimental Shock: Production of Ischemic Necrosis of the Skin by an Intradermal Injection of Endotoxin or Vasopressor Amine*

CARL G. EVERS, B.S. . . . . 418

*Modern Bronchology*

ROBERT E. PRIEST, M.D., JAMES A. DONALDSON, M.D.,

JOHN R. HILGER, M.D., RICHARD R. LUND, M.D. . . . . 431

*Social, Legal, and Medical Aspects in Illegitimacy*

MRS. ELIZABETH NOWICKI, M.S.,

MR. JAMES N. BRADFORD, L.L.D., IRWIN H. KAISER, M.D. . . . 442

MEDICAL SCHOOL ACTIVITIES . . . . . 454

FACULTY PUBLICATIONS . . . . . 455

---

Published semi-monthly from October 15 to June 15 at Minneapolis, Minnesota

# Staff Meeting Report

## Studies on Experimental Shock:

### Production of Ischemic Necrosis of the Skin by an Intradermal Injection of Endotoxin of Vasopressor Amine\*†

Carl G. Evers, B.A.‡

#### INTRODUCTION

In 1928 Shwartzman<sup>1</sup> reported the production of cutaneous hemorrhagic necrosis in rabbits by an intradermal and an intravenous injection of bacterial filtrates. Since then, it has been shown that many substances, injected intradermally, are capable of producing similar lesions if given in association with an intravenous injection of Gram-negative endotoxin.<sup>2,3</sup> It has been demonstrated also that the administration of substances such as heparin<sup>4</sup> or nitrogen mustard<sup>5,6</sup> inhibits the development of the dermal lesion.

In 1956 Thomas<sup>7</sup> reported that dermal hemorrhagic lesions resembling the cutaneous Shwartzman lesion could be produced in rabbits by: (1) an intravenous injection of endotoxin followed by an intradermal injection of epinephrine or levarterenol, or (2) an intradermal injection of a mixture of endotoxin and epinephrine.

Zweifach, Nagler, and Thomas<sup>8</sup> described also an altered state of reactivity of the vessels of the rat meso-appendix to topical epinephrine following an intravenous injection of endotoxin. The results of these studies led these investigators to postulate that endotoxin altered the reactions of blood vessels to epinephrine in such a manner that the hormone became capable of producing necrosis.

In 1958 Gatling<sup>9</sup> reported the production of hemorrhagic skin lesions in rabbits by an intradermal injection of epinephrine or levarterenol following an intravenous injection of horse serum to which the animals previously had been sensitized. This investigator postulated that circulating antigen and its antibody were necessary for the production of the lesion, and he presented data identifying the lesion with that of the Arthus phenomenon.

In 1959 Anderson and Brunson<sup>10</sup> described certain lesions pro-

\*This report was given at the Staff Meeting of the University of Minnesota Hospitals on April 10, 1959.

†This study was made in conjunction with the Department of Pathology, University of Minnesota Medical School.

‡Senior medical student

duced in rabbits subjected to acute rotational stress. They showed that the lethality, as well as the incidence and severity, of the lesions was increased greatly if the shock procedure was carried out in conjunction with an intravenous injection of endotoxin. It was suggested that these effects were mediated through adrenal medullary hormones.

The present paper reports the results of a series of experiments in which cutaneous necrosis developed in rabbits given an intradermal injection of endotoxin or a vasopressor amine in conjunction with rotational shock. These lesions, while similar in some respects to those described by Thomas<sup>7</sup> and Gatling,<sup>9</sup> exhibit striking differences in other respects, as will be described.

#### MATERIALS AND METHODS

Hybrid albino rabbits of both sexes weighing approximately 1.5 kilograms, were used in the study. They were fed Purina® rabbit pellets and were given free access to water.

The animals were subjected to a 15-minute period of rotation in a modified Noble-Collip drum<sup>11</sup> (450 revolutions). The drum was modified to the extent that it had no baffles, and was padded with foam rubber to reduce trauma. This duration of rotation, as described previously,<sup>10</sup> produced a state of marked prostration and shock in the animals.

In conjunction with rotation in the drum, the animals were given an intradermal injection of endotoxin or a sympathomimetic amine. For this purpose the abdominal hair was depilated—in most cases prior to drum rotation—using the method described by Pitesky and Last.<sup>12</sup> (No significant differences in the dermal lesions were observed between those depilated before and those depilated after rotation.) In most of the animals two test substances were injected at separate sites on the abdomen.

Endotoxin, epinephrine, and levarterenol were used in the initial studies. The endotoxin consisted of the lipopolysaccharide fraction derived from *E. coli* (0:111 B4) obtained from Difco Laboratories, Detroit, Michigan. Dilutions were made in sterile, isotonic, pyrogen-free saline solution and given in amounts of 100  $\mu$ g. in a volume of 0.2 ml. The epinephrine and levarterenol were given in dosages of 100  $\mu$ g. in a volume of 0.1 ml. Two groups of control animals were used: One was given intradermal injections of the test substances without being subjected to rotation; the other was given an intradermal injection of 0.2 ml. sterile isotonic saline solution in conjunction with drum rotation.

## THE MEDICAL BULLETIN

In later studies a variety of other substances was used. These included phenylephrine (Neosynephrine®), ephedrine sulfate, isopropylarterenol (Isuprel®), heparin, nitrogen mustard, and certain phenothiazine derivatives. The use of these materials is described in the text which follows.

### EXPERIMENTAL RESULTS

#### *Effects of Intradermal Endotoxin, Epinephrine, or Levarterenol in Rabbits Subjected to Rotational Shock*

The results obtained by an intradermal injection of Gram-negative endotoxin, epinephrine, or levarterenol are summarized in Table 1. The figures in the table include only those animals which survived longer than four hours after rotation. As shown, cutaneous necrosis developed in a high percentage of the animals given the test substances simultaneously with onset of rotation. No lesions were produced in control animals given only intradermal endotoxin, epinephrine, or levarterenol, or in those given intradermal saline solution simultaneously with drum rotation.

TABLE 1  
INCIDENCE OF CUTANEOUS NECROSIS IN RABBITS GIVEN  
INTRADERMAL INJECTIONS OF ENDOTOXIN, EPINEPHRINE,  
OR LEVARTERENOL SIMULTANEOUSLY WITH ROTATIONAL SHOCK

Material Injected	Number of Animals	Dermal Necrosis
Endotoxin	30	21 (70%)
Epinephrine	14	10 (71%)
Levarterenol	15	9 (60%)
Controls*	12	0 ( 0%)

\* See text for details.

The lesions were similar in all groups of animals, and were evident on inspection within four hours after rotation. They were characterized by a localized area of ischemia at the injection site, in which the skin was a pearly-white color. During the following few hours the skin became dry, brown, and parchmentlike in consistency. The area of involvement extended from the injection site for varied distances and invariably was greater in animals given epinephrine or levarterenol than in those given endotoxin.

Dilatation of superficial blood vessels over the area was noted

occasionally, but frank hemorrhage in or around the lesion was never observed. In the following 18 to 24 hours the skin became progressively drier and more brittle, and cracks or fissures appeared, but little edema was observed. Within 72 hours, areas of eschar formation appeared, and fragments of the dried skin began to drop off. In 96 hours, extensive eschar formation was present, and desquamation began to occur.

To determine the role of ischemia in causation of the lesions, the animals were given an intravenous injection of fluorescein (2 ml. of a 2 per cent solution) at varied times after the intradermal injections, and the abdomens were examined under ultraviolet light (Woods lamp) for evidence of fluorescence. In those animals which had been given epinephrine or levarterenol, as much as 50 per cent of the abdominal skin area, was noted to be nonfluorescent for as long as six hours after intradermal injection. In those given endotoxin, on the contrary, the period of ischemia and nonfluorescence diminished by the end of two to three hours, and at six hours the injection site was marked by high intensity fluorescence.

Microscopic examination of the skin in animals which died or were killed at varied times after intradermal injection and rotation showed similar changes in all groups, with one exception. The early changes were manifested by complete ischemia of the skin and subcutaneous tissues, with necrosis of the superficial portions of the epidermis. At 18 to 24 hours the epidermis was marked by a heavy crust of material composed of necrotic squamous cells, nuclear debris, and minimal amounts of fibrin and red blood cells. These changes persisted for as long as five days. Rarely was occlusion of blood vessels observed, and the arterial walls displayed no evidence of necrosis. In all lesions, there was a striking absence of hemorrhage. In the lesions produced by endotoxin, varying degrees of inflammatory cellular reaction composed of heterophilic and mononuclear cells were observed; in some, the reaction was quite sparse but in others it was severe and extended into the underlying connective tissue. In those lesions produced by the vasopressor substances, very little inflammatory cellular reaction was noted in lesions examined as long as three to five days after rotation. Sections from animals of both groups at this time showed extensive deposits of subepidermal hyaline material and varied degrees of connective tissue proliferation. One other change, which appeared in both groups, was the development of extensive areas of muscle calcification unaccompanied by any cellular reaction.

*Effect on Cutaneous Necrosis of Variation in the Interval Between Intradermal Injection and Drum Rotation*

It has been reported that the systemic effects produced by drum rotation and intravenous injections of endotoxin are dependent on the interval between rotation and administration of endotoxin.<sup>10</sup> To study the effect of time variation on the production of local dermal necrosis, a series of animals was given injections four hours before, and another series four hours after, drum rotation. Substances used for injection were endotoxin, epinephrine, and levarterenol in the same dosages and volumes as previously described.

As may be seen in Table 2, the incidence of lesions was low when the test substances were injected four hours before rotation. Cutaneous ischemic necrosis developed in only one of eight animals given endotoxin, and in only two of nine given epinephrine; furthermore, the size and extent of these lesions were considerably less than those described in the previous groups of animals. When the materials were injected four hours after rotation, however, cutaneous necrosis developed in a high percentage of the animals. These lesions were similar in incidence and severity to those that occurred in the animals given intradermal injections of these substances simultaneously with rotation (Table 1).

TABLE 2  
EFFECT ON DERMAL NECROSIS OF VARIATIONS IN THE  
INTERVAL BETWEEN SKIN INJECTION AND ROTATION

Procedure	Material Injected	No. of Animals	Dermal Necrosis
Injection 4 hours prior to rotation	Endotoxin	8	1 (13%)
	Epinephrine	9	2 (22%)
	Levarterenol	3	0 (0%)
Rotation 4 hours prior to injection	Endotoxin	7	5 (71%)
	Epinephrine	4	3 (75%)
	Levarterenol	3	2 (66%)

*Production of Dermal Necrosis in Rabbits by Injections of Other Vasopressor Substances in Conjunction with Drum Rotation*

In the studies described by Thomas<sup>7</sup> and Gatling,<sup>9</sup> dermal necrosis failed to develop in rabbits given ephedrine, suggesting that vasoconstriction *per se* was not an important factor in the production of the hemorrhagic lesions. To test the effects of other vasopressor amines on the development of the lesions in rabbits subjected to rotational shock,



a series of animals was given intradermal injections of the following substances simultaneously with the onset of drum rotation: ephedrine sulfate, phenylephrine hydrochloride, and isopropylarterenol hydrochloride. The ephedrine was injected in a dosage of 100  $\mu$ g. in 0.5 ml., phenylephrine in a dosage of 100  $\mu$ g. in 0.1 ml., and isopropylarterenol in a dosage of 10  $\mu$ g. in 1.0 ml.

The results, summarized in Table 3, show that a high percentage of the animals in each group developed dermal lesions. These were similar in appearance and severity to those produced by endotoxin, epinephrine, or levarterenol.

TABLE 3  
INCIDENCE OF CUTANEOUS NECROSIS IN RABBITS GIVEN  
INTRADERMAL INJECTIONS OF SYMPATHOMIMETICS  
SIMULTANEOUSLY WITH ROTATIONAL SHOCK

Material Injected	Number of Animals	Dermal Necrosis
Phenylephrine	6	5 ( 83%)
Ephedrine	8	4 ( 50%)
Isopropylarterenol	4	4 (100%)

#### *Effects of Heparin, Nitrogen Mustard, or Phenothiazine Derivatives on the Development of the Cutaneous Lesions*

It has been shown that the dermal Shwartzman phenomenon is inhibited by heparin<sup>4</sup> or nitrogen mustard<sup>5,6</sup> but that the administration of chlorpromazine, a phenothiazine derivative, does not influence its development.<sup>7</sup> Thomas<sup>7</sup> reported that the dermal epinephrine-endotoxin lesions were prevented by administration of chlorpromazine, but were enhanced by the administration of heparin or nitrogen mustard. Gatling<sup>9</sup> on the other hand, reported that in his experiments heparin "ameliorated" but did not prevent dermal hemorrhagic necrosis.

To test the effects of these materials on the drum-induced dermal lesions described previously, experiments were carried out in which heparin, nitrogen mustard, or a mixture of promazine-promethazine was given to rabbits subjected to drum shock simultaneously with an intradermal injection of endotoxin, epinephrine, or levarterenol.

Heparin sodium, in a concentration of 10 mg/ml, was given intravenously in a dosage of 20 mg. to a group of four rabbits immediately prior to drum rotation and to an intradermal injection of 100

$\mu\text{g}$ . of endotoxin and epinephrine. The results, summarized in Table 4, show that heparin in this dosage failed to prevent the development of the dermal lesions, which occurred in all of the animals given either endotoxin or epinephrine.

Another group of four rabbits was given an intravenous injection of nitrogen mustard, in a dosage of 1.5 mg/Kg, three days prior to intradermal injections of endotoxin and epinephrine in conjunction with drum rotation. The results were comparable to those obtained with heparin (Table 4), in that in all of the animals extensive areas of severe ischemic dermal necrosis developed.

TABLE 4  
EFFECT OF HEPARIN, NITROGEN MUSTARD, OR PHENOTHIAZINES ON THE PRODUCTION OF DERMAL LESIONS

Intravenous Injection*	Intradermal Injection	No. of Animals	Dermal Necrosis
Heparin	Endotoxin	4	4 (100%)
	Epinephrine	4	4 (100%)
Nitrogen Mustard	Endotoxin	4	4 (100%)
	Epinephrine	4	4 (100%)
Phenothiazine	Endotoxin	5	1 (20%)
	Levarterenol	4	1 (25%)

\* Details of administration in text.

On the contrary, the lesions were either prevented or markedly attenuated by prior administration of certain phenothiazine derivatives, as shown by the following experiment: A group of rabbits was given an intravenous injection of a mixture of 2.5 mg. each of promethazine and promazine. This mixture was used because it has been shown to modify the pressor responses to epinephrine and levarterenol.<sup>13</sup> After the administration of this mixture, each animal was given an intradermal injection of endotoxin and levarterenol and was subjected to drum shock. Only one of the animals in each group exhibited ischemic dermal necrosis, which was considerably less severe and more localized than in the animals given endotoxin or levarterenol alone in conjunction with drum rotation.

#### DISCUSSION

A previous report<sup>10</sup> described the systemic lesions produced in rabbits by acute rotational shock alone and in conjunction with an intravenous injection of Gram-negative endotoxin. The effects in those subjected to rotation alone were similar to the changes produced in rabbits given a single intravenous injection of endotoxin,

suggesting that the rotational procedure acted in a manner basically similar to that of endotoxin. The acute stress procedure, undoubtedly accompanied by an increased secretion of products from the adrenal gland, led the authors to postulate that adrenal medullary hormones in some manner participated in the actions of endotoxin, or that the actions of endotoxin were mediated through adrenal medullary hormones.

The occurrence of ischemic and hemorrhagic intestinal lesions in rabbits subjected to drum rotation suggested also that there might be absorption into the blood stream of either Gram-negative microorganisms, or products thereof (lipopolysaccharides) which could contribute to the development of systemic lesions. Thus, it seemed plausible that drum-shocked animals not only might have increased quantities of adrenal hormones in their circulatory system, but also, and perhaps simultaneously, might have endotoxin or endotoxinlike substances derived from the intestinal flora.

The experiments described by Thomas<sup>7</sup> (in which dermal hemorrhagic necrosis was produced by an intradermal injection of epinephrine in rabbits given intravenous endotoxin, or by an intradermal injection of a mixture of endotoxin and epinephrine) suggested an ideal method by which to test the hypotheses mentioned above, i. e., through the series of experiments described here.

The results of these studies show that cutaneous necrosis may, indeed, be produced in shocked rabbits by an intradermal injection of epinephrine (or levarterenol) or endotoxin. Although the method used was similar to that used by Thomas,<sup>7</sup> and by Gatling,<sup>9</sup> the resulting lesions bear little gross or microscopic similarity to the lesions reported by those investigators.

These differences warrant serious consideration. First, the lesions described in these experiments appear to be due primarily to a prolonged period of ischemia. Evidence for this fact is their gross appearance, the absence of fluorescein penetration into the injected sites for extended periods of time, and absence of dilated vessels, petechiae or hemorrhage. Histologically, also the lesions are characteristic of ischemic necrosis.

Second, these lesions resolve by desquamation of the skin in and about the sites of injection, associated with subepidermal accumulations of hyaline material and connective tissue proliferation. They do not, in contrast to the lesions described by Thomas, "gradually fade in color."

Finally, it should be emphasized that similar dermal lesions were

TABLE 5

COMPARISON OF THE FEATURES OF CUTANEOUS LESIONS REPORTED BY VARIOUS AUTHORS

Author or Reaction	Gross Features					Microscopic Features			Fate of Lesion
	Ischemia or pallor	Petechiae	Hemorrhage	Edema	Induration	Vascular lesions	Hemorrhage	Cellular Infiltrate	
Swartzman <sup>1</sup>	Transient	+	+	±	-	+	+	+	Fades
Thomas <sup>7</sup>	*Transient	+	+	-	-	±	+	-	Fades
	†Transient	+	+	+	+	±	+	+	Fades
Gatling <sup>9</sup>	Transient	+	+	+	+	+	+	+	Fades
Evers	Persistent	-	-	-	-	±	-	+(Endotoxin) -(Vasopressor)	Desquamates

\*Reaction produced by intradermal epinephrine or endotoxin after an intravenous injection of endotoxin

†Reaction produced by intradermal injection of mixture of endotoxin and epinephrine

produced by injections of other vasopressor amines such as ephedrine, isopropylarterenol, or phenylephrine. In this respect they differ sharply from those reported previously, since neither Gatling<sup>9</sup> nor Thomas<sup>7</sup> succeeded in producing dermal hemorrhagic necrosis by administration of such substances as ephedrine.

The lesion induced by epinephrine (or other vasopressor) in this study is similar to the lesions described by Thomas in its striking absence of inflammatory change. On the other hand, the lesion induced by endotoxin resembles that which Thomas produced by intradermal injections of mixtures of epinephrine-endotoxin, in that it often shows a heavy infiltrate of inflammatory cells. The lesions are similar also to those described by Thomas in exhibiting no evidence of vascular occlusion or vascular fibrinoid deposition. A comparison of the various features of the lesions is shown in Table 5.

The influence of several modifying agents on the production of dermal necrosis is summarized in Table 6. As shown there, the

TABLE 6  
COMPARISON OF MODIFYING ACTION OF VARIOUS  
SUBSTANCES ON CUTANEOUS LESIONS

Author or Reaction	Modification of Lesion			
	Heparin	Cortisone	Phenothiazine	Nitrogen Mustard
Shwartzman <sup>1</sup>	Prevents	Enhances	No effect	Prevents
Thomas <sup>7</sup>	Enhances	Prevents	Prevents	Enhances
Gatling <sup>9</sup>	Ameliorates	?	No effect	?
Evers	No effect	?*	Prevents	Enhances

\*All animals died within 4 hours after pretreatment with cortisone and rotation in drum.

lesions observed in the present series of experiments resemble more closely those of Thomas<sup>7</sup> than of other investigators, in that (1) they are prevented by administration of phenothiazine derivatives (chlorpromazine or promazine-promethazine), and (2) they are either unaltered or enhanced by administration of heparin or nitrogen mustard. In an attempt to study the effects of cortisone on the shock-induced dermal lesions, rabbits were pretreated for three days with cortisone acetate, following which they were subjected to rotation in conjunction with intradermal injections of epinephrine or endotoxin. Unfortunately, it was not possible to obtain definitive results, since all animals so treated died during the period of rotation.<sup>14</sup>

From these observations and other data now extant, it appears reasonable to conclude that vasospasm, with prolonged dermal is-

chemia, played a major role in the development of the lesions in this series of experiments. This period of ischemia appears to be particularly severe in the vasopressor-produced lesions, to such an extent that an inflammatory reaction is inhibited, but it is less severe and of shorter duration in the endotoxin-induced lesions. Furthermore, the inhibition of vasospasm by agents known to exert adrenolytic effects, such as the phenothiazine derivatives, prevented the development of the lesions. But agents such as heparin, on the contrary, did not affect the development of the lesion, indicating that vascular thrombosis and hemorrhage are relatively unimportant in this regard. It is difficult, however, to assess the role of nitrogen mustard, since its administration seems to enhance the development of the lesions.

That vasospasm may not be the only factor in producing these lesions is shown by other studies<sup>7</sup> in which cutaneous necrosis failed to develop in rabbits that were given repeated intradermal injections of epinephrine alone. Similarly, certain other materials such as normal rabbit plasma or old tuberculin, given intradermally just prior to drum rotation, have been shown to produce lesions comparable in all respects to those described here.<sup>14</sup> Furthermore, it has not been possible to produce cutaneous lesions in rabbits given epinephrine or endotoxin intradermally during hemorrhagic shock,<sup>15</sup> a state which is usually accompanied (at least transiently) by peripheral vasoconstriction.

These observations, and the recorded differences in the dermal lesions, suggest two hypotheses: (1) The shock state induced by drum rotation differs in its pathogenesis from the shock induced by endotoxin or hemorrhage. (2) Certain other, endogenous, agents or factors, in addition to those injected intradermally, participate in production of dermal lesions in rabbits subjected to drum shock. The nature and origin of these factors, if such exist, and the mechanisms involved in the production of rotational shock, remain obscure, and their elucidation requires further investigation.

#### SUMMARY AND CONCLUSIONS

Ischemic cutaneous necrosis was produced in rabbits subjected to rotational shock in conjunction with an intradermal injection of epinephrine, levarterenol, or endotoxin. The incidence of the lesions was approximately 70 per cent when the test substances were given simultaneously with, or four hours after, drum rotation but was less than 25 per cent when they were administered four hours prior to rotation.

The lesions were evident grossly within four hours after rotation.

They were characterized by extensive pale, flat ischemic areas which progressed rapidly to desiccation and, later, to desquamation. The histologic features consisted of necrosis of the superficial epidermis with a paucity of inflammatory reaction except in the endotoxin-induced lesions. Vascular occlusion was significantly absent. Changes observed three to five days after rotation consisted of extensive accumulations of subepidermal hyaline material and connective tissue proliferation. Similar dermal lesions were produced by rotational shock in association with an intradermal injection of ephedrine, phenylephrine, or isopropylarterenol.

The lesions were prevented by intravenous administration of a mixture of promazine and promethazine but were unaffected by prior administration of heparin. Pretreatment with nitrogen mustard appeared to increase the severity of the lesions.

The pathogenesis of the lesions, and their similarity to dermal lesions described by other authors, are discussed. It is concluded that vasospasm, although playing a major role in causation of the lesions, is probably not the only factor involved.

## REFERENCES

1. Schwartzman, G.: Studies on *Bacillus Typhosus* Toxic Substances: I. Phenomenon of local skin reactivity to *B. typhosus* culture filtrate, *J. Exp. Med.* 48:247, 1928.
2. Schwartzman, G.: *Phenomenon of local tissue reactivity*, New York, Paul Hoeber, Inc., 1937.
3. Thomas, L. and Stetson, C. A.: Studies on the Mechanism of the Schwartzman Phenomenon, *J. Exp. Med.* 89:461, 1949.
4. Good, R. A. and Thomas, L.: Studies on the Generalized Schwartzman Reaction: IV. Prevention of the Local and Generalized Schwartzman Reactions with Heparin, *J. Exp. Med.* 97:871, 1953.
5. Stetson, C. A. and Good, R. A.: Studies on the Mechanism of the Schwartzman Phenomenon: Evidence for the Participation of Polymorphonuclear Leucocytes in the Phenomenon, *J. Exp. Med.* 93:49, 1951.
6. Becker, R. M.: Suppression of Local Tissue Reactivity (Schwartzman Phenomenon) by Nitrogen Mustard, Benzol, and X-ray Irradiation, *Proc. Soc. Exp. Biol. & Med.* 69:247, 1948.
7. Thomas, L.: The Role of Epinephrine in the Reactions Produced by the Endotoxins of Gram-negative Bacteria; I. Hemorrhagic Necrosis Produced by Epinephrine in the Skin of Endotoxin-treated Rabbits. *J. Exp. Med.* 104:865, 1956.
8. Zweifach, B. W.; Nagler, A. L.; and Thomas, L.: The Role of Epinephrine in the Reactions Produced by the Endotoxins of Gram-negative Bacteria: II. The Changes Produced by Endotoxin in the Vascular Reactivity to Epinephrine, in the Rat Meso-appendix and the Isolated, Perfused Rabbit Ear, *J. Exp. Med.* 104:881, 1956.

THE MEDICAL BULLETIN

9. Gatling, R. R.: Altered Reactivity to Epinephrine in the Hypersensitive Rabbit, *J. Exp. Med.* 108:441, 1958.
10. Anderson, J. M. and Brunson, J. G.: The Influence of Acute Stress on the Response of Rabbits to Intravenous Endotoxin, *Circ. Res.* 7:37, 1959.
11. Noble, R. L. and Collip, J. B.: A Quantitative Method for the Production of Experimental Traumatic Shock Without Hemorrhage in Unanesthetized Animals, *Quart. J. Exper. Physiol.* 31:201, 1942.
12. Pitesky, I. and Last, J. H.: An Effective Depilatory Formula for Use on Laboratory Animals, *Science* 108:657, 1948.
13. Hodgson, C. J. and Brunson, J. G.: Unpublished observations.
14. Brunson, J. G. and Evers, C. G.: Unpublished observations.
15. Thomas, L.: Personal communication.



## Staff Meeting Report

### Modern Bronchology\*

Robert E. Priest, M.D.†

James A. Donaldson, M.D.‡

John R. Hilger, M.D.§

Richard R. Lund, M.D.¶

Rapid advances in anesthesiology and in the chemical control of infection have made possible the surgical treatment of intrathoracic lesions during the last two decades. Exact preoperative diagnosis has become important in cardiology and in the study of pulmonary and esophageal disease. The foundations of broncho-esophagology were laid long ago, but many refinements have been added recently, and doubtless more will follow. This paper considers the essentials of adequate pulmonary study by present standards.

Accurate and simplified nomenclature to denote various parts of the lung, the use of bronchoscopic telescopes, improvement in collection of specimens for histologic and cytologic study, and development of precision in bronchographic study—all these are parts of an integrated pulmonary evaluation. Each of them entails the participation of one or more members of the thoracic surgery team. This team includes the physician who originally suspects and diagnoses the pulmonary disease, the thoracic surgeon, the radiologist who has special knowledge and interest in pulmonary topographic anatomy and pathology, the pathologist who is trained in pathologic cytology as well as histology, the anesthesiologist, and the bronchoscopist. Each member of the team must be familiar with much of the knowledge and with the points of view of the others, for the patient is best served when the entire group is closely integrated.

Each member of the thoracic surgery team must perform his function with the utmost precision. Each must have considerable knowledge of pulmonary physiology and anatomy, and each must be willing to pay attention to the smallest detail to attain better quality in his part of the entire study. In short, what may be called "precision bronchology" is indispensable, precision being the sum total of many

\*This report was given at the Staff Meeting of the University of Minnesota Hospitals on April 17, 1959.

†Clinical Associate Professor, Department of Otolaryngology

‡Medical Fellow, Department of Otolaryngology

§Medical Fellow, Department of Otolaryngology

¶Medical Fellow, Department of Otolaryngology

small details each as nearly perfect as possible, none very important by itself, but all necessary to make up a really precise whole.

For many years the senior author, serving as bronchologist and carrying out pulmonary studies prior to lung surgery, has been privileged in working closely with thoracic surgeons who have had experience in the management of all types of pulmonary disease. These thoracic surgeons have said many times that the bronchologist could serve them best when he learned to "think like a thoracic surgeon."

As time has gone on, the precision of these bronchologic efforts has increased. What factors distinguish a precise bronchologic study from a mediocre one? As a beginning, consider what is meant by precision. The dictionary defines it as "sharply or exactly limited as to meaning; exact, definite, not loose, vague or equivocal." This definition standardizes the word "precision" but not with respect to any particular usage. In actual practice, "precision" may mean almost anything. Its meaning varies with the development of the field to which it is applied. The higher the development, the more minute the detail connoted by the term "precise." The following examples from Collier<sup>1</sup> illustrate this idea.

Early in the nineteenth century, a machinist advertised a boring mill "capable of turning the cylinders of steam engines accurate to plus or minus the thickness of a shilling." A shilling is three thirty-seconds of an inch thick. In 1959, steam engine cylinders made to an accuracy of only three thirty-seconds of an inch would be considered extremely crude, for today's tolerances are within a few thousandths of an inch.

As a second illustration, consider the problems of the highway construction engineer. While a highway construction engineer could probably maintain the straightness of a road to plus or minus one foot per mile, a difference of plus or minus one yard per mile would be accurate enough for most purposes. In an international boundary survey, however, one foot per mile would represent relatively poor accuracy. Thus, what constitutes precision in one field is not precision in another; and what is precision at one stage of the development of an art or craft is not precision at a later stage.

Turning again to bronchologic precision we ask, What can be expected of the bronchologist? The exact information delivered by the bronchologist will be of greatest interest to the thoracic surgeon, because he will have to operate on the patient. The family physician or internist will be interested in the same information but he will seek *qualitative* data, while the thoracic surgeon is more interested in

*quantitative* information. Is a certain lesion cancerous? Can it possibly be removed? These are qualitative problems. How far is it from the carina? Is the bronchus rigid; if so, exactly where? These are quantitative questions, and it is these that will concern us as we ask: *What can the thoracic surgeon expect from the bronchologist?*

The thoracic surgeon can expect that the bronchologist will be intensely interested in his own work; that he will study diligently to perfect his knowledge of pulmonary anatomy, physiology, and pathology; that he will fully merit being called a bronchologist or student of the bronchi rather than a bronchoscopist, who looks at the bronchi but may not fully understand what he sees. The papers of Jackson and Huber,<sup>2</sup> of Boyden et al.,<sup>3</sup> and of Kane<sup>4</sup> are essential to this study.

The thoracic surgeon can expect the bronchologist's description of the entire respiratory system to be sufficiently exact to enable him to picture the respiratory system in his mind's eye just as though he himself had made the examination. The thoracic surgeon should reasonably expect the bronchologist to study the patient's problem before performing bronchoscopy. The surgeon and bronchologist should discuss the entire problem and examine the x-rays, and the bronchologist should talk to the patient about the bronchoscopic procedure. A few minutes of explanation in preparing the patient for bronchoscopy will reduce his nervous tension and thereby greatly increase the quality of the studies.

The thoracic surgeon can expect to learn the condition of the patient's pharynx and larynx, including motility and structural state of the vocal cords. He can expect to be informed of the position, size, and shape of the trachea, as well as any abnormality produced by extrinsic pressure or by intrinsic tumors or ulcers. He can expect to learn whether or not the tracheal mucous shows signs of inflammatory reactions or of suppuration.

The thoracic surgeon can expect the bronchologist to describe the appearance of the tracheal carina. It may be straight and slim covered with normal mucosa; it may be broadened due to the patient's habitus or to tumor masses lying in the angle between the right and left main bronchi. It may be kinked during the expiratory phase of respiration, and straight during the inspiratory phase, suggesting the presence of tumors adjacent to the carina. It may be attached to the large vessels by infiltration of tumor and therefore make excursions with the vessels in a transverse direction—excursions that will be out of phase with the respiratory excursions.

The thoracic surgeon can reasonably expect the bronchologist to be thoroughly familiar with bronchial anatomy and to examine the orifices of all major branch bronchi present within the right and left bronchial trees. Such examination should include routine telescopic observations of the upper lobe bronchi with the right-angle telescope and occasionally with the retrograde telescope. Examination of the bronchi of the middle and lower lobes should include observation with the foroblique telescope; but the bronchus of the apical division of the lower lobes should be examined with the right-angle telescope. Right-angle and foroblique telescopes should be used routinely rather than only in cases presenting special problems. The same observation described in connection with the trachea should be made routinely of the mucosa of the bronchi of both bronchial trees.

Routine collection of specimens by aspiration should be carried out in the manner described by Clerf.<sup>12</sup> Material should be collected from the appropriate branch bronchus, as indicated by previous study of the chest x-rays and by study of the patient before bronchoscopy, as well as by bronchoscopic findings. Specimens removed with the aspirating device should be subjected to certain routine tests, including cytologic study of the secretions for tumor cells by a qualified clinical pathologist. The Papanicolaou technique, while often extremely valuable, is subject to limitations based on the experience of the pathologist. Early in the senior author's experience, false positives were obtained using this procedure, and some patients had portions of lungs removed when, as it now appears, carcinoma was not actually present. Inflammatory metaplasia of cells in lesions such as bronchiectasis is the most frequent cause of this difficulty. A second routine test that should be applied to all specimens removed by aspiration is culture for tubercle bacilli. All specimens should be labeled immediately as to their exact source within the bronchial tree, listing if possible the exact bronchus from which they were aspirated. Thus it is preferable to say that one has aspirated the "medial basal bronchus of the right lower lobe," rather than merely "the right lower lobe bronchus." Sometimes such accuracy may not be necessary or even possible, but if one strives for a high level of routine accuracy he is more apt to obtain information of value to the thoracic surgeon.

When it is possible to make a biopsy of a tumor using bronchoscopic forceps, what does the thoracic surgeon want to know about the bronchi? He wants to know how much clearance he has between the end of the tumor and the point where he will have to resect in order to effect a cure. If the tumor is so situated as to give him

ample clearance, he wants to know whether or not there is rigidity of the bronchus proximal to the tumor, suggesting tumor infiltration within or adjacent to its wall. He also wants to know if the bronchus is narrowed, as though compressed by masses lying outside of it. On several occasions in our experience patients have had to undergo bronchoscopy twice because the bronchoscopist in the first instance did not localize the tumor accurately enough, even though he had obtained a biopsy that was positive for carcinoma. In these cases the thoracic surgeon could not tell whether or not there was room to attempt a resection. Aspiration studies should be made on all patients from whom biopsy specimens are obtained. This gives the pathologist known positive material on which to practice his cytology. (When excessive bleeding follows biopsy this is not possible, of course.)

The question of measurements within the bronchi has been raised by several authors. A bronchial yardstick and an intrabronchial caliper have been devised by Emerson.<sup>5,6</sup> An experimental recording bronchial caliper has been used by Andrews.<sup>7</sup> The presence of such instruments on a bronchoscopic table is of unquestionable value. On the other hand, one must not forget that for most purposes the simple instruments always present can assure reasonable accuracy of measurement. This is especially true of longitudinal measurements of the bronchi (but not so true of measurement of bronchial diameters). For example, one can use an ordinary suction tip and ruler, making a first measurement with the suction tip placed against the tumor. The suction tip can then be placed against the nearest anatomic landmark, for example, the tracheal carina, and a second measurement can be made. This simple method gives excellent results and removes from the thoracic surgeon's mind any doubt as to the accuracy of the bronchologist's observation. Such statements as "a long way down the left main bronchus," "half way down the left main bronchus," "it was a pretty big one," and so forth have no place in the accurate bronchology of today.

The preparation of proper bronchographic studies using contrast medium injected into the tracheobronchial tree has been discussed by many authors and will only be touched on here. As in other phases of precise bronchology, the making of bronchograms must be carried out with a detailed plan. The patient must be psychologically prepared. Adequate anesthesia must be obtained, the requirements as to kind and amount of anesthetic agent varying in different patients. In some patients the application of topical anesthesia within the tracheobronchial tree is adequate. In some, particularly bronchiectatic pa-

tients, the bronchi must be emptied by bronchoscopy and suction, and additional anesthetic must be applied to the areas laid bare by the removal of secretion. In some patients drugs such as codeine ( to decrease the desire to cough), sedatives, or muscle relaxants must be given intravenously during bronchoscopy. In adults it is undesirable to use sedatives in such large doses as to interfere with breathing, but a smaller quantity can sometimes be used to induce sedation with distinct advantages.

The contrast medium should be injected under fluoroscopic control and preferably with cooperation between the radiologist and the bronchologist. In some hospitals in which the radiologist is too busy or insufficiently interested to do this work, the bronchologist may be forced to perform the entire procedure himself. At the University of Minnesota Hospitals the radiologists have been greatly interested; as a result, the quality of bronchographic studies has continually risen, until we now are completely dissatisfied with anything except a very accurate demonstration of all major and most minor bronchi. This effort has enabled us to demonstrate small areas of bronchiectasis as described by Overholt and Walker,<sup>8</sup> which form a basis for recurrent asthma or pulmonary bleeding; we would have missed such areas completely in years past, and we have reason to believe that less exact studies of the bronchial tree overlook them even now. Recently several techniques for bronchographic studies in children have been described.<sup>9,10</sup> These require careful planning but they permit entirely satisfactory bronchographic studies of patients at almost any age.

Overholt<sup>11</sup> commented on the diagnosis of early pulmonary cancer and the relationship of the various branches of medicine concerned with this disorder. His statements are worth examining by everyone engaged in bronchology. His primary tenet was that the positions of some lesions in the lung make their histologic diagnosis impossible except through biopsies obtained on thoracic exploration. He stated the belief that sometimes lesions which are clearly visible by x-ray are passed over by the family doctor, the internist, or the bronchologist as being unimportant in the face of apparently normal bronchoscopic findings. Overholt asserted that repeated bronchoscopy is sometimes carried out in such cases in a fruitless effort to determine the type of lesion, and that valuable time is lost before surgery is finally initiated. We are in accord with this point of view. We do not, however, subscribe to Overholt's idea that in most instances bronchoscopy is best carried out on the day of thoracic exploration, because we feel it advisable to study the case thoroughly and to get all advance informa-

tion possible. The thoracic surgeon can work more efficiently if he can draw upon cell studies, a biopsy report, and studies of paraffin sections rather than frozen sections. On the other hand, we certainly agree that loss of time due to such studies should be minimal. Adequate pulmonary evaluation can be made with no significant time loss, two or three days after the initial evaluation. An understanding of how rapidly this entire field has developed can be derived from the words of Dr. Louis Clerf, designer of the Clerf specimen aspirator and Professor Emeritus of Laryngology and Bronchoscopy at the Jefferson Medical School, Philadelphia. At the meeting of the American Broncho-esophagological Association in March, 1959, Dr. Clerf said, among other things:<sup>12</sup>

"While a junior student in medicine during 1910 I saw my first endoscopic case. The patient, a little girl, aged three years, had a coin in the esophagus. Her father, a fireman, underpaid as usual, was not able because of economic reasons to follow Dr. DaCosta's advice, namely, to take her to Pittsburgh to see Dr. Chevalier Jackson. Dr. DaCosta then decided to do the esophagoscopy and presenting the case before his Clinic indicated that chloroform was the anesthetic of choice. He then passed an esophagoscope which I found later was a 9 mm. adult tube. As is so often the case everyone watched the operator but later someone noted that the patient had ceased breathing. This apparently was discovered too late for after attempts at resuscitation the child was pronounced dead. Dr. DaCosta devoted the remainder of the clinic hour to a discussion of 'tragedies of surgery' . . .

"In 1912 as an interne at Jefferson Hospital I had opportunity to observe a bronchoscopy for a brass headed tack which was localized at the lower end of the trachea. The removal was unsuccessful and was complicated by the occurrence of extensive subcutaneous emphysema which extended from the crown of the head to Poupart's ligament. This was undoubtedly the most remarkable case of emphysema I have ever witnessed. The question arose whether one should make multiple skin incisions or introduce needles subcutaneously to drain off the air. Fortunately nothing was done, the emphysema slowly subsided and the patient coughed up the tack five days later; this was indeed a very happy solution of a complicated problem. . . .

"In 1924, during the Presidency of Dr. Ellen J. Patterson, I became a member of this Association at its 7th annual Meeting in St. Louis and presented my thesis covering *Experiences with 50 Foreign Body Cases in the Air and Food Passages*. . . .

"It is interesting to recall the changes that have been observed in the overall picture in endoscopy. In 1922, Dr. Gabriel

Tucker and I started to treat cases of lung suppuration by tracheal aspiration performed through a direct laryngoscope and the instillation of gomenol. This latter was considered the miracle drug of that day, and remarkable claims were made in the treatment of pulmonary suppuration. Esophagosopic examination was performed more frequently than diagnostic bronchoscopy which still was in its infancy but with increasing cases of pulmonary suppuration and later the use of lipiodol as a diagnostic aid, bronchoscopy was more frequently performed. I recall in 1924, the first case of pulmonary carcinoma at the Clinic, which was diagnosed bronchoscopically by biopsy during life. Up to that time the literature on pulmonary carcinoma referred to postmortem observations. Dr. Thomas McCrae, Professor of Medicine, the physician in this case, presented it to the students and emphasized the importance of diagnostic bronchoscopy and expressed the belief that this was indeed a great advance which would help immeasurably in the successful management of this disease.

"Another activity in those days was the bronchoscopic treatment of pulmonary abscess. Cases following tonsillectomy were very common for in 1927 I presented a series of 50 cases before this Society. Thoracic surgery had not arrived at the point where pulmonary abscess could be treated as successfully and bronchoscopy offered more."

It is truly remarkable that the science of broncho-esophagology has evolved from such crude beginnings to its precision of today.

#### CASE REPORTS

*Case 1.* The patient, a 67-year-old white man, was admitted to the Veterans Hospital because of cramping abdominal pain of six weeks duration. The patient also had complained of a productive cough for four or five years with occasional blood flecking of his sputum. In addition to the gastrointestinal x-ray study, sputa were collected for tubercle bacilli and tumor cell studies. The third sputum specimen was reported as suspicious for tumor cells. The patient had a complete pulmonary workup, including:

Posteroanterior and lateral chest films—normal

Bronchoscopy and left bronchogram—normal

Bilateral planigrams of lung fields—normal

Planigram of mediastinum—normal

Twelve sputa were collected and one appeared definitely positive for tumor cells.

Bronchoscopy was again requested three weeks later. The nasopharynx, oropharynx, hypopharynx, vocal cords, trachea, carina, right main stem bronchus and its subdivisions were reported to be normal. A definitely invasive lesion of 5 mm. diameter was noted on the lower lip of the left upper lobe orifice. This same mucosal area had been described as normal at bron-



choscopy three weeks earlier. This lesion undoubtedly represented an early mucosal breakthrough that had been too minute to be recognizable at the earlier examination.

Biopsy was accomplished with the Hollinger upper lobe resecting telescope, the flexible arm being directed laterally until the area of the lesion was reached; a direct mucosal bite was taken. The pathologic finding was squamous cell carcinoma.

On December 29, 1958, the patient was subjected to radical left pneumonectomy. The pathologist reported negative mediastinal nodes and normal bronchial mucosa. Microscopic examination of the site of the previous biopsy showed early submucosal extension of a squamous cell carcinoma surrounded by islands of carcinoma in situ.

*Case 2.* This patient was a 10-month-old girl who had a sudden onset of paroxysms of coughing five weeks before admission. She had been hospitalized elsewhere after a week of coughing because it was suspected that she had aspirated a foreign body. Bronchoscopy revealed only mucosal inflammation and a thick mucous secretion. She was treated with antibiotics for tracheobronchitis, and after two weeks, chest x-ray revealed obstructive emphysema of the left lung. She was referred here for further investigation.

On admission striking decrease of the breath sounds was noted in the left side of the chest, especially in the left base posteriorly. There was a mild inspiratory wheeze. Although respirations were rapid, no retraction or cyanosis was apparent. Blood studies revealed leukocytosis, and there was a slight temperature elevation. Chest x-ray showed an obstructive type of emphysema on the left with depression of the left hemi-diaphragm, and extension of the left lung across the midline in the anterior superior mediastinum. The heart and mediastinum were also shifted to the right.

The differential diagnosis here included tracheobronchitis with a mucus plug, pertussis, congenital atelectasis on the right, or an aspirated foreign body with obstructive emphysema. Bronchoscopy was indicated.

Under basal anesthesia, a 3½ mm. Jackson bronchoscope was introduced and passed to the level of the carina. The right main bronchus was observed to be normal, but a foreign body was seen in the left main bronchus. This was a sharp object approximately 3 mm. in diameter and of undetermined length. The object was grasped with a forceps—a rather difficult maneuver because of the small size of the bronchoscope necessary in this infant. Then the foreign body, forceps, and bronchoscope were all removed together. The foreign body appeared to be a piece of straw or the stem of a flower, 3 to 4 mm. in diameter and more than 2½ cm. long.

The bronchoscope was re-introduced to examine the site of the foreign body. The left main bronchus was now patent, and except for mucosal swelling and irritation, no other injury was apparent.

The child continued to wheeze until about 4 days after bronchoscopy; a chest x-ray taken at that time showed almost complete resolution of the emphysema.

The table below indicates the volume of endoscopic work done in the several hospitals in which our residents are active, during the one-year period ending January 1958. In Ancker Hospital, the endo-

## THE MEDICAL BULLETIN

scopic work is divided between the ear, nose, and throat services and the surgical services, as indicated in the table. Except for the work listed as being done by General Surgery, all the figures represent individual patients operated on by ear, nose, and throat residents:

BRONCHOSCOPY			
	Diagnostic	Foreign Body	Aspiration
Minneapolis Veterans Hospital	314	0	72
University of Minnesota	155	3	7
Ancker Hospital	47		
	50*	0	1
Minneapolis General Hospital	76	1	0
	<hr/>	<hr/>	<hr/>
Total	642	4	80

ESOPHAGOSCOPY		
	Diagnostic	Foreign Body
Minneapolis Veterans Hospital	50	0
University of Minnesota	78	5
Ancker Hospital	9	
	1*	11
Minneapolis General Hospital	27	1
	<hr/>	<hr/>
Totals	165	17

\*Performed by the Surgery Department

This is being carried on in as precise a manner as possible. The members of the otolaryngology department feel that with the experience offered by so large a volume of cases our residents can be trained to be truly competent broncho-esophagologists.

### REFERENCES

1. Collier, George X. M.: What Price Precision? Part I, QST, A Radio Amateurs Journal 36:42, 1952.
2. Jackson, C. L. and Huber, J. F.: Correlated Applied Anatomy of the Bronchial Tree and Lungs with a System of Nomenclature, Dis. Chest 9:319, 1943.
3. Boyden, E. A., et al.: Minnesota Studies on the Anatomy and Variations of the Bronchopulmonary Segments.
  - a) The Whole Lung
    - Boyden, E. A.: Surgery 18:706, 1945.
    - Boyden, E. A.: Dis. Chest 15:657, 1949.

THE MEDICAL BULLETIN

- b) Right Upper Lobe  
Boyden and Scannell: *Am. J. Anat.* 82:27, 1948.  
Scannell and Boyden: *J. Thoracic Surg.* 17:232, 1948.  
Boyden: *Azygos Lobe and Pre-eparterial Bronchi*, Radiology, (June) 1952.
  - c) Middle Lobe  
Boyden and Hamre: *J. Thoracic Surg.* 21:172, 1951.
  - d) Right Lower Lobe  
Smith and Boyden: *J. Thoracic Surg.* 18:195, 1949.  
Ferry and Boyden: *J. Thoracic Surg.* 22:188, 1951.
  - e) Left Upper Lobe  
Boyden and Hartmann: *Am. J. Anat.* 79:321, 1946.  
Boyden: *Surgery* 20:828, 1946.  
Scannell: *J. Thoracic Surg.* 16:530, 1947.  
Boyden: *Surgery* 26:167, 1949.
  - f) Left Lower Lobe  
Berg, Boyden, and Smith: *J. Thoracic Surg.* 18:216-236, 1949.
  - g) Agenesis of Right Lung  
Thomas and Boyden: *Surgery* 31:429, 1952.
  - h) Boyden, E. A.: Lateral Views of the Segmental Bronchi and Related Pulmonary Vessels in an Injected Preparation of the Lungs, *Radiology* 61:183, 1953.
  - i) Boyden, E. A.: A Critique of the International Nomenclature on Bronchopulmonary Segments, *Dis. Chest* 23:266, 1953.
4. Kane, Irving J.: Segmental Localization of Pulmonary Disease on the Postero-Anterior Chest Roentgenogram, *Radiology* 59:229, 1952.
  5. Emerson, E. B., Jr.: A Bronchial Yardstick, *J. Thoracic Surg.* 21:516, 1951.
  6. Emerson, E. B., Jr.: Intrabronchial Caliper, *Arch. Otolaryng.* 55:724, 1952.
  7. Andrews, A. H.: Observations on Bronchial Movements and Elasticity by Means of a Recording Bronchial Caliper, *Ann. Otol., Rhin. & Laryng.* 61:1181, 1952.
  8. Overholt, R. H. and Walker, James H.: Hidden or Unsuspected Bronchiectasis in the Asthmatic, *Ann. Otol., Rhin. & Laryng.* 61:1198, 1952.
  9. Wishart, D. E. S.: Bronchography in Bronchiectasis in Children, *Ann. Otol., Rhin. & Laryng.* 56:404, 1952.
  10. Priest, Robert E.: Bronchography in Infants and Children, *Ann. Otol., Rhin. and Laryng.* 61:651, 1952.
  11. Overholt, Richard H.: Virus Pneumonia, Tuberculosis, Cancer: That is The Problem, Supplement to the Fourth in a Series of Monographs on Cancer of the Lung, *Am. Cancer Soc., Inc.*
  12. Clerf, Louis: Personal communication outlining his remarks quoted in this paper.

## Staff Meeting Report

### Social, Legal, and Medical Aspects of Illegitimacy\*

Elizabeth Nowicki, M.S.†

James N. Bradford, L.L.D.‡     Irwin H. Kaiser, M.D.§

#### A. THE SOCIAL ASPECTS OF ILLEGITIMACY (Mrs. Nowicki)

This topic has been selected for discussion by the Social Service Department because of the many questions that arise when unmarried pregnant women come to doctors for help. Therefore, this meeting was planned to provide information about these women, the problems they encounter, and the resources available for helping them.

In the past decade, much has been written about unwed mothers and the problems they face. "Girls in Disgrace," "Black Market Babies," "School Girl Mothers," "I Married a Bigamist," "Afraid to Keep My Baby," "I Wouldn't Let My Son Marry the Mother of His Baby"—these are some of the stories found in popular magazines today, dealing with personal experiences of the illegitimate child and his mother. The best-known story on this subject is Nathaniel Hawthorne's "The Scarlet Letter," which is a classic psychological study of the effects of adultery upon the characters. Hester Prynne is a "fallen woman," portrayed in such a way that the reader cannot but admire the courage she displays in her public confession. The father of the child suffers more moral degradation because he would not acknowledge his part in the social "crime."

Hawthorne's tale was an attempt to probe the moral consequences of adultery, but the material being written today is, as indicated by the above titles, sensational and often lurid. These articles, as well as newspaper columns purporting to give advice by feature writers, frequently have positive values. After reading them, a girl may not feel so alone in her problem; perhaps she will seek help as others

\*This report was given at the Staff Meeting of the University of Minnesota Hospitals on April 24, 1959.

†Senior Social Worker, Department of Social Service

‡Special Assistant, Attorney General, State of Minnesota

§Associate Professor, Department of Obstetrics and Gynecology

have done; or her family may receive some comfort or direction in learning how this situation might be handled. Serious literature on this subject is also being written by social workers, psychiatrists, doctors, ministers, and sociologists attempting to study causes, problems, and treatment.

The rise in the number of out-of-wedlock births has become a serious concern. The national Bureau of Vital Statistics reported about 200,000 such births for 1955, representing an increase of more than 120 per cent during the past two decades and accounting for about five per cent of the yearly total of 4,163,000 births in the nation.

In Minnesota the number of illegitimate births from 1941-1958 varied from 2.0 to 2.8 per cent of all live births. The maximum was 2.8 per cent in 1945. In 1957 more than two thousand children were born out of wedlock, representing 2.35 per cent of 85,000 live births in Minnesota.

The University Hospitals, because of its location, functions, areas served, and affiliation with the Booth Maternity Home, sees a higher percentage of illegitimate births than the average for the nation. The average on the maternity wards is 15 per cent of the total number of births, or about 120 illegitimate children per year.

In comparing the age range of unmarried mothers reported by the State Department of Welfare with that reported by the University Hospitals, it was found that most women in both groups were from 18 to 21 years old; the University Hospitals however, had a larger percentage of unmarried mothers in the ages between 12 and 18 years.

Another trend has been the increase in the number of illegitimate pregnancies among very young girls. The median age of unmarried mothers during 1957 was 21.3 (i.e., half of the mothers were under 21). The most important trend noted nationally in the last 10 years is a 40 per cent increase in births to unmarried mothers aged 15 to 17 years old. This increase in number of babies born to young mothers exceeds the proportionate rise in babies born to the total female population.

The problems of illegitimate children and unwed mothers have been of concern for centuries. The treatment of these mothers and children have varied, but even in the most civilized cultures, they are still considered a class apart, and the concepts of moral judgment and punishment persist in spite of the more humanitarian attitudes of today.

The concern of doctors, ministers, and social workers has produced better programs for assistance to unwed mothers. Church organiza-

tions, the Salvation Army, Florence Crittendon Homes, can be found in all parts of the country, and all states have laws that provide specific protection for the mother and her child. But in spite of the advanced programs, there are still remnants of punitive attitudes and unkind public opinion. The majority of these women, for example, must leave their home communities in order to be protected from the censure of their neighbors. In some states, a woman may not be able to obtain financial assistance, food, and shelter for herself and her child unless she is willing to name the father of the child. Moreover, in most states, the word "illegitimate" must appear on the child's birth certificate; and in many other states, a birth certificate of a different color is used to designate an out-of-wedlock birth.

Who are these women who have children out of wedlock? Many long-held beliefs about them—that they were innocent girls who were seduced, that they were "born bad," were mentally deficient, or were always from the "wrong side of the tracks"—have not proved true. Some of these girls are seduced, of course, but not nearly as many as supposed. Mentally deficient and mentally ill women do have illegitimate children, but they are not in the majority. Thus, of the 107 patients who are included here, only four had been in institutions for the mentally deficient, and three others had had or were having psychiatric treatment. Many of these unwed mothers have come from homes which have little to offer in the way of security, supervision, and family solidarity, but the homes are not always "on the wrong side of the tracks." In fact, most of these girls do not fall into a neat pattern; they come from every walk of life and every type of home, and they display a wide range of mental ability. Most of these patients have attended or are attending high school, and some are college students or college graduates.

Among the 107 unwed patients on the Obstetrical Service in the past fiscal year 1957-58, the age distribution was as follows:

Age—(Range 12 to 49 years)	
12-18 years . . . . .	28
19-24 years . . . . .	41
25-30 years . . . . .	15
31-36 years . . . . .	12
37-49 years . . . . .	11

---

107

THE MEDICAL BULLETIN

The marital situation of these patients is summarized below:

Marital Status	
Single	74
Divorced	14
Separated	18
Widowed	1
	<hr/>
	107

The fact that one cannot always explain why an apparently normal, intelligent woman will have a child out of wedlock when she may be fully aware of the problems involved has influenced study of other factors with the hope that understanding can culminate in treatment of the cause. Authorities on this subject agree that most of these women have some type of emotional disorder, whether of long or short duration, in which the pregnancy may be incidental. This disorder is evidenced by a defect in relationships usually within the family and most frequently with one or both parents. The domineering mother or father, or the passive parent unable in either case to have a normal relationship of love and acceptance with the child, is perhaps most frequently blamed for this poor adjustment.

One of the patients recently interviewed in Social Service at the University Hospitals was a lonely and unhappy girl who wanted to go home but was so afraid of her father she could not do so. Her whole life seemed to have been affected by this punishing man who mistreated his wife and family. This girl became pregnant by the first boy she had ever dated. She said he had seemed very kind and she had been sure they would be married; she was very bewildered when he ceased being interested in her.

Although the defect in family relationships is basic, other factors contribute to illegitimacy: In the age group 18 to 21, the girl may be on her own for the first time, often glad to leave the guidance of her parents and eager for experience, but unable to cope with her new freedom. In the older group, age 34-49, various situations exist: the woman separated from her husband and seeking companionship; the woman who hopes to marry the father of her baby; and the woman who may really wish a child even without a husband.

Regardless of the situation, most of these patients are lonely, uncertain women, greatly suffering from strong feelings of guilt and lack of self-esteem, often desperately disturbed, and confronted by unmet

needs. What are these needs of the unmarried mother? They are the needs primarily of a woman who is about to have a child. But in addition she requires the emotional, financial, and physical support that would ordinarily be provided by a husband. This need must be filled as well as possible by her own family and by community resources. Social attitudes complicate matters by making it necessary to consider secrecy and confidentiality. The unmarried mother needs a place to stay, medical care, and money to make this possible, as well as wise, and sympathetic, help in making plans for herself and her expected child. She and the persons helping her also need legal counsel in the arrangements for financial aid and care of the baby.

In Minnesota, the general attitude toward unmarried mothers is liberal, and several excellent facilities exist where women may live during pregnancy and receive help in making satisfactory plans for the future. In the Twin Cities, there are: the Booth Memorial Home, St. Paul, operated by the Salvation Army and affiliated with the Obstetrical Department of the University; the Catholic Infant Home, St. Paul; and the Lutheran Girls Home, Minneapolis. Girls may live in these homes during pregnancy, and schooling is provided for those eligible for the services of the local departments of education. Work in homes is found for those who need to secure financial assistance. All these facilities provide casework services to help the girl plan adequately.

The function of the county welfare boards and the private social agencies in this area is to help the girl in handling the problems of her situation and in making a plan for herself and her child. Agencies safeguard the information they receive and keep their contacts with the girl in greatest confidence.

In hospitals with a Social Service Department, such as University of Minnesota Hospitals, a social worker is assigned to the Obstetrical Service. Her duties include casework service to the patients and cooperative work with appropriate agencies. She serves as liaison between the staff and social agencies for effective communication between hospital and community in meeting the patient's needs.

Professional people are concerned not only with these immediate needs but also with the more far-reaching aspects of illegitimacy. What research, they ask, is being directed at the causes of these situations? What follow-up is made to help the girl with future adjustments in keeping her baby or in putting it up for adoption? Many agencies, while equipped to follow up these cases, frequently are not able to do so. Patients who leave home during pregnancy may



not wish a referral to an agency in their communities. They are often eager to return to school and work, and this urgency overshadows their desire for help. Their families, who through help with future adjustments might be able to help the girl herself, may hesitate to seek further counseling after the immediate crisis has passed.

Some contact with an agency is maintained by the women who keep their children and need financial assistance. Just how much help is available depends upon the agency's as well as the woman's ability to seek and use help. The fact that 17 out of 107 patients seen here in one year were having their second or third illegitimate child indicates that more study, as well as more financial aid, is needed.

In connection with the availability and use of community services, it is interesting to note that out of 107 patients during one year, 12 entered the University Hospitals in labor without having had any prenatal care. Clearly, more is needed than agencies and easily available hospitals. Several of these patients said that they had no money and did not want to ask for help. One said there was too much "red tape" connected with county help. One patient planned to pay her own way and had saved only \$75 when she had a premature baby; a newcomer to the city, said she had not known of any agency that could help her, that she had no doctor, minister, or friends in whom she wished to confide, and that she expected the hospital to place the child.

Because these problems are usually complicated, early referral to an agency for assistance is of utmost importance. The experience of the Social Service Department here has shown the difficulties of trying to formulate sound plans with patients who come without counseling. Since hasty decisions are often regretted later, patients are never forced to make a quick decision about giving up their children. Temporary boarding homes can be found, but some women find this plan is really not what they wanted, and decide to keep their children instead.

Some patients almost ignore the fact of their pregnancies by not seeking help; frequently these are women who later show little interest in their babies. Several patients, all minors, were brought in by their parents, who knew they were pregnant but did nothing until the situation was urgent. One mother said she did not want to force her daughter, who did not like doctors, to go to one. (This patient, incidentally, has since had a second out-of-wedlock pregnancy, but this time she had medical care, the mother, meanwhile, having deserted the family.) One girl's mother said she was too busy to take

## THE MEDICAL BULLETIN

her daughter to a doctor and thought it was not the thing for her father to do. Other patients who had had illegitimate children before said it did not seem important.

The question raised by people interested in this subject is: What lasting effect does the experience have on the girl? Material is not available to provide a completely satisfactory answer, but some research has been done on this question.<sup>1</sup> The Inwood Maternity Home<sup>2</sup> in New York conducted a study of girls in 1954, eight years after they left the institution. Personal interviews were held with 54 of 73 girls residing in all parts of the country. The study revealed that 70 per cent had married but that 20 per cent of these were separated from their husbands. Of the children, 50 per cent had been adopted; 30 per cent were living with the mother; 15 per cent were living with relatives or friends; and 5 per cent were residing in foster homes.

One interesting point brought out in this study was the fact that many of the women who kept their children had since had additional illegitimate children. Only one woman of the 27 who gave up their children for adoption had another out-of-wedlock child, as compared to seven of the 16 who kept their children. This might indicate that the women who gave up their children were able to make better total adjustments and to lead more satisfactory lives.

In a study completed in 1956, the Community Welfare Council of the Greater Minneapolis Area had this to say in its Conclusions and Recommendations.<sup>3</sup>

“ . . . the committee is convinced that the unmarried mother is most effectively served when certain factors are operating in a community:

1. When there is close coordination between social, medical, legal and counseling help.
2. When there is a recognition that the unwed mother's condition is related to causative factors and that she is generally in need of some help in working out these basic problems.
3. When service to the unmarried mother at the earliest possible time is recognized as vital in this helping process.
4. When there is public approval of services to provide necessary financial assistance, counseling, and other help to the unwed mother.
5. When it is recognized that mobility is closely identified with unmarried motherhood and when, therefore, services can be provided as needed, without respect to residence or financial status.
6. When services include confidentiality as a basic ingredient.”

These suggestions are all related to the woman's status as an unmarried mother. It is thought that her pregnancy may be only an incidental manifestation of her basic emotional problems, which requires help in understanding and solution. Along with the further study and continued follow-up that is clearly needed, the general public must be educated to a greater awareness and real understanding of the unmarried mother's situation and her needs. For it is only when her basic emotional problems are understood that we can effectively assist her to make a mature and healthy adjustment.

REFERENCES

1. Young, Leontine: *Out of Wedlock*, New York, McGraw-Hill Company, 1954.
2. Levy, Dorothy: Inwood House Follow-up Study on Unmarried Mothers, Paper presented at the National Conference of Social Work, Atlantic City, New Jersey, May 11, 1954.
3. The Unmarried Mother in Hennepin County, Committee Report of the Family and Child Welfare Division, October 1956.

B. THE LEGAL ASPECTS OF ILLEGITIMACY (Mr. Bradford)

Generally speaking three disciplines are involved in the problems created by unmarried mothers and children born out of wedlock. They are the professions of medicine, social work, and law. They are not necessarily involved in the order named, because that is determined by the circumstances of the unmarried mother or the child.

To resolve the complex problems presented by unmarried mothers and their offspring the members of the professions most concerned must be aware of their respective roles and cooperate so that each dovetails with the other.

A rough simile would be to say that the laws of our state constitute the adhesive and also the lubricant for the proper fusion and functioning of these professions in regard to the problem of illegitimacy.

What protections do the laws of the state of Minnesota establish for unmarried mothers and children born out of wedlock? With which of these laws are doctors concerned?

Looking at these laws in the order in which they appear in our statutes we come first to the Department of Public Welfare and its Commissioner.

Minnesota Statute § 256.01 enumerates the specific duties of the Commissioner. He is empowered to administer and supervise all

forms of public assistance to the state, including aid to dependent children and all child welfare activities; he is further directed to promote the enforcement of laws protecting defective, illegitimate, dependent, neglected, and delinquent children, and to license and supervise child caring and child placing agencies, boarding, and foster care facilities.

To aid the Commissioner in carrying out the duties imposed upon him by § 256.01, and to protect children in foster care, we have Minnesota Statute § 257.03. In essence, this section requires that any person receiving a child in his home with intent to adopt said child or keep him permanently, except a person receiving a child from an authorized agency, must notify the Commissioner within 30 days after receiving the child in his home. Moreover, no person shall solicit, receive, or accept any payment, promise of payment, or compensation for placing or assisting to place a child in foster care. Payment of confinement expenses, medical, or hospital bills has been construed to constitute payment within the meaning of § 257.03.

Minnesota Statute § 257.04 provides that upon receiving the notice required by § 257.03, the Commissioner or his designated agent (the county welfare board) shall visit the home, supervise it, and take any appropriate action to assure protection of the child's welfare and that of his foster parents.

Minnesota Statute § 257.05 regulates and controls the importation of children into this state for foster care purposes or for adoptions. It also requires that the Commissioner be notified.

Minnesota Statute § 257.06 similarly regulates and controls the exportation of children for foster care or adoption. Further protection is afforded a child in foster care by the provisions of Minnesota Statute § 257.07, which requires a written agreement between the person placing such child and the one receiving him.

Maternity shelters or hospitals, are defined and made subject to license and supervision by the Commissioner of Public Welfare, as are foster care facilities, by the provisions of Minnesota Statute § 257.081. The Commissioner of Public Welfare has rule-making powers to facilitate the accomplishment of his obligations under this section. The statutory definition of his obligations under this section. The statutory definition of maternity shelters distinguishes and exempts facilities which give obstetrical care and treatment and are subject to license by the department of health.

Minnesota Statute § 257.09 provides for the supervision and licensing of foster care facilities and provides further that "no un-

licensed person or agency shall receive a child for care or placing out, place a child in foster care, [or] in any way assist with plans for his placement in foster care. . . .”

“Placing children in foster care” is defined by Minnesota Statute § 257.081 Subd. 5 as “. . . placing children in any of the following foster care facilities . . . It also means placement in a private home for the purpose of legal adoption.”

Minnesota Statute § 257.14 requires that the licensee of an infant’s home, upon receipt of an infant therein for care, shall use due diligence to ascertain the legitimacy of such child and to notify the commissioner if the child is believed to be illegitimate.

Minnesota Statute § 257.15 protects the information concerning such child’s illegitimacy and restricts disclosure except to authorized persons with due regard to the welfare of the child and its mother.

Minnesota Statute § 257.16 relates to county child welfare boards and obligates them to perform such duties as the Commissioner may require of them. The County Welfare Boards have now replaced the old county child welfare boards and perform their functions.

Minnesota Statutes § 257.18 to § 257.33 deal with illegitimate children, proceedings to establish paternity, and the duties of the Commissioner of Public Welfare in regard to children born out of wedlock and unmarried mothers. In summary, these statutes provide:

(a) that in addition to being signed by the woman, a complaint alleging paternity may be signed by the Board of County Commissioners, the Commissioner of Public Welfare, or his agent;

(b) that the state lends its name to the proceedings as party plaintiff and that the county attorney prosecute the action;

(c) that in addition to support for the child, confinement or lying-in expenses be recoverable.

Further, our State Supreme Court has held that the mother of a child born out of wedlock has sufficient standing as a party to appeal from a judgment that defendant was not the father (1956, 246 Minn. 299.75 NW (2d) 195); it has also maintained that such a mother has a definite personal financial interest in the amount of support awarded the child by court in paternity proceeding and that as an aggrieved party she can appeal this decision (1950, 231 Minn. 1, 42 M. W. 2d 680, 18 ALR 2d 929). The county attorney is also charged with the duty of enforcing such orders for support as the court may make.

(d) The Commissioner is authorized to make a lump sum settle-

ment with an admitted or adjudicated father for the support of the child.

(e) It is made the duty of the Commissioner of Public Welfare ". . . when notified of a woman who is delivered of an illegitimate child, or pregnant with child likely to be illegitimate when born, to take care that the interests of the child are safeguarded, that appropriate steps are taken to establish his paternity."

The Commissioner is further empowered to "offer his aid and protection in such ways as are found wise and expedient to the unmarried woman approaching motherhood."

From the foregoing it is clear that in order to implement fully the benefits obtainable from the laws dealing with children born out of wedlock and with unmarried mothers, each profession should respect the others' integrity and sphere of operation, and should utilize the skills, services, and functions of other interested disciplines to realize the spirit and objectives of the laws.

#### C. THE MEDICAL ASPECTS OF ILLEGITIMACY (Dr. Kaiser)

From a medical standpoint, illegitimately pregnant women differ from their married sisters in only a few respects. As has been indicated, they are in similar age and social groups, with a preponderance of younger primiparas among the unmarried women.

Despite the oversimplifications that women vomit more readily with unwanted pregnancies and that most unmarried youngsters are unwillingly pregnant, hyperemesis gravidarum is most unusual in the latter group. This is not due to the fact that unmarried women generally come to prenatal care late, for the history of early pregnancy is almost invariably benign. We have no idea of the course in those women who deal with the situation by securing criminal abortion, except when this procedure goes badly and there is an opportunity to obtain a history; even this group tends to conform to the pattern. All this can be taken to mean that whatever social problems illegitimate pregnancy creates, it also serves deep-seated neurotic needs for the mother. The majority of these women use the pregnancy for some purposes of their own, however inexpressible this may be and however unwise it may seem. This in part accounts for the regular appearance of young women with serious disease, usually of long standing and often disfiguring, who have not married because of their handicaps but who have become pregnant apparently as a means of demonstrating their femininity. In this group the patients with serious heart disease present a major problem because they are disin-

clined to be treated as sick, and much persuasion is required to bring them to an acceptance of medical care. The dwarfs who fall into this category may present problems of contracted pelvis which are ordinarily easily diagnosed and handled.

The accidents of pregnancy are of course not respecters of social status. The occasional elderly primigravida and more rarely, the true juvenile may present difficulties at delivery because of a less than normal vaginal capacity which leads to vaginal laceration. The other hazards of delivery and the postpartum course are not unique to illegitimately pregnant women.

There is, however, one area in which major, and as yet virtually untouched, problems exist—and that is the adjustment of the mother after delivery. In no area is there any thought-out program of rehabilitation, and, indeed, in view of the difficulties of follow-up study, there is no clear agreement as to what is required. The differences in status of illegitimately pregnant women from one culture to another and from one social class to another make certain that external influences help in finally solving the problems that provide the neurotic push to out-of-wedlock pregnancy. One can be certain that if suitable services were provided, the ultimate salvage would be improved. Note that the laws of Minnesota protect the baby but make no provision for the protection of the mother. A major task remains to be done in this area.

## Medical School Activities

On April 23, the Department of Bacteriology and Immunology had a special lecturer, DR. P. L. BAZELEY, Director, Commonwealth Laboratories, Melbourne, Australia. Dr. Bazeley lectured on the subject Plasma Protein Factors in Tissue Cultures.

PROFESSOR F. HIMMELWEIT, Director of Virus Research, Wright-Fleming Institute, St. Mary's Hospital Medical School, London, England, was guest of the Department of Bacteriology and Immunology for a lecture on April 24. The subject was Aspects of the Prevention and Evaluation of Influenza Virus Vaccine.

At the Annual Meeting of The American College of Physicians held in Chicago on April 23, 1959, DR. WESLEY W. SPINK, Professor of Medicine at the University of Minnesota Medical School, was elected First Vice President of the College for 1959-60. He was also elected to the Board of Regents. Dr. Spink has been a member of the Board of Governors of the College during the past nine years, representing Minnesota.

### IN MEMORIAM

DR. CHARLES N. HENSEL, '08  
St. Paul, Minnesota

DR. JOHN MAHLON TIERRELL, '00  
Minneapolis, Minnesota



## Faculty Publications

- GOLTZ, ROBERT W. and LYNCH, FRANCIS W.: Nevus Lipomatosus Cutaneous Superficialis, A.M.A. Arch. Dermat. 78:479, 1958.
- GOLTZ, ROBERT W.; FUSARO, RAMON M.; and JARVIS, JAMES: Observations on Glycogen in Epithelial Tumors, J. Invest. Dermat. 31: No. 6, 1958.
- GOLTZ, ROBERT W.; FUSARO, RAMON M.; and JARVIS, JAMES: The Demonstration of Acid Substances in Normal Skin by Alcian Blue, J. Invest. Dermat. 31: No. 3, 1958.
- HALL, WENDELL H.: The Management of Staphylococcal Infections with Antibiotic Combinations, Rocky Mountain Med. J. 55:40, 1958.
- HILDING, A. C.: Ciliary Streaming Through the Larynx and Trachea, J. Thoracic Surg. 37:108, 1959.
- KENNEDY, B. J.: Fluoxymesterone in the Therapy of Advanced Breast Cancer, Proc. Am. Assn. Cancer Res. 2:314, 1958.
- KENNEDY, B. J.: Fluoxymesterone Therapy in Advanced Breast Cancer, New England J. Med. 259:673, 1958.
- KENNEDY, B. J.; MELBY, J.; GOETZ, F.; MORAN, W.; and ZIMMERMANN, B.: Primary Hyperaldosteronism Due to Hyperfunction of the Adrenal Cortex Corrected by Partial Adrenalectomy, Proc. of the 40th Meeting of the Endocrine Soc., June, 1958 (Abstract)
- KEYS, ANCEL: Undernutrition, in *Diseases of Metabolism*, 4th ed., Garfield G. Duncan, editor, 1959.
- LYNCH, FRANCIS W. and RUKAVINA, JOHN G.: The Effect of an Intravenous Chelating Agent, Edathamil Disodium (NA-2-EDTA), in Three Cases of Sarcoidosis, J. Invest. Dermat. 31:259, 1958.
- LYON, RICHARD H.; LICHSTEIN, HERMAN C.; and HALL, WENDALL H.: The Influence of Age on the Metabolic Activity of Mycobacterium Tuberculosis, Proc. Soc. Exp. Biol. & Med. 99:79, 1958.
- LYON, RICHARD H.; LICHSTEIN, HERMAN C.; and HALL, WENDALL H.: Metabolic Rate of Rapidly Multiplying Human Tubercle Bacilli (H37Ra), Trans. 17th Conf. on the Chemotherapy of Tuberculosis 283: Feb., 1958.
- McDONALD, FRANK M.: The Medical Management of Bronchiectasis, Med. Clin. of N.A. 43:209, 1959.

THE MEDICAL BULLETIN

- McDONALD, FRANK M.: Tuberculosis, in *Outlines of Internal Medicine*, 9th ed., C. J. Watson, ed., Dubuque, Iowa, Wm. C. Brown Co., 1958.
- McDONALD, F. M.; GORDON, G. B.; EICHENHOLZ, A.; and SEMBA, T.: Studies on the Mechanism of Bicarbonate Reabsorption, *Clin. Res.* 7:76, 1959.
- McDONALD, F. M. and STEAD, W. W.: The Evaluation of Pulmonary Function in Clinical Practice, in J. A. Myers' *Diseases of the Chest including the Heart*, in press.
- MAGRAW, R. M.: Emotional Problems in Medicine, *Outlines of Internal Medicine*, 9th Ed., C. J. Watson, ed., Dubuque, Iowa, Wm. C. Brown, Co., 1958.
- MAGRAW, R. M. and DULIT, E. P.: The Patient's Presenting Complaint—Signpost or Goal, *Univ. of Minn. Med. Bulletin*, 29:329, 1958.
- MELBY, J. C.; ECGDAHL, R. H.; and STORY, J. L.: Effect of Progressive Removal of the Brain on Adrenal Cortical Hypersecretion Due to *Brucella Melitensis*, *Clin. Res.* 6:280, 1958.
- MELBY, J. C.; BRADLEY, MARY; and SPINK, WESLEY W.: The Influence of Tri-iodothyronine on the Lethal Effect of Bacterial Endotoxin and Infection Due to *Br. melitensis*, *Clin. Res.* 6:280, 1958.
- MELBY, J. C. and SPINK, WESLEY W.: Comparative Studies on Adrenal Cortical Function and Cortisol Metabolism in Healthy Adults and in Patients with Shock Due to Infection, *J. Clin. Invest.* 37:1791, 1958.
- MELBY, JAMES C. and SPINK, WESLEY W.: Experimental and Clinical Studies on Adrenocortical Function in Shock, *Univ. of Minn. Med. Bull.* 30:61, 1958.
- MORAN, W.; GOETZ, FREDERICK J.; MELBY, J.; ZIMMERMAN, B.; and KENNEDY, B. J.: Primary Hyperaldosteronism Without Adrenal Tumor, *Am. J. Med.* (in press).
- OLWIN, THOMAS K. and FLINK, E. B.: The Treatment of Diabetic Acidosis, *Journal-Lancet* 78:37, 1958.
- PRASAD, ANANDA S. and FLINK, E. B.: The Base Binding Property of the Serum Proteins with Respect to Calcium, *J. Lab. & Clin. Med.* 51:345, 1958.
- PRASAD, ANANDA S. and FLINK, E. B.: The Determination of Ultrafiltrable Calcium in a Variety of Clinical Conditions, *J. Lab. & Clin. Med.* 52:1, 1958.

## WEEKLY CONFERENCES OF GENERAL INTEREST

### *Physicians Welcome*

- Monday, 9:00 to 10:50 A.M. OBSTETRICS AND GYNECOLOGY  
Old Nursery, Station 57  
University Hospitals
- 12:30 to 1:30 P.M. PHYSIOLOGY-  
PHYSIOLOGICAL CHEMISTRY  
214 Millard Hall
- 4:00 to 6:00 P.M. ANESTHESIOLOGY  
Classroom 100  
Mayo Memorial
- Tuesday, 12:30 to 1:20 P.M. PATHOLOGY  
104 Jackson Hall
- Thursday, 11:30 A.M. to 12:30 P.M. TUMOR  
Todd Amphitheater  
University Hospitals
- Friday, 7:45 to 9:00 A.M. PEDIATRICS  
McQuarrie Pediatric Library,  
1450 Mayo Memorial
- 8:00 to 10:00 A.M. NEUROLOGY  
Station 50, University Hospitals
- 9:00 to 10:00 A.M. MEDICINE  
Todd Amphitheater  
University Hospitals
- 1:30 to 2:30 P.M. DERMATOLOGY  
Eustis Amphitheater  
University Hospitals
- Saturday, 7:45 to 9:00 A.M. ORTHOPEDICS  
Powell Hall Amphitheater
- 9:15 to 11:30 A.M. SURGERY  
Todd Amphitheater  
University Hospitals

For detailed information concerning all conferences, seminars, and ward rounds at University Hospitals, Ancker Hospital, Minneapolis General Hospitals, and the Minneapolis Veterans Administration Hospital, write to the Editor of the BULLETIN, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14, Minnesota: