Pulmonary Emphysema, Adrenocortical Hyperplasia and Peptic Ulceration*

MARJORIE J. WILLIAMS, M.B.CH.B.** AND JULIUS L. MENDEL, PH.D.

Temple, Texas

INTRODUCTION

An increased incidence of peptic ulceration in patients with pulmonary emphysema has been well documented and it has been suggested that the association might be due to enhanced and adrenocortical activity. Recently Sjaastad and associates* performed certain blood and urine steroid determinations in a group of men with pulmonary emphysema, several of whom had peptic ulcers. These workers concluded that there was no evidence of enhanced adrenocortical activity in men with pulmonary emphysema and that the increased incidence of peptic ulceration could not be attributed to hypercorticism. These studies, while thorough, were by no means exhaustive. On the other hand, an impression had developed from necropsy studies performed at this hospital that adrenocortical hyperplasia was a fairly common finding in men with pulmonary emphysema. The present investigation was undertaken to evaluate this impression by systematic morphologic study of necropsy material.

MATERIALS AND METHODS

During a four-year period, 1958 through 1961, 513 necropsies were performed on men. Of these, 434 were suitable for inclusion in the present investigation. Suitability depended upon the availability of microscopic sections of both lungs and adrenals for review and upon the uniform fixation and sectioning of the specimens. Ten cases were excluded because of very extensive carcinomatous metastases to the adrenals and one because of secondary amyloidosis affecting the adrenals. No other selection was exercised. No attempt was made to assess any case in relation to the patient's smoking habits, history of asthma or of any other conditions which might predispose to emphysema. The vast majority were long-term residents of Texas and came from semi-rural areas.

The lungs were removed from the body en bloc with the main stem bronchi and the trachea. They were filled with 10 per cent neutral formalin through the trachea under gravity. The lungs were then submerged in a jar containing formalin for a minimum of three days. Gross examination was carried out by cutting each lung into slices about 1 cm. in thickness. The emphysematous lungs were classified in accordance with the recommendations of the American Thoracic Society. The degree of involvement, either moderate or severe, was determined by correlation of gross and microscopic findings.

The adrenals were dissected as free as possible of fat and weighed. When the combined weight of both glands exceeded 20 gm., hyperplasia was suspected. Multiple sections were made through the fresh specimens and the thickness of the cortices evaluated. The specimens were fixed in either Zenker's solution or 10 per cent neutral formalin. All the grossly circumscribed cortical nodules encountered in the series were classified after microscopic study as hyperplastic changes rather than as true encapsulated adenomas. The final determination of the presence of cortical hyperplasia was determined by correlation of gross with microscopic findings, utilizing the criteria described by Cohen and associates* and by Ashworth and Garvey.*

*From the Laboratory Service, Veterans Administration Center.
**Presently at Department of Medicine and Surgery, Pathology and Allied Sciences Service, Washington, D. C.
Each stomach and duodenum was examined for the presence of chronic peptic ulceration.

All microscopic sections were stained with hematoxylin and eosin. In this investigation, routine slides in the files were utilized for review. The adrenals and the lungs were studied separately without knowledge as to the condition of the other organ.

The lungs were classified in the following manner: (1) emphysema present when the disease was severe or moderate, (2) emphysema, absent, when the disease was not present or was of minimal extent. The adrenal cortices were classified as: (1) hyperplastic; (2) non-hyperplastic.

Chi square determinations were used for all statistical analyses. Probability values are shown in the text.

**RESULTS**

In the series of 434 necropsies on men, the findings were as follows: 243 patients with emphysema of severe or moderate degree; 191 with little or no emphysema; 154 with hyperplastic adrenal cortices; 280 with nonhyperplastic adrenals; and 49 with peptic ulcers. The average age for the patients with emphysema was 63 years and for those without, 61 years. Chronic lung diseases, such as primary cancer, tuberculosis and chronic inflammation were present in a significant number (p<0.001) in the emphysema group compared with the non-emphysema group. Chronic obstructive respiratory disease constituted a major clinical problem in only about one-third of the patients with emphysema.

Among the cases with emphysema, 60 patients had severe lung destruction and 183 moderate disease. The emphysematous changes were lobular, usually with a mixture of the subtypes, in about 75 per cent and paracicatrical in about 25 per cent. The lungs of all patients with severe disease exhibited the lobular type of emphysema.

A significant association between pulmonary emphysema and adrenocortical hyperplasia was detected (p<0.001), (Table 1). However, no statistically significant relationship was noted when the incidence of peptic ulceration was compared with that of the adrenocortical hyperplasia.

The occurrence of hypertensive cardiovascular disease was distributed fairly evenly among the patients with emphysema and without emphysema. A similar distribution was noted for cancer. Therefore, the high incidence of adrenocortical hyperplasia in men with emphysema cannot be attributed to co-existent hypertension¹ or cancer.² Although cancer as a whole showed no linkage with emphysema, significant association of this disease with lung cancer was apparent (p<0.001), (Table 1). No predominance of "stress" factors with the exceptions of lung disease, hypoxia, and peptic ulceration were noted among the emphysema patients as compared with those without emphysema.

**DISCUSSION**

A significantly increased incidence of adrenocortical hyperplasia and of peptic ulcer has been demonstrated by morphologic necropsy studies in men dying with severe or moderate pulmonary emphysema. The hyperplastic changes in the adrenals were defined using generally accepted criteria. Such changes are usually considered to be the morphologic manifestation of increased adrenocortical hormone production. None of the patients had overt clinical hyperadrenocorticism, but minor manifestations may not have been detected since they were not specially sought. In this connection, it is of interest that many of the patients with carcinoma of the lung, who showed morphologic or chemical evidence of hyperadrenocorticism, had no suggestive symptoms.³ Although peptic ulceration had a significant association with pulmonary emphysema, no evidence of its linkage with adrenocortical hyperplasia emerged from the present study. This observation is interesting and suggests that adrenocortical hyperactivity bears no direct relationship to peptic ulceration. However, it has been
TABLE 1—ASSOCIATION OF PULMONARY EMPHYSEMA WITH CERTAIN CONDITIONS SHOWN BY CASES

<table>
<thead>
<tr>
<th>Conditions Analyzed</th>
<th>Pulmonary Emphysema</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Present (in 243 cases)</td>
<td>Absent (in 191 cases)</td>
<td>P Values</td>
</tr>
<tr>
<td>Adrenocortical Hyperplasia</td>
<td>Present</td>
<td>103 (42.4%)</td>
<td>51 (26.7%)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>140 (57.6%)</td>
<td>140 (73.3%)</td>
</tr>
<tr>
<td>Peptic Ulceration</td>
<td>Present</td>
<td>39 (16.0%)</td>
<td>11 (5.8%)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>204 (84.0%)</td>
<td>180 (94.2%)</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>Present</td>
<td>39 (16.0%)</td>
<td>12 (6.3%)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>204 (84.9%)</td>
<td>179 (93.7%)</td>
</tr>
</tbody>
</table>

noted by others that the gastric response to steroid administration is unpredictable.4

The mechanism underlying the association between pulmonary emphysema and adrenocortical hyperplasia is obscure. Hypoxia either as a specific or a non-specific "stress" factor must be considered. Yet no particular relationship between left heart failure and adrenocortical hyperplasia was noted and the present material did not permit study of the adrenals in patients with severe hypoxia such as is found with certain congenital heart lesions. Further study of adrenocortical function in hypoxic individuals might produce valuable information. The possibility of a coincidental association between pulmonary emphysema and adrenocortical hyperplasia, though unlikely, cannot be completely dismissed. Possibly tissue utilization of adrenocortical hormones may be increased in patients with emphysema and the cortices may have proliferated in order to supply an increased need. Such circumstances would account for the absence of clinical hyperadrenocorticism as it might be assumed that the steroids were all utilized by the tissues. The studies of Sjaastad and others18 indicate that abnormalities of steroid excretion are not a factor. Croxatto and Barnafi14 have discussed the hormone-like effect of active polypeptides which are formed naturally, as a result of tissue injury, or under artificial conditions. It is intriguing to speculate that damage to the lung tissue such as occurs in emphysema may lead to the formation of an active polypeptide with adrenocorticotrophic properties.

**SUMMARY**

Analysis of morphologic necropsy findings in 434 men demonstrated a statistically significant association between pulmonary emphysema and adrenocortical hyperplasia and between pulmonary emphysema and peptic ulceration.

**Resumen**

El estudio de los hallazgos morfológicos en la necropsia de 434 hombres demostró una asociación con significación estadística entre el enfisema pulmonar y la hiperplasia adrenocortical y entre el enfisema pulmonar y la úlcera péptica.

**Résumé**

Une analyse des constatations morphologiques faites à l’autopsie de 434 hommes mit en évidence une association statistiquement nette entre emphysème pulmonaire et hyperplasie surrenale et entre emphysème pulmonaire et ulcère gastrique.

**Zusammenfassung**

Eine Analyse morphologischer Sektionsbefunde bei 434 Männern erwies eine statistisch signifikante Verknüpfung zwischen einem Lungenemphysem und einer Nebennierenrindenhyperplasie und zwischen Lungenemphysem und peptischem Geschwür.

**References**

THE USE OF 14" x 14" FILMS FOR CHEST EXAMINATION*

Recently it has been proposed that 14" x 14" films be used routinely for chest x-ray examination (Dui. Chest, 38:124, August, 1960). It has been stated that this size is adequate for 96 per cent of patients, that use of this size results in a reduction dose, and that there is a saving of about $0.13 per film.

It is the viewpoint of the Joint Committee of the American College of Radiology and the American College of Chest Physicians that such choices should be at the discretion of the individual radiologist. However, because of official requests for information which have reached this committee, we feel constrained to comment.

Since there are some patients (2 to 20 per cent) who because of their size require the use of 14" x 17" films, and since anything less than this size is not adequate for examination of the abdomen in adults, it is obvious that the 14" x 14" size cannot completely replace the larger size cassettes in a general radiologic practice. The practice of using 14" x 14" film in 14" x 17" cassettes requires such careful control in positioning the film in the darkroom and using the proper end of the cassette when positioning for examination that, particularly in a busy department, the number of repeated examinations because of technical errors in these details would undoubtedly nullify any advantages of potential radiation and cost savings. The necessity of purchasing additional cassettes and intensifying screens in the 14" x 14" size would also tend to obviate any cost savings. It should be noted that the cost of the film represents only a small portion of the total cost of a radiologic examination and that any savings in this minor cost may well be negated by additional costs for the more expensive items.

It is certainly laudable to attempt to limit the patient dose in any radiologic diagnostic procedure, and it is a well-accepted fact that limitation of the size of the field is one of the most effective measures in lowering this dose. However, with chest radiography such a small contribution to lifetime gonadal dose is made, even using the 14" x 17" format, that a saving of 18 per cent does not seem significantly large. It would also seem that repeated examinations due to incorrect positioning or to patient size might, on the average, make this saving much less. Of course, unless the x-ray beam is carefully confined to the 14" x 14" area there will be no sparing of dose, when intermixed sizes are used there is more of a possibility that the beam will be diaphragmed to the largest size utilized, and no dose saving realized.

In much of Europe, the 14" x 14" size is standard, but chest examinations are made by fluoroscopic localization (with consequently increased dose) and additional films of the costophrenic angles are almost routine.

Based on these considerations, the Joint Committee cannot officially favor the use of the 14" x 14" size as a routine one for chest examinations, but recognizes that, at the discretion of an individual radiologist and with appropriate consideration of the difficulties described above, such a format may be useful in selected situations.

*Approved by the Joint Committee at its annual meeting in Atlantic City, June 18, 1963.

Joint Committee on Chest X-ray
American College of Chest Physicians
American College of Radiology

For reprints, please write Dr. Williams at Veterans Administration/113/, Washington 25, D. C.