STATUS THYMICO-LYMPHATICUS*

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The first description of death caused by an enlargement of the thymus gland was recorded by Felix Platter,[1] Professor of Medicine at Basle, who died in 1614. Ever since this time a controversy has been going on between whether lymphatism (usually diagnosed by an enlargement of the thymus) could ever be responsible for death from minor causes, e.g. after the administration of an anaesthetic or the performance of a minor surgical operation.

In England the argument was more or less settled after the appearance of an article by Greenwood and Woods in 1927,[2] and the report of the Status Lymphaticus Investigation Committee in 1931.[3] The corpse of lymphatism was successfully buried, but since Selye[4] started his theory of the general adaptation syndrome, and the use of cortisone and allied steroids began in clinical medicine, the thymus has assumed a new importance, and many efforts have been made in the medical press to revive the corpse and give it a new lease of life. For these reasons, and also owing to the fact that in our own country inquest magistrates still accept lymphatism as a cause of death following on anaesthesia, I thought it advisable to review the recent literature on the subject, mention some of my own experimental work, and see if I could get any nearer to the truth in the matter.

Definition. For those who believe that this condition exists the description of Marine[5] is the best: 'Status lymphaticus may be defined as a constitutional defect, usually congenital (though it may be acquired), dependent on an inadequacy of some function of the suprarenals, sex glands and autonomic nervous system, and associated with lowered resistence or increased susceptibility to a great variety of non-specific physical and chemical agents. Anatomically it is characterized by delayed involution or hyperplasia of the thymus, hypertrophy and hyperplasia of the lymph glands and lymphoid tissue of the various organs, under-development of the chromaffin, gonadal (suprarenal cortex, interstitial cells of testes and ovaries) and cardiovascular systems and certain peculiarities of external configuration.'

Incidence

The figures for the incidence of status thymico-lymphaticus quoted below were obtained from a questionnaire I sent to all specialist anaesthetists, pathologists, and public hospitals in South Africa. The response from the anaesthetists was very poor; only about 10% replied. In order to get comparative figures questionnaires were also sent to anaesthetists attached to some of the leading medical schools in England, Europe and America. In all 500 questionnaires were sent out and 210 answers were received.

I would not attach much importance to the comparison of the total overseas death rate with our own, in the first place because these are figures from leading medical schools where one would expect the standard of anaesthesia to be very high; whereas the South African figures include the hospitals which are not attached to medical schools. Secondly some doubt existed in the minds of many anaesthetists about what was actually meant by the question, 'Total number of deaths associated with anaesthesia during the last 5 years'. What I wanted was a record of all cases like those referred to the district surgeon under the Inquest Act, but most overseas anaesthetists only gave a return of cases where they thought the anaesthetic alone was responsible. The important point I wish to make is that it appears that the pathologists attached to the leading medical schools in England, Europe and America no longer make the diagnosis of status thymico-lymphaticus as a cause of death following the administration of an anaesthetic.

TABLE. I. ANAESTHETIC DEATHS 1950-1954 (QUESTIONAIRE RETURNS).

Country	*No. of Operations*	*Total Deaths*	*Deaths per 1000 cases*	*Deaths from Lymphatism*
U.S.A. ..	162,700	59	0·30	0
England and Europe ..	225,000	103	0·45	0
South Africa	518,900	445	0·86	19

Deaths from lymphatism in South Africa—0·037 per 1000 cases (3·7 per 100,000).

Physiology

There is still no evidence that the thymus produces an internal secretion; its main function seems to be the production of lymphocytes.

The thymus reaches its maximum size at puberty (11 to 15 years), and then undergoes an 'age involution', until at the age of 65 it is about one quarter the size it reached at puberty. After puberty there also occurs a rapid reduction of the bulk of parenchyma in the organ; while at the same time the interstitial connective tissue usually assumes the character of adipose tissue and forms a progressively greater part of the organ.[6]

The thymus also undergoes an 'acute or accidental involution' after exposure to various forms of stress. This involution is controlled by the adrenal glands. Dougherty[7] and his co-workers have apparently proved that the size of the lymphoid tissue (including the thymus) is dependent on the ability of the adrenal cortex to induce dissolution of lymphocytes. They have demonstrated an absolute lymphopenia in the circulating blood after the administration of whole adrenocortical extract and, as a result, a reduction in the size of lymphoid tissue.

The thymus is decreased in size in marasmus, wasting diseases, starvation and inanition. Hyperplasia of the thymus is associated with castration, Graves' disease, Addison's disease, myasthenia gravis, lymphatic leukemia, acromegaly, rickets (rarely), congenital

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hypoplasia of the adrenals, congenital abnormalities like hare-lip and cleft palate, anencephaly, and so-called thymic death.

Recently it was reported that 1·5 g. of flavonoids had been extracted from 15 kg. of calf thymus. These extracts are supposed to delay the onset of 'heat', and also to diminish fertility.[8]

Diagnosis

It is very difficult to diagnose a condition which probably does not exist. If one believes that lymphatism is always accompanied by adrenocortical insufficiency then chemical examination of steroid levels in the blood (17-OH-corticosteroids) and urine (17-keto-steroids) should be helpful in suspected cases. The Thorn test might also be useful. In infants who suffer from pressure symptoms cyanosis, hoarseness and stridor may be present. Kemp[9] believes that border-line cases are often found in pale well-nourished children with a placid disposition. He also mentions 3 signs which he found of value in recognizing these poor-risk cases before anaesthesia, as follows: (1) *Sargent's white-line sign*—a delay in reddening when the skin of the abdomen or chest is lightly scratched with a toothpick or match, (2) *Orroya's sign*—an appreciable delay in the contraction of the pupil which should immediately occur when a light is suddenly flashed in a child's eye, and (3) *Schridde's sign*—a prominence of the lymphoid follicles on the pharyngeal wall between the tonsils. I have never been able to elicit these signs on examining children before tonsillectomy.

Radiological Diagnosis. According to most radiologists the diagnosis of enlargement of the thymus is very difficult because the thymus can easily be confused with other shadows in the mediastinum. The pictures with the least distorted view of the mediastinum are the postero-anterior roentgenograms taken in the upright position at the end of inspiration. A lateral view should also be taken.[10] To my mind the only two indications for radiological examination of the thymus before operation are (1) where the infant shows signs of pressure symptoms, when one might discover an obscure tumour in the mediastinum, and (2) where the parents suffer from a thymus 'phobia'.

Post-Mortem Findings

The autopsy reports differ according to the beliefs of the individual pathologist who conducts the post-mortem. The conditions reported include a hypertrophy of the thymus and general hyperplasia of the lymphatic system, atresia of the aorta and endocardial signs of degeneration.[2] Hypoplasia of the adrenals is a common finding.

It must be pointed out that the normal thymus, even in children, is much larger than was previously supposed, and one should not diagnose this condition on the size of the thymus alone. It may be useful to quote the views of some prominent pathologists on this subject. Boyd:[11] 'Since most subjects who come to autopsy have been ill for more than 3 days the pathologist's eye become adjusted to the involuted thymuses, so that the prominent thymus of the healthy, well-nourished subject appears enlarged to him. In other words, the anatomical picture called status thymico-lymphaticus is the normal state of the thymus and lymphoid tissue of the healthy person. The inconspicuous thymus and lymphoid tissue commonly called normal is the involuted thymus of the poorly nourished or diseased person.' Greenwood and Woods:[2] 'The present use in certification and in evidence in coroner's courts of the phrases status lymphaticus and status thymico-lymphaticus is, we suggest, a good example of the growth of medical mythology. A nucleus of truth is buried beneath a pile of intellectual rubbish, conjecture, bad observations, and generalization. This heap of rubbish is described in the current scientific jargon and treated as an orthodox shrine.' Young and Turnbull[3] reporting on the Status Lymphaticus Investigation Committee in 1931: 'In the opinion of the Committee the facts elicited in the present inquiry are in harmony with those of Hammar (1926 and 1929) and Greenwood and Woods (1927) in affording no evidence that so-called "status lymphaticus" has any existence as a pathological entity.'

Against these opinions Symmers[12] of the Bellevue Hospital, New York, reported 249 cases of lymphatism in 4,000 autopsies. In a carefully recorded series of over 500 autopsies in children dying suddenly Carr[13] also reports 49 deaths associated with pathological changes in the thymus and lymphatic systems.

AUTHOR'S EXPERIMENTAL WORK: (1) ANIMAL EXPERIMENTS

The object of these experiments was to determine (*a*) whether the size of the thymus has any influence on the induction time and sleeping time in rats, (*b*) the role of the thymus in 'stress', and (*c*) whether any relationship could be established between the size of the thymus and the size of the adrenals in normal and orchidectomized rats.

Method

Male albino rats (wistar strain) from 6 weeks to 3 months old were anaesthetized with open ether and the testes *or* adrenal glands removed. These rats, with an equal number of controls, were then kept under observation from 3-6 weeks under identical conditions, and fed on the same standard rat diet-'comproids' and milk. The adrenalectomized animals were also given normal saline in addition to tap water. All the animals for adrenalectomy were given 1 mg. of cortisone 2 days before and 3 days after operation. A certain number of adrenalectomized or orchidectomized rats were also given 1-3 mg. cortisone daily by intramuscular injection, until the time of autopsy, usually for not longer than 3 weeks.

After an interval of 3-6 weeks the operated animals together with controls were placed in a large tin, 6 at a time, with a glass top, and anaesthetized with 2 litres of oxygen blown through a glass bottle containing either 100 c.c. of ether or 50 c.c. of chloroform, and the induction time, and sleeping time, for each rat determined by means of a stop-watch.

Immediately on recovery from the anaesthetic the animals were killed instantly and weighed, and their thymus and adrenal glands dissected out and weighed.

Under open ether anaesthesia about half the experimental animals with controls were exposed to stress by crushing of all four limbs and severe pulling of the entire gut, stomach and liver. The whole gut was then left exposed, and the animal kept under observation until he showed signs of waking up. Immediately on recovery from the anaesthetic the animals were killed instantly, weighed, and their thymus and adrenal glands dissected out and weighed.

Over 300 rats were sacrificed in these experiments.

Findings

(*a*) In the 180 rats anaesthetized with ether or chloroform there were no deaths, irrespective of the size of the thymus. The adrenalectomized animal can apparently stand even chloroform induction well without the aid of cortisone or atropine. The largest

TABLE II. RECORD OF 4 OF THE EXPERIMENTS ONLY

Expt. No.	*Anaesthetic used*	*Weight Rat (g.)*	*Weight Thymus (mg.)*	*Induction Time (minutes and seconds)*	*Sleeping Time (minutes and seconds)*
12	Ether	170	153	1,00	4,20
		159	165	1,35	2,40
		180	228	0,45	3,55
		174	153	1,15	2,45
		211	268	2,30	1,05
		159	211	1,45	3,45
		215	433	1,30	3,15
		186	323	2,00	3,55
15	Ether	109	135	2,45	1,20
		170	193	3,40	1,50
		90	102	2,05	2,05
		134	219	2,30	2,15
		157	189	2,30	1,45
		143	400	2,15	1,45
23	Chloroform	224	231	1,46	1,14
		269	367	1,45	1,25
		206	200	1,35	0,40
		259	397	1,10	0,36
		258	122	2,00	0,32
		259	186	2,00	0,35
		292	120	1,30	1,05
		242	152	1,35	0,55
24	Chloroform	230	78	2,50	0,30
		220	124	3,55	2,15
		228	142	1,30	0,45
		244	126	3,30	0,40
		203	206	3,10	0,35
		256	290	1,45	0,45
		264	414	2,40	0,40
		279	319	3,55	0,35

thymuses were found in those animals that had been adrenalectomized or orchidectomized 4 weeks before the commencement of the experiments. The smallest thymuses were found in those animals that had received cortisone for 3 weeks after operation. A considerable diminution in the size of the adrenal glands was also noticed after large doses of cortisone (2-3 mg. daily). *No relationship could be established between the weight of the thymus gland and the induction time and sleeping time in rats.* See Table II.

(*b*) 150 rats were exposed to surgical trauma under ether anaesthesia as already described. There were no deaths that could be attributed to the stress *per se*. Even the adrenalectomized animals without cortisone did not succumb. It would appear that once the adrenalectomized animals have survived for about 3 weeks they can withstand a considerable amount of stress, owing to the development of accessory adrenal cortices in other parts of the body. Three animals died during anaesthesia, but these deaths can all be explained. One rat died from haemorrhage, one from overdose of ether before we commenced the 'stress', and one from an artificially induced pneumothorax, the result of bad surgery.

From these experiments the conclusion is reached that rats suffering from artificially-induced 'lymphatism' do not die suddenly after exposure to various forms of surgical trauma under ether anaesthesia.

(*c*) It has often been stated that an inverse ratio exists between the size of the thymus and the adrenals, in other words, that a large thymus is usually accompanied by hypoplastic adrenal glands.[14]

No such relationship could be established in normal or orchidectomized rats. All our glands were weighed

TABLE III(A)

Orchidectomized Rats		*Control Rats*		*Orchidectomized Rats receiving Cortisone 1–3 mg. daily*	
Weight Thymus (mg.)	*Weight Adrenals (mg.)*	*Weight Thymus (mg.)*	*Weight Adrenals (mg.)*	*Weight Thymus (mg.)*	*Weight Adrenals (mg.)*
336	32	162	36	49	16
428	35	186	36	68	19
347	36	218	35	60	14
435	29	201	35	53	14
244	34	126	34	66	22
286	39	167	30	82	14
378	40	69	29	89	18
224	41	77	24	72	13
312	34	165	25	177	26
340	26	153	31	139	21
217	36	156	31	141	32
299	39	101	39	130	25
254	38	143	25	65	22
255	36	105	28	203	28
347	34	145	39	146	27
234	32	158	29	137	20

TABLE III(B)

Adrenalectomized Rats	*Control Rats*		*Adrenalectomized Rats receiving Cortisone 1-2mg. daily*
Weight Thymus (mg.)	*Weight Thymus (mg.)*	*Weight Adrenals (mg).*	*Weight Thymus (mg.)*
400	218	35	135
336	189	31	193
376	164	30	102
306	163	30	89
318	155	26	90
382	170	25	69
290	157	27	113
260	144	28	110
506	169	31	121
368	218	25	161
341	132	31	82
348	143	28	182
250	159	33	134
393	173	28	158
331	211	34	92
247	128	35	68

on a Mettler analytical balance which gives the correct weight up to 1/10,000 g. Table 3 gives the weights of some of these glands for rats weighing between 150-200 g.

2. AUTHOR'S OBSERVATIONS ON HUMAN TISSUES

The object of this investigation was to determine (*a*) the average size of the thymus gland for each age-group, and (*b*) whether one could establish a relationship between the size of the thymus and adrenal glands by weight, and histological examination.

Method

About 100 adrenal and thymus glands were collected at post-mortems of patients *who died suddenly* from accidental death, injury, suicide or homicide. These glands were then cleaned, weighed, and examined histologically. Wherever possible the weights of the

TABLE IV. AVERAGE WEIGHTS OF THYMUS GLAND IN GRAMS ACCORDING TO AGE

Age (years)	*Our average weights*	*Hammar*	*Schridde*
0– 1	20·6	13	13
1– 5	22·8	23	17
6–10	26·5	26	20
11–15	30·8	38	25
16–20	26·5	26	20
21–25	25·8	25	19
26–35	14·3	20	14
36–45	21·7	16	10
46–55	16·6	13	7
56–65	8·6	16	4
66–75	5·8	6	3

bodies and of the spleen were also obtained. Boyd[11] has emphasized the fact that (with the exception of tumours of the thymus, leukemia, and exopthalmic goitre) the weight of the thymus is reduced by any fatal illness, which has lasted longer than 24 hours. Selye[15] also lays stress on the fact that the weight of the adrenal glands is affected by various diseases owing to the general adaptation syndrome elicited by them. For these reasons one should only consider as true weights the weights of organs obtained from patients who did not succumb after a prolonged illness.

Findings

(*a*) The average weight of the thymus gland for each age-group is given in Table IV. These weights are compared with those given by Hammar[16] in 1906 and Schridde[17] in 1923, also in cases of sudden death (accident, homicide or suicide).

(*b*) *No relationship could be established between the weight of the thymus and adrenal glands.* Even with our largest thymuses the weights of the adrenal glands were still within normal limits for the age-group. Soffer[18] talks about the existence of an autonomous 'see-saw' arrangement between these two glands. In our own series we could not establish such a relationship.

All these glands were sectioned, stained with haemotoxylin and eosin and examined histologically. In those patients who presented thymus glands above the average weights the adrenal glands were also stained with Sudan IV stain and examined for lipids. These glands undergo autolysis after death so that the final results are not always reliable.

Histological Findings

(*a*) *Thymus Glands.* Apart from increased adipose tissue in the larger glands we could find nothing abnormal in these sections.

(*b*) *Adrenal Glands.* A few adrenal glands taken from subjects with large thymuses (over 50 g.) showed a generalized diminution of lipids in all three zones of the adrenal cortex. Similar changes were however also found in control adrenal glands where the thymus glands were of average size. Most of the glands were normal in appearance in spite of increase in the size of the thymus glands.

From the histological examination of our own sections we could not establish a relationship between the thymus and the adrenal cortex. Our largest thymus glands were not always accompanied by hypoplastic adrenals showing histological changes.

THEORIES ON THE CAUSE OF DEATH

Various theories have been advanced by pathologists and pediatricians to explain these deaths. No single theory will explain all deaths. If children in the category of lymphatism do not all react in the same way to various forms of stress, this might be a reason why so many theories have been postulated. Some of the more important theories are discussed below:

Mechanical Obstruction. Anatomically it is possible for the thymus to cause pressure not only on the trachea, but also on the great vessels and the recurrent laryngeal nerves. Theoretically this is particularly likely to happen during the first year of life; afterwards, although the thymus is increasing in size, the chest is growing at a much greater rate, so that obstruction by the thymus is very unlikely.[11] I doubt if direct pressure of the thymus could ever cause death, even during anaesthesia. According to experiments conducted by Tammassia[19] the thymus must weigh at least 180 g. before it can completely compress the trachea. This is much larger than the heaviest thymuses ever reported.

Anaphylaxis. Symmers[12] believes that death is due to anaphylaxis, sensitization and shock as the result of the release of nucleoproteins formed during the destruction of innumerable germinal follicles in the thymus gland. This theory of auto-intoxication is no longer accepted.

Rupture of a Hypoplastic Cerebral Artery. Of the anatomical abnormalities associated with status thymico-lymphaticus a general hypoplasia of the arteries has often been mentioned. These changes are supposed to be common in the aorta and cerebral vessels. Cerebral haemorrhage might well be a cause of sudden death in young people; but often there is no associated enlargement of the thymus gland.[3] These deaths might just as well be taken as examples of congenital aneurysms of the cerebral arteries.

Adrenal Insufficiency. Wiesel[20] was the first to postulate the theory of adrneal insufficiency. He suggested that a sudden fall of blood pressure due to hypoplasia of the chromaffin tissue of the adrenal glands resulted in insufficient production of adrenaline and that this

deficiency led to a sudden increase in vagal tone, with cardiac dilatation.

Campbell[21] believes that death is due to hypoplasia of the medulla resulting in an insufficiency of adrenaline in cases of 'stress' with the result that there is not sufficient dilatation of the coronary arteries to supply more blood to the heart muscle.

Aldrich[22] and others believe that these patients suffer from a *vagotonia*, as a result of the reduced adrenal activity. These vagotonic symptoms might take the form of increased stimulation of the vagus or parasympathetic, or a reduction in the activity of its normal antagonist, the sympathetic. In my opinion patients can die from these causes without showing any evidence of lymphatism. We also know that the size of the thymus is not affected by the secretions of the adrenal medulla, and that the medulla is not essential to life.

Perhaps the most reasonable hypothesis is that advanced by Kemp,[23] of Vancouver, who believes that status lymphaticus is the result of the normal postnatal absorption of the foetal adrenal cortex in infants suffering from hypothyroidism. In this connection it is of interest that in 1929 Williamson and Pearce[24] apparently proved that the thymus was not a distinct organ, but part of the thyroid gland, and that it acted as a reservoir for the secretory products of thyroid activity. I shall discuss this theory of adrenocortical insufficiency below.

DISCUSSION

Whether or no status thymico-lymphaticus exists as a pathological entity is a matter for the pathologists to decide. One is, however, struck by the fact that in the recent literature on the causes of sudden and unexplained deaths in infants and children, not associated with anaesthesia, status thymico-lymphaticus is no longer mentioned as a cause. Most of these deaths are eventually traced down to the heart and lungs after careful histological examination of these tissues.[25] What concerns us as anaesthetists is whether this condition can be responsible for death during anaesthesia. In my opinion, even if the condition exists this should never happen under a skilful anaesthetist. My own experience and reading suggest that other less nebulous causes can usually be found to explain these fatalities, if adequate investigation is made. Quite a number of anaesthetic complications, apart from the size of the thymus, can cause death with more or less similar post-mortem findings, or with none. To mention only a few, one thinks of laryngospasm, bronchospasm, chronic hypoxia, reflex vagal inhibition, ventricular fibrillation, and simple overdose of anaesthetic in a susceptible individual.

In the older records chloroform was the chief agent blamed for these deaths. We now know that chloroform can cause sudden ventricular fibrillation in susceptible patients, irrespective of the size of the thymus gland. But no particular anaesthetic seems to be free from blame.

It is said that these deaths are particularly likely to occur in children after operations for tonsillectomy or adenoidectomy. On going through the records of thymic deaths during throat operations one is struck by the suddenness of death in most cases. I venture to suggest that these deaths could with equal sincerity have been diagnosed as being due to *reflex vagal inhibition*. We know that the threshold for peripheral vagal stimulation is much lower in the neck than elsewhere. It is particularly likely to happen under light anaesthesia, with inadequate premedication. In some of these cases where the diagnosis of status thymico-lymphaticus has been made the size of the thymus is well within normal range, and in most of them the weight of the thymus is not given or was not taken.[3] It is significant that in Pretoria during the last 5 years at least 10,000 children were operated on for tonsils or adenoids with no deaths from status thymico-lymphaticus. In Johannesburg, where no death from this cause was reported, the figure must be considerably higher.

The thymus is supposed to be hypertrophied or persistent in toxic goitre, and in myasthenia gravis, to mention only two conditions frequently requiring surgery. I have not found these cases more difficult to anaesthetize, or worse anaesthetic risks, than normal cases. We also have no record of eunuchs dying suddenly after the administration of an anaesthetic or from trivial or emotional causes.

The only reasonable theory of death during operations on patients suffering from lymphatism seems to be that of adrenocortical insufficiency, and this requires further examination. Most 'thymic deaths' reported were in children who showed no signs of adrenal disease before operation, and in most cases death occurred very suddenly, before any resuscitative measures could be instituted. If these deaths were due to adrenal exhaustion one would expect at least a delayed interval, with signs of collapse, before death finally set in. Many of these deaths occurred during induction, or during minor operations, where the patient was not exposed to much 'stress'. We know that there is an increased secretion of corticoids during periods of stress; and even if there were a certain amount of hypoplasia of the cortex beforehand one would expect the remaining cortex to secrete enough corticoids to meet the situation during minor operations.[26] We know too, that general anaesthesia in itself is not the type of stress requiring an increased secretion of steroids.[27] It is also accepted that a normal adrenal gland never suffers from exhaustion, and keeps on secreting until just before death.[28] If there was marked atrophy of the adrenals beforehand then one would expect symptoms indicative of chronic adrenocortical insufficiency before operation, e.g. hypotension and pigmentation.

In children frank Addision's disease is rare, and one might therefore argue that a latent adrenocortical insufficiency without symptoms would also be rare. In infants one would expect an enlargement of the thymus in congenital adrenal hypoplasia as a result of failure of development of the adult adrenal cortex after neonatal involution of the foetal cortex. The cases reported suffering from this condition have, however, all showed symptoms like diarrhoea, vomiting, listlessness or pigmentation which would have enabled the pediatrician to make his diagnosis, and which would have put the anaesthetist on his guard before the commencement of the anaesthetic.

In infants and children suffering from Waterhouse-Freidrichsen syndrome as a result of acute infections,

one would expect the thymus to be enlarged; but these cases would be bad risks for any surgical operation.

Patients who died from status thymico-lymphaticus during anaesthesia can be compared with those cases who died post-operatively from acute adrenocortical insufficiency. Recently quite a few cases were reported in the literature of patients who had succumbed from operations after having been on cortisone for a long period, some time before the operation. None of these cases showed signs of Addison's disease to warn the surgeon, and none received supportive therapy (cortisone or ACTH) pre-operatively to help them over the period of stress during the operation.[29,30] At post-mortem all these cases showed atrophy of the adrenal glands with marked loss of weight. Microscopically there was an absence of vacuoles on sections stained with haemotoxylin and eosin. Sections stained with Sudan IV showed diminished quantities of lipid throughout all three zones of the cortex. The medulla was normal.

In our own sections, even with the thymuses much larger than average, we seldom found such changes in the adrenal glands (see above). In a large number of reported cases of so-called 'thymic death' during anaesthesia the adrenals were normal on macroscopic and microscopic appearance. Other writers have reported a hypoplasia of the adrenals, but in the majority of cases there was no mention of the adrenal glands at all.[3-31]

Another notable feature in these deaths after previous cortisone therapy is that *death never occurred on the table.* The patients may have collapsed on the table, but there was always an interval of a couple of hours after the onset of symptoms of collapse before the time of death. Death usually occurred within 24 hours after operation in spite of blood transfusions, intravenous cortisone etc. In the 'thymic deaths', death usually occurred on the table; collapse came on very suddenly, and there was no time for resuscitation. This is not what one would expect from patients suffering from a latent adrenocortical insufficiency, as even with a hypoplasia of the cortex one would expect some increased secretion of steroids during stress to keep the patient going until adrenal exhaustion finally sets in. In other words one would have expected these patients to behave in the same way as those patients who had been on cortisone therapy for a long time; but this was not the case.

CONCLUSION

From my own observations on animals, and on human tissues, and from the arguments advanced in the discussion, I would like to put forward the hypothesis that those deaths described in the literature as thymic deaths could not have been due to an acute adrenocortical insufficiency. There is not sufficient evidence to put the blame on the adrenal cortex. Some other cause must be found and I have mentioned a few likely causes in the discussion.

Until equivocal evidence supports the concept of status thymico-lymphaticus the use of this term as a cause of death during anaesthesia should be discouraged, even if the ultimate diagnosis should prove to be 'death due to cause unknown'. Such a line of action is likely to stimulate thorough investigation into the mysteries which still surround some deaths under anaesthesia.

To my mind the only way we shall ever solve the riddle of anaesthetic deaths is for the pathologist, anaesthetist and surgeon to meet together, before the autopsy, in a frank and open discussion of all the facts of the case. This would materially assist the pathologist in making his diagnosis. The procedure would be very much simplified and suspicion removed if the Inquest Act were changed so that the anaesthetist would not always be faced with a public inquest every time he had a death on the table, whether or no the anaesthetic played a part in such a death.

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