The Autopsy and Clinical Diagnosis

E. McGooGAN, MB, MRCPath

Senior Lecturer in Pathology, University of Edinburgh, and Honorary Consultant Pathologist to the Lothian Health Board

The Working Party on Medical Aspects of Death Certification[1] expressed concern at the high rate of diagnostic inaccuracies revealed by the autopsy, and this caused them to propose measures to reverse the present downward trend in autopsy rates. In spite of the acquisition of many new sophisticated diagnostic techniques, comparison of clinical and autopsy diagnoses reveals many inaccuracies[2].

These concerns do not appear to be widely understood or accepted by clinicians. Some certainly give the autopsy a very low rating, as witness some of the responses to a questionnaire[3] circulated by Dr Cameron and I to clinical consultants in the South Lothian District. Dr Cameron[2] quotes several adverse opinions, to which I add one more: 'I discourage the request of a PM except in those cases where the diagnosis is uncertain'.

To ascertain whether these attitudes are justified, or whether the hospital autopsy, in addition to improving the accuracy of death certification and mortality statistics, has a role in refining clinical diagnostic expertise, it was necessary to obtain relevant facts and figures. For this purpose, we conducted a prospective review of 1,152 consecutive routine hospital autopsies[4]. These did not include any Fiscal, neonatal or paediatric cases. The clinical data were recorded and authenticated by a senior clinician before autopsy. Comparison of clinical and autopsy diagnoses showed that, with an autopsy rate of 25 per cent, autopsy failed to confirm 39 per cent of main clinical diagnoses, and also failed to confirm 66 per cent of other conditions considered to have contributed to death.

We tried to relate the frequency of confirmation to the clinician’s confidence in his diagnosis; in 47 per cent of cases the diagnoses were certified as ‘fairly certain’; ‘uncertainty’ was expressed in only 16 per cent. We found that, even when clinicians were reasonably confident of their diagnoses, their main diagnoses were not confirmed in 25 per cent of cases (Table 1).

Table 1. Confirmation of main diagnosis in relation to clinical confidence.

|               | Cases certified clinically (%) | Cases confirmed at autopsy (%) |
|---------------|-------------------------------|-------------------------------|
| Fairly certain| 47                            | 75                            |
| Probable      | 35                            | 55                            |
| Uncertain     | 16                            | 36                            |
| Unspecified   | 3                             | 50                            |

One might expect that accuracy in diagnosis would increase with the time the patient had been in hospital. This was not so; Table 2 shows that correlation of diagnoses was actually poorer in those patients who had been in hospital for some weeks than in those who died within three days of admission.

To set these findings in perspective, the significance of the diagnostic discrepancies had to be judged. This was difficult but, in doing so, we tried to be conservative and avoid over-estimating significance. Nevertheless, we reckoned that more than half the discrepancies were clinically significant in that they might have affected investigation or management. Table 3 illustrates some examples.

Table 2. Confirmation of main diagnoses in relation to time in hospital.

| Time in hospital | Cases confirmed at autopsy (%) |
|------------------|-------------------------------|
| 0-3 days         | 66                            |
| 4-7 days         | 58                            |
| 8-28 days        | 61                            |
| >28 days         | 54                            |

Since our hospital patients are increasingly elderly, it is worth noting that the frequency of diagnostic discrepancies increases with increasing age; we found that, below 54 years, major diagnoses were correct in almost 80 per cent. Thereafter there was a progressive fall in an almost step-like fashion until, in patients over 65, fewer than half

Table 3. Examples of significant discrepancies revealed at autopsy.

| Clinical diagnoses | Autopsy diagnoses                                      |
|--------------------|--------------------------------------------------------|
| 1. Cerebrovascular accident | Gastric ulcer with haemorrhage (no cerebrovascular lesion) |
| Cerebral thrombosis  |                                          |
| 2. Renal failure | Diverticulitis with perforation Peritonitis |
| Congestive cardiac failure | Aortic aneurysm                                   |
| Aortic aneurysm |                                          |
| 3. Acute myeloid leukaemia | Miliary tuberculosis with leukaemoid reaction |
| 4. Carcinoma of colon | Ileocolitis? Crohn's disease Bronchiectasis |
| Pulmonary tuberculosis |                                          |

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of the main diagnoses were confirmed (Table 4). Since autopsies are much less likely to be performed on the elderly, one may assume that an even greater number of diagnostic errors pass undetected.

The fact that we were working on a very low (25 per cent) autopsy rate caused one of our senior clinical colleagues to suggest that our depressing findings were due to selection of difficult cases — that the clinicians were asking for autopsies particularly in cases where there were known diagnostic problems. Although this seemed questionable, since the clinicians were reasonably confident of almost half of their main diagnoses and yet asked for autopsies, it seemed appropriate to mount a second prospective survey. In this, we attempted over a period of six months to do autopsies on all deaths occurring in a group of clinical units. This raised the autopsy rate to 65 per cent — more than twice the rate in the previous survey[5]. The number of cases was much smaller than in the first series, 154 in all. We did indeed find a much higher rate of confirmation; 85 per cent of main diagnoses and 58 per cent of causes of death were confirmed. Nevertheless, this leaves discrepancies in 15 per cent of main diagnoses and in 42 per cent of causes of death.

In this second survey, rather than making judgements on the significance of discrepancies ourselves, we consulted the responsible clinicians on every apparent discrepancy, and came to a joint decision on the question: 'Had the autopsy diagnoses been suspected in life, would this have altered investigation and/or management?' On this basis we found that, in the entire series, there were clinically significant diagnostic errors in 23 cases (15 per cent); 94 per cent of main diagnoses were said to be 'certain' or 'fairly certain', but 12 per cent of these were not confirmed (Table 5).

As an additional check on significance, we had asked the clinicians — before the autopsy was done — whether, in the absence of the survey, they would have requested an autopsy. There was no significant difference in the frequency of confirmation whether the clinician believed he would have asked for an autopsy or not (Table 5).

So much for general statistics; let us now look at actual disease processes in which we found diagnostic discrepancies. We labelled diagnoses as 'agreed', 'over-diagnosed' and 'under-diagnosed'. A clinical condition was considered over-diagnosed when it was disproved at autopsy and under-diagnosed when an autopsy diagnosis had not been anticipated clinically. This was purely a record of diagnoses made or not made; disagreement between pathologists and clinicians on the relative importance of a condition was not registered as misdiagnosis. Some discrepancies may not carry implications for clinical management, others do. I have extracted from our first survey[6] some of those conditions which clearly carry implications for clinical management (Table 6).

| Table 4. Confirmation of main clinical diagnosis in relation to age of patient. |
|------------------|------------------|------------------|
| Age              | Main diagnosis not confirmed at autopsy (%) | Main diagnosis confirmed but other significant discrepancies revealed at autopsy (%) |
| <45 years        | 22               | 68               |
| 45-54 years      | 27               | 77               |
| 55-64 years      | 32               | 79               |
| 65-74 years      | 39               | 83               |
| >75 years        | 53               | 87               |

| Table 5. Prospective review of 154 autopsies. |
|---------------------------------------------|
| Confirmed at autopsy (%)                   |
| Main clinical diagnosis                    |
| certain or fairly certain                   | 94%  | 88 |
| Autopsy would 'normally'                    | 110  | 85 |
| have been requested                           |       |
| Autopsy would not 'normally'                  | 44   | 86 |
| have been requested                           |       |

A clinical diagnosis of pulmonary tuberculosis was made in 15 cases: 7 were confirmed, but 8 were disproved (i.e. over-diagnosed). All the over-diagnosed cases had been considered by the clinicians to be significant, and in 4, death had been attributed to tuberculosis. In the same period, 7 cases were revealed for the first time at autopsy (i.e. they were under-diagnosed) and all 7 had caused or contributed to death.

We also encountered a wide range of bacterial and fungal infections, most of which were diagnosed for the first time at autopsy (31 of 39). These included infective endocarditis, meningitis, acute pyelonephritis and mycotic infections. Almost all were significant, 13 contributing to death. In some, these were surprising findings completely at variance with the clinical diagnoses. In others, the clinical background might have suggested the possible diagnosis; e.g. bacterial endocarditis occurring in known rheumatic heart disease; mycotic infections complicating treatment with broad spectrum antibiotics and steroids; and aspergiloma arising in an already diseased lung.

In a series of varied acute abdominal conditions, many were diagnosed for the first time at autopsy (Table 6); these included peritonitis (irrespective of cause): there was a surprisingly large number under-diagnosed. Other
poorly diagnosed conditions included perforated peptic ulcer, strangulated hernia, acute appendicitis and diverticulitis. This is clearly a difficult diagnostic area; patients are gravely ill and, in some, time for making a diagnosis was limited. Many of the clinical diagnoses offered were other forms of acute abdominal lesions but in some instances the clinical diagnoses bore no relation to the revealed pathology (e.g. acute myocardial infarction, cerebral ischaemia) (Table 6). Acute cardiorespiratory conditions account for a large proportion of autopsy diagnoses.

Pulmonary embolism (Table 6) is a notoriously ill-diagnosed condition. Our figures show that, while it was commonly over-diagnosed, it was much more commonly missed. This was true even when the emboli were of major significance. In fact it is probable that these figures are an under-estimate of under-diagnosis since small emboli may be easily overlooked at autopsy. In the under-diagnosed cases the majority of the emboli had caused death, or, more commonly, had contributed to death. The clinical diagnoses offered, though many and varied, included ischaemic heart disease, various respiratory diseases, and a few cases of acute abdomen. The frequency with which pulmonary embolism was missed emphasises the need for a high index of suspicion. It has been said by a clinician that ‘the unforgivable clinical sin is not in missing the diagnosis, but in not considering it’.

We included in the figures for myocardial infarction only definite diagnoses of the condition (Table 6). In sudden death, the clinical diagnosis was accepted on the basis of ECG and/or biochemical changes whether or not there were morphological changes at autopsy. Over-diagnosis and under-diagnosis were both common. It is of note that many of the under-diagnosed cases occurred in patients suffering from chronic myocardial ischaemia. In about one-third of over-diagnosed cases, myocardial infarction had apparently been mimicked by such conditions as acute abdomen and pulmonary embolism.

Intact saccular aortic aneurysms present at autopsy were mainly incidental findings, but it is surprising that, even when quite large, the majority of these were missed clinically. Ruptured and dissecting aneurysms are another matter, often presenting dramatically as acute events (Table 6). Almost half of those discovered at autopsy had been missed clinically. Occasionally the clinical diagnosis illustrated a classical problem of differential diagnosis—acute myocardial infarction—but at other times it seemed to have little bearing on the true diagnosis.

One of the most common problems of differential diagnosis is the distinction of cerebrovascular from cardiovascular disease (Table 6). Most under-diagnosed cases of cerebrovascular disease were graded by the pathologist as contributory or incidental (38 and 19 respectively) rather than the main diagnosis, and some were probably clinically silent. Of the 38 which the pathologists considered had contributed to death, many were undoubtedly overshadowed by the major cause of death. The significance of these is questionable, but it is not so for the 47 over-diagnosed cases. It is not obvious why so many cases were over-diagnosed, especially since the majority (39 of 47) had been thought clinically to be the cause of death. In some, possibly as many as 28 of the 47 cases, the diagnosis may have been mimicked by cerebral ischaemia caused by hypotension, due to a potentially treatable condition such as, for example, a myocardial infarction, perforated peptic ulcer, gastrointestinal haemorrhage or pulmonary embolus. Most of the over-diagnosed cases (41 of 47) were labelled ‘cerebral haemorrhage’ or ‘CVA’ and this suggests that these terms were used loosely as convenient labels for the cause of death.

In the more accessible parts of the body most clinical diagnoses of malignant neoplasms are confirmed (Table 7); for example, carcinoma of breast and melanoma. In other sites, discrepancies are quite numerous and include both over- and under-diagnosis. Carcinoma of bronchus was the most common neoplasm in our series and provided the largest group of misdiagnoses. Considering that it is relatively accessible to investigation, it is surprising that about one-third went undiagnosed. In some misdiagnosed cases the evidence suggested a problem in differential diagnosis, for example tuberculosis and bronchial carcinoma. In others, the tumour, as a relatively chronic condition, may have been concealed by a more acute incident such as a myocardial infarction, cerebrovascular accident or pulmonary embolus. Carcinoma of pancreas is a well recognised diagnostic problem for which little can be offered in the way of therapy, so the significance of diagnostic discrepancies is uncertain. Lesions of the gastrointestinal tract, like those of the bronchus, are accessible to investigation, and yet there are considerable numbers of misdiagnoses of carcinoma of stomach and colon (Table 7).

The diagnosis of primary liver cancer was poor, in spite of evidence which might have suggested it; e.g. in five of the 10 under-diagnosed cases the clinical diagnosis was liver failure or cirrhosis.

In the group of non-Hodgkin’s lymphomas the large proportion of under-diagnosed cases carried important implications for therapy. In both the over- and under-diagnosed cases there was confusion with disseminated epithelial malignancies.

Cameron[2] avers that nothing replaces the autopsy as a means of monitoring not only the final diagnoses but

| Table 7. Malignant neoplasms. |
|-------------------------------|
|                               | Agreed | Under-diagnosed | Over-diagnosed |
| Breast                        | 28     | 0               | 1              |
| Melanoma—skin                 | 5      | 0               | 0              |
| Bronchus/lung                 | 88     | 46              | 15             |
| Oesophagus                    | 21     | 1               | 2              |
| Stomach                       | 17     | 11              | 7              |
| Large bowel                   | 19     | 12              | 13             |
| Liver                         | 2      | 10              | 1              |
| Pancreas                      | 7      | 10              | 9              |
| Kidney                        | 4      | 7               | 0              |
| Lymphoma (non-Hodgkin’s)      | 10     | 8               | 4              |
also the diagnostic aids that have contributed to them. There have been many advances in diagnostic procedures and therapy in the last 40 years. However, I would suggest that our findings, which have been confirmed by other workers[7-9], show that, despite the recent advances in diagnostic techniques, we still have much to learn. The autopsy has a key place in the investigation of disease in hospital practice and presumably in general practice, although we have not had the opportunity of examining the latter.

I believe that, in a sense, the problems of the autopsy are of particular importance to the younger generation of practitioners. New investigative techniques have been at their disposal for most of their careers, and they are perhaps particularly in danger of taking a CAT scan or an endoscopy report as absolute, without questioning its accuracy or specificity. For example, in my own area of special interest, cytology, I am frequently asked to do fine needle aspirations of abdominal lesions in patients with suspected disseminated malignant disease in order to obviate the need for diagnostic laparotomy and other troublesome and expensive investigations. Without autopsy, how can we vouch for their accuracy?

I think, therefore, that we must question the view of clinicians who attribute falling autopsy rates to the increase in modern diagnostic techniques and blandly assume that the autopsy is now superfluous. We should also be suspicious of the clinician quoted by Cameron[2] as saying that ‘we are not usually seeking more information’. Should we not always be seeking more information?

Fortunately for the autopsy, there are other attitudes—witness the responses of two clinicians when asked for their explanations of falling autopsy rates: one replied simply ‘laziness’; the other ‘apathy’[3].

In most cases permission for autopsy can be obtained when properly requested. In our second survey[5], the success rate varied from one clinical unit to another; at its lowest, 50 per cent, and at its highest, 90 per cent. In response to the question ‘How often do relatives refuse permission?’ one consultant replied that he was hardly ever refused, and added: ‘pressure is brought to bear on the reluctant, because I believe that the autopsy is of fundamental importance’.

Two replies we received from senior clinicians in Edinburgh in answer to the question ‘Would you like to have an autopsy on every patient who dies in your unit?’ appear to sum up the situation. The first said: ‘Certainly not—it would be wasteful of medical manpower, NHS monies and morally unjustified’; the second said: ‘Yes. It is one of the most important forms of quality control and a good encouragement to honesty’.

These may be taken to exemplify the range of clinical attitudes. I would suggest that the outcome of present trends will depend on which predominates.

This article is based on a paper read at the Conference on Death Certification and the Autopsy held at the Royal College of Physicians in May 1984.

References

1. Medical Aspects of Death Certification: a joint report of the Royal College of Physicians and the Royal College of Pathologists (1982) Journal of the Royal College of Physicians of London, 16, 4.
2. Cameron, H. M. (1984) Journal of the Royal College of Physicians of London, 18, 236.
3. McGoogan, E. and Cameron, H. M. (1978) Scottish Medical Journal, 23, 19.
4. Cameron, H. M. and McGoogan, E. (1981) Journal of Pathology, 133, 273.
5. Cameron, H. M., McGoogan, E. and Watson, H. (1980) British Medical Journal, 281, 985.
6. Cameron, H. M. and McGoogan, E. (1981) Journal of Pathology, 133, 285.
7. Britton, M. (1974) Acta Medica Scandinavica, 196, 203.
8. Goldman, L., Sayson, R., Robbins, S., Cohn, L. M., Bettman, M. and Weissberg, M. (1983) New England Journal of Medicine, 308, 1000.
9. Bauer, F. W. and Robbins, S. L. (1974) Journal of the American Medical Association, 221, 1471.