breakage. This strategy improved amplification efficiency, as was demonstrated for the detection of a single-copy gene.

We examined the effects of the restoration technique on a freshly isolated plasma DNA, obtained from a breast cancer patient (fig 1). The freshly isolated, non-restored DNA sample showed positive amplification for both the 110 and 171 bp β -globin amplicons (lanes 1 and 3). The corresponding PCRs where restored breast cancer plasma DNA was used as template displayed higher efficiency for both primer sets assayed, based on the band intensity (lanes 2 and 4). The restoration treatment does not increase the length of DNA chains but repairs those sites where some nucleotides have been lost.¹³

Given the increase in amplification efficiency obtained from the freshly isolated sample, we decided to try the restoration technique on archived plasma DNA samples. We selected 12 plasma samples from lung cancer patients stored at -20°C for 1 year or longer. These samples were selected based on the inability to amplify the β -globin gene on DNA isolated from them using standard PCR procedures. Using equivalent DNA input for each non-restored–restored pair, the two amplicons assayed could be obtained from the 12 restored samples, unlike the non-restored controls in which the result continued to be negative. Four of the 12 samples are shown in fig 2, where lanes 1–4 (fig 2A) show positive amplification with restored DNA, and lanes 5–8 (fig 2B) show no amplification on the corresponding non-restored samples.

A benefit of the restoration technique involves the quantity of template needed to obtain similar amplification efficiencies between restored and non-restored samples. Figure 1 showed that the amplification efficiency of newly isolated plasma DNA can benefit from the restoration technique, requiring less DNA input, thereby increasing the number of experiments on a given isolate. This is beneficial if the sample is difficult to obtain, very rare or no longer available. Restored DNA from the sample shown in fig 2A, lane 2 could not only be amplified, but could also be diluted $>1:10$ and still produce the amplicon of interest (data not shown).

In summary, the quality of plasma DNA isolates obtained from archived samples can be significantly improved by introducing a pre-PCR treatment. The technique is based on the filling and restoration of single-strand breaks in DNA molecules, using the complementary strand as template. The procedure allowed the amplification of two short segments from a single-copy gene on samples which could not be amplified by other strategies. However, since the procedure involves a “de novo” synthesis of DNA chains, it is not suitable for the evaluation of epigenetic features of DNA such as the methylation status of specific genes.

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Take-home messages

- A simple pre-treatment step can improve the integrity of archived plasma DNA.
- The pre-treatment technique is modified from a protocol used to restore the integrity of archived paraffin-embedded tissue DNA samples. Restoration is based on “de novo” synthesis, where single-chain breaks are repaired using the complementary strand as template.
- DNA restoration improves the detection of many genetic features, but it is not applicable for the detection of epigenetic markers such as CpG island methylation status.

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The effect of automated test rejection on repeat requesting

We present our experience of the effect of automated test rejection and computerised reminders on repeat requesting behaviour of hospital clinicians and general practitioners. In 2000, four tests (thyroid-stimulating hormone (TSH), ferritin, glycated haemoglobin and B12 + folate), which are frequently requested, were selected. Following discussion with key local clinicians, test-specific trigger intervals within which a repeat was unlikely to show clinical change were decided. A computerised scheme of automatic test rejection was introduced in 2000 and the effect on these four tests assessed by retrospective interrogation of the laboratory database in 2001. The data supported the contention that tests are being unnecessarily repeated. Re-audit after 4 years looked at the effect of these reminders on physician repeat requesting practice. Against a background increased workload of 37.4% for these tests over the 4-year period, the mean percentage of declined tests fell from 4.0% in 2001 to 2.8% in 2005. This suggests a positive learning effect on requesting behaviour from continuous computerised reminders about appropriate test repetition intervals.

Introduction

The appropriate use of laboratory tests is necessary for optimal patient care. Laboratory utilisation has steadily increased during the past several decades in many health care jurisdictions around the world.^{1,2} Inappropriate requesting can make up a large proportion of laboratories' workloads and cost the health care system significant amounts of money. There have been numerous attempts over the years to modify the diagnostic test-ordering behaviour of physicians, mostly because of perceived, or real, overutilisation.^{3–7} Repeat testing is one component of requesting which can be modified. A study in an immunology laboratory in Hong Kong concluded that unnecessary test repeats within 12 weeks of previous analyses constituted 16.8% of its total workload, with an estimated annual cost consequence of US\$ 132 151 (£66 344).⁸

In this report we present our experience of the effect of automated test rejection and computerised reminders on repeat requesting behaviour of hospital clinicians and general practitioners (GPs).

Methods

The study was conducted in the Clinical Chemistry Laboratory in the Royal Devon and Exeter Hospital in South West England with a workload of 306 000 patient requests annually in 2000–01 rising to 427 000 in 2004–05.

In 2000, four tests (thyroid-stimulating hormone (TSH), ferritin, glycated haemoglobin and B12 + folate), which are frequently requested, were identified as suitable. A literature review was performed and, following

Table 1 Trigger intervals and recommended testing intervals

	TSH	Ferritin	B12 + folate	Glycated Hb
Interval trigger	25	25	30	30
Recommendation	Hyperthyroid: start: 4–6 weeks; controlled, 3 months Hypothyroid: start, 6 weeks; controlled, 1 year Untreated euthyroid: 1 year	2 months	2 months	3 months

Hb, haemoglobin; TSH, thyroid-stimulating hormone.

discussions with key local clinicians (endocrinologists, diabetologists, renal physicians and haematologists), test-specific time intervals within which a repeat test was unlikely to show clinical change were agreed together with recommendations for longer intervals (table 1).

These were, and continue to be, fed back to the clinicians with a reporting comment on every occasion of receipt of a repeat request within the trigger interval. A repeat request was defined as one that followed a preceding test of the same type before the test-specific time interval had elapsed. A computer-based scheme of automatic test rejection was introduced in October 2000 and the effect on these four tests assessed by retrospective interrogation of the laboratory database over a 3-month period in 2001. The data supported the contention that tests are being unnecessarily repeated. Non-performance results in significant budgetary savings. The decision was taken to continue with the system, to identify whether the repeats came from the same source or different source locations, the spread of intervals over which they were made and whether sending these reminders over time had any effect on physician behaviour regarding repeat requesting. Re-audit took place 4 years later.

Results

In total, 33 112 requests for TSH, glycated haemoglobin, ferritin and B12 + folate were received over 3 months in 2005 compared with 24 094 in 2001, an incremental workload of 37.4% over this 4-year period (fig 1). In 2005, of the requests for these tests, 939 were repeats meeting our criteria for rejection, making up 2.83% of the total number received. The fully recovered cost estimated for these declined repeat tests would have been £2700, which can be extrapolated to £10 800 per annum (approximately £3000 reagent cost at current prices) showing a significant saving. The percentage of repeats decreased from 4.0% in 2001 to 2.8% in 2005 (fig 2). Looking at the source of repeat requesting, of the total 939 requests which were rejected in 2005, 616

Figure 1 Total requests received for all the four tests over a 3-month period.

(66%) were from the same source, of which 320 came from the acute hospital trust and 296 were from GP surgeries and other community sources. In terms of the time intervals between repeats, 43.3% were requested within 1–10 days, 36.6% within 11–20 days and 20% within 21–30 days of the previous request.

Discussion

Appropriate diagnostic test use is a cornerstone of optimal medical practice. Inappropriate performance is not only a waste of resources, but it can also potentially result in patient harm—for example, inappropriate x-ray exposure. There have been a plethora of reports on the implementation of educational or other programmes aimed at curbing the costs of inappropriate testing. Most describe utilisation of tools such as education programmes,⁹ incentives for clinicians,¹⁰ information about costs of tests, audit of ordering profiles and feedback on ordering patterns, guidelines, decision support systems and process changes.¹¹ In our audit, we saw a positive effect of automated test rejection and computerised reminders on physician behaviour regarding repeat requesting.

One change with great potential to affect physician behaviour further is computerised order entry. Such order communication systems for laboratory and radiological tests have been in use for many years. The literature supports the claim that such systems, in the context of appropriate education and wider policy setting, can reduce the cost of testing and improve efficiency of care.^{12–13}

Our audit was performed at only one medium sized hospital site. There was no attempt to determine whether the original tests were ordered appropriately. Early repeats which were subsequently analysed on the basis of representation of need by the requesting physicians were not included in the data set collection as rejections. Though the trigger intervals selected are remarkably short, the longer recommended intervals are also mentioned in the reporting comment sent to the requestors and, if implemented, should result in proportionately greater

Figure 2 Total percentage of tests rejected over a 3-month period.

Take-home messages

Automated test rejection and continuous computerised reminders about appropriate test repetition intervals:

- Have a positive learning effect on repeat requesting behaviour of hospital clinicians and general practitioners.
- Contribute towards health care savings.

savings than those already identified. Only four tests were selected, and the usefulness of extending the analysis to other tests is an area for further investigation.

Conclusion

Our complete audit cycle demonstrates that automated test rejection and computerised reminders have a beneficial influence on physician repeat requesting behaviour and also contributes towards health care savings.

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