human exon. Lanes X, Y, and Z contain DNA amplified from the ALDH2 gene of different humans. The homoduplex in lane Z migrates behind the baboon homoduplex but ahead of homoduplex in lane X. This indicates that lane Z is an ALDH2-1 homozygote and lane X is a 2-2 homozygote. The 2-1 homoduplex is electrophoretically faster than the 2-2 homoduplex because of the higher thermal stability of the 2-1 component. The specimen in lane Y contains both the fast- and slow-migrating DNA homoduplexes, indicating ALDH2-1/2 heterozygosity; the additional two slower bands in lane Y are the heteroduplexes. For the 34 human samples examined, the results obtained for ALDH2 genotype by the CDGE method were identical to those previously obtained by allele-specific oligonucleotide probing.

References
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Small-Group, Case-Based Clinical Biochemistry Course for a Medical Laboratory Science Curriculum, Peter L. Schwartz, Christopher J. Lovell-Smith, and Ernest G. Loten (Dept. of Pathol., Univ. of Otago Med. School, P.O. Box 913, Dunedin, New Zealand; author for correspondence: fax int + 64 3 479-7136, e-mail peter.schwartz@stonebow.otago.ac.nz)

Problem-based learning has become increasingly popular since its introduction at McMaster University School of Medicine in 1969 (1–3). Barrows (4) has proposed a "taxonomy" of problem-based learning methods, ranging from "lecture-based cases" at the lowest level to "closed-loop problem-based" at the highest. If one accepts such a wide definition, biochemistry and clinical biochemistry have featured prominently among courses utilizing the method (5–9), which have mainly been courses for medical or science students. In contrast, we developed a case-based course in clinical biochemistry for an undergraduate program in medical laboratory science.

The University of Otago established a 4-year curriculum leading to the Bachelor of Medical Laboratory Science (BMLSc) degree for 30–40 students per year in 1991. The course in clinical biochemistry, which all students take during the third year of the curriculum, was first offered in 1993. Its format is derived from a successful course introduced in 1988 for medical students (8, 10, 11).

The semester-long course has no lectures. Instead, small groups (maximum 10 and usually subdivided during discussions) work with problems or cases that bring out and allow application of the principles and facts we want the students to learn. The problems and cases are well circumscribed and mostly brief, and the learning is mainly (though not entirely) teacher directed, so the course is closest to but at a slightly higher level than "case method" in Barrows' taxonomy (4). The course has a large laboratory component, which, wherever possible, relates to and flows from the problems and cases.

The course has 12 modules, each lasting a week. Each module includes cases and problems closely related to the week's theme, plus one to five relevant analytes, the tests for which the students study in detail and record in personal logbooks.

Analytical techniques and instrumentation are emphasized, but extensive consideration is also given to pathophysiology, data interpretation, and principles that are fundamental to the practice of a clinical chemistry laboratory (including precision, accuracy, calibration, quality assurance, reference ranges, basic statistics, sampling techniques, and patient preparation). Emphasis and content conform to international recommendations for such a program (12).

A typical week proceeds as follows: Monday morning (1 h) is a small-group session where students receive one or more clinical cases or problems. The students discuss what kinds of laboratory tests might be relevant and what questions and issues arise. Before
they leave, they receive a set of objectives for the week's
topic, a list of suggested readings from the textbook (and
other sources, where appropriate), and a self-assessment
quiz.

*Tuesday morning* (2 h) is another small group session
where students discuss some of the self-assessment ques-
tions and then consider those cases or problems that
require laboratory work. The method(s) to be used and the
relevant principles of laboratory practice are highlighted,
and the students make preparations to carry out any
assays required.

*Tuesday afternoon or Wednesday* (2–3 h) is the practical
session. Students learn about, and either perform or see
demonstrated, the assays that are required for assessing
the samples from the patients/cases/problems for the
week.

*Friday morning* (2 h) is a final small group session
where the students consider the pathophysiology and
clinical application of the week's topic. There may be
discussion of more of the self-assessment questions and of
some new short cases or problems on paper. Students
apply to the main cases/problems the results of the vari-
ous assays that were run in the laboratory. Before they
leave, the students are given complete sets of answers to
the self-assessment quiz.

The weekend is for consolidation. No new material is
presented until the following Monday.

Assessment of the students' performance is consistent
with the philosophy of the course—i.e., being problem-
oriented and requiring the kinds of application of knowl-
dge demanded during the small-group sessions. All exam-
ination questions are problems in multiple parts and
call for responses in the students' own words; multiple
choice questions are not used. In each of two in-course
tests and in the theory component of the final examina-
tion, individual questions require consideration of more
than one of the following: analytical methods and (or)
instrumentation; laboratory principles such as precision,
quality control, and calibration; data interpretation; and
pathophysiology. (In addition, there is a final laboratory
examination, and a component of the final mark is deter-
mixed by each student's contribution to his or her group.)

During 1993, we administered a questionnaire partway
through the new course to determine how the students
were coping and to identify areas requiring modification;
during 1994, one of the class representatives arranged a
comprehensive end-of-year evaluation by the students of
each of the course components for the year. The clinical
biochemistry course proved popular from the outset. How-
ever, the students in 1993 felt overwhelmed by the
amount and the detail of reading expected. They rated the
laboratory part of the course lower than the theory part
mainly because, during that first year, no major instru-
ments of any sort were devoted entirely to the students'
use and they felt they did not get enough "hands on"
experience. In response, a different textbook was recom-
ended for 1994, and an automated analyzer was dedi-
cated to the students' use.

The other courses studied during 1994—microbiology,
ematology, and pathology—were all taught in a tradi-
tional lecture/laboratory/tutorial format. The students'
satisfaction with our course was confirmed by their re-
sponse to a question that was asked only about the clinical
biochemistry course: To the question, "How effective did
you find the approach taken (i.e., sessions rather than
lectures)?" the mean response (± SD) was 1.7 ± 1.0, where
1 was "very effective" and 5 was "ineffective." In summa-
rizing the ratings and the students' comments, the orga-
nizer of the questionnaire stated: "There was a general
view from the class that this method of teaching was very
effective. Small group sessions were found to be beneficial
in understanding and remembering the material covered.
. . . the view of the class towards the Clinical Biochemistry
course was very positive, and [it] was the most highly
praised paper."

Students still expressed worries about the opportuni-
ties for practical experience in the laboratory sessions and
there were some complaints about the textbook. In 1995, a
second dedicated automated analyzer will be available
and we are evaluating other textbooks as potential re-
placements for the current text.

The students' satisfaction was matched by their perfor-
mance in final examinations. For 1993 and 1994, unad-
justed mean scores (% ± SD) were 71.2 ± 8.7 and 71.1 ±
9.7. These results are similar to those of the medical
students (range 65.2 ± 9.8 to 71.8 ± 10.7) on comparable
problem-solving examinations since their case-based
course was introduced in 1988, results that represent a
consistent 15–20% improvement over the medical stu-
dents' examination performance in the previous tradition-
ally taught course (10, 11).

In addition, in 1994, on average, individual students
achieved higher marks in clinical biochemistry than in
any of the other papers for the year. The mean score of
71.1 ± 9.7 in clinical biochemistry was significantly
higher than mean scores on final examinations in micro-
biology (63.5 ± 14.9; 0.01 < P < 0.02), hematology (64.9 ±
12.1; P < 0.01), and pathology (65.8 ± 13.1; 0.01 < P < 0.02)
by t-tests for paired samples. Although types of questions
and marking standards obviously differed among the
various disciplines, 16 of the 30 students in the class
received the highest mark for the year in clinical bio-
chemistry; in each of the other courses, no more than 8
students had their highest mark.

The students have received the new clinical biochemis-
ty course enthusiastically and have performed well. They
see the laboratory component as needing further improve-
ment—which we shall deal with by increasing the oppor-
tunities for practical experience.

We believe that the most important features promoting
success of the course are

- the provision of objectives and self-assessment tools,
- the requirement that each student prepare for discus-
sion by studying all aspects of the topic relevant to a
case rather than delegation of separate tasks to individ-
uals,
- the use of subgroups rather than full groups for discus-
sion,
- the continual availability of a committed tutor at group
discussions,
- the definition of appropriate problem-solving activities
for the small group sessions, and
- a break for coffee and cookies during any session lasting
2 h or longer.

We have described the new course in the belief that
others might find it a useful model. It incorporates many
important features of problem-based learning without the
disruption and perceived threat associated with imple-
mentation of a full interdisciplinary problem-based pro-
gram. Our style of problem-based learning can be confined to a single discipline and is likely to be acceptable to both teachers and students who have traditional educational backgrounds and philosophies. It retains enough structure and direction by teachers to satisfy teachers' concerns while still passing substantial responsibility to students and requiring them to be active learners.

Evidence on the overall efficacy of problem-based learning is inconclusive (13–15), but students seem to learn as well in a problem-based course as in a traditional one. What evidence we have supports this conclusion. What is clearer from reported studies is that teachers and students enjoy problem-based courses more than traditionally taught ones and students work more enthusiastically in problem-based courses (13, 15). Again our findings are corroborative. We can warmly recommend a course designed along the lines described here. As long as the program is well planned and is put into effect with commitment and enthusiasm, teachers and students are likely to respond very positively.

This paper is dedicated to Colin Watts, one of the key people in developing the BMLSc curriculum and a teacher in the clinical biochemistry course. He died in October 1994, just before the first cohort of students was to graduate. We thank Stephanie Easthope for organizing the evaluation of the third-year BMLSc courses at the end of the 1994 teaching year.

References

Effect of Light and γ-Irradiation on Pyridinolines and Telopeptides of Type I Collagen in Urine, Aubrey Blumsohn, Anthony Colwell, Kim Naylor, and Richard Eastell. [Dept. of Human Metab. and Clin. Biochem., Univ. of Sheffield, Sheffield, UK; 1 address for correspondence: Dept. of Human Metab. and Clin. Biochem., Clin. Sci. Center, Northern General Hosp., Herries Rd., Sheffield S6 7AU, UK; Fax (0114) 2618775, E-mail a.blumsohn@sheffield.ac.uk]

Pyridinoline (Pyd) and deoxypyridinoline (Dpd), nonreducible cross-links formed between neighboring collagen molecules, are excreted in a peptide-associated (~60%) or free form (1). Excretion of total Dpd (TDpd) measured by HPLC correlates well with bone resorption determined by radioisotopes such as radiostrontium kinetics (2) and has several advantages over hydroxyproline as a measure of bone resorption. Bone resorption can also be assessed by measurement of immunoreactive free Pyd (FPyd) or free Dpd (FDpd) (3, 4), or cross-linked telopeptide fragments of type I collagen (5, 6).

Ultraviolet (UV) light is well known to accelerate degradation of purified Pyd (7, 8). Recent studies have found that brief exposure of urine samples to artificial laboratory lighting results in extensive degradation of Dpd (9), raising doubts about the validity of previous clinical studies involving these analytes. We have therefore evaluated the effect of UV light, ambient laboratory light, and γ-irradiation on stability of Pyd, Dpd, and telopeptides of type I collagen in urine.

We measured total TDpd and Pyd (TPyd) by HPLC after acid hydrolysis with isodesmosine as an internal standard (10). FDpd and FPyd were measured by HPLC without the hydrolysis step. Immunoreactive Pyd was measured by ELISA, with an assay that preferentially recognizes free pyridinolines [Pyrilinks™, Metra Biosystems, Palo Alto, CA (M-iFPyd)]. Free immunoreactive Dpd was measured with the Metra Biosystems Pyrilinks-D™ ELISA (M-iFDpd) and a recently developed RIA (3) (N-iFPDp; Nichols Institute, San Juan Capistrano, CA). The N-terminal telopeptide of type I collagen [Osteomark Assay; Ostex International, Seattle, WA (NTx)] and the C-terminal telopeptide of type I collagen [Crosstip Assay; Osteometer, Copenhagen, Denmark (CL)] were measured by ELISA. Sample aliquots were stored at −20°C, and samples from each study were measured within a single analytical batch where possible. The within-run analytical CV was <5% for all immunoassays, and <10% for determinations by HPLC. The study protocol conformed to the revised Helsinki Declaration of 1983.

We performed three separate experiments:
1) Effect of UV light. Aliquot (10 mL) of fresh undiluted urine from healthy male volunteers (n = 6, mean TDpd 146.3 nmol/L, range 23–394 nmol/L) were exposed to a low-intensity UV source for up to 72 h (20.1 μW/cm² at 254 nm, and 16.9 μW/cm² at 297 nm, incident surface area of urine 13 cm²). Samples were exposed in open vessels with frequent replacement of evaporative losses determined by weighing. An aqueous calibrator containing pure Dpd at 192 nmol/L (10) was exposed under the same conditions. Fig. 1 shows the effect of UV light on the concentration of each analyte. For both Pyd and Dpd, the free fraction was considerably more unstable than the conjugated fraction determined by HPLC. The apparent instability of free immunoreactive Pyd and Dpd were somewhat less than...