So far as function and specific therapy are concerned the main interest centres on the patients without follicles but having an otherwise well-formed gonad, and those with ovaries containing follicles. The histological pattern in the former group (Cases 11 to 13) suggests a congenital deficiency in the number of follicles and the possibility that the follicles have been used up in the slow but constant partial maturation of follicles in childhood. It has been shown that the number of ova diminishes from 2×10^6 at birth to 3×10^5 at age 7,[16] and maturing follicles have been reported at all ages of childhood.[17] The fertility of this group is suspect but a firm opinion would require the assessment of ovarian response to gonadotrophin stimulation and repeat laparoscopic biopsy to detect any ovarian tissue response and to ascertain whether follicular formation can be promoted. So far there has not been an opportunity to investigate these patients in this way.

There was failure of maturation of follicles in the second group of patients (Cases 14 to 20). The size of the adult ovary is in part due to an increase in the stromal compartment. This increase is thought to be the result of new formation associated with repeated follicular maturation.[18] The smallness of the ovaries in these patients might therefore have been due to infrequent and poor maturation of follicles. In cases 14, 15, 19, and 20 the increase in the number of follicles could have been more apparent than real and due to crowding within a small ovary. Nevertheless, the resemblance to children's ovaries was striking. Further observation will be necessary to determine whether these seven patients really form two distinct subgroups. Gonadotrophin therapy to induce ovulation is obviously indicated but the presence of severe degeneration of ova in some of these cases may indicate a process other than mere lack of pituitary gonadotrophins. Four patients stimulated with HMG and HCG produced ovulatory responses and two patients became pregnant. There is a lack of information regarding the functional anatomy of the ovary. Many of the changes noted in these ovaries give rise to problems relating to capsular thickness and structure, quality of cortical and medullary stroma, the frequency of primordial follicles, and the mechanism and timing of follicular maturation. Laparoscopy supplies a method whereby some of these questions may be answered.

Laparoscopy and gonadal biopsy made the major contribution to the diagnosis, prognosis, and management of patients with primary amenorrhoea. Endocrine and chromosomal investigations provided additional information and helped in the selection of patients for induction of ovulation with gonadotrophins. This approach to the investigation of amenorrhoea provides a method for study of the functional anatomy of the ovary about which few data are available.

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Computers in Medicine

Computer Simulation Model of an *X*-ray Department

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Summary

A computer simulation model has been designed to predict the effects of changes in the work load and resources of an *x*-ray department. The model has been used to produce histograms of patient waiting times and to show the effect on these of introducing changes in the speed of processing films and in the numbers of cubicles and radiographers available. The predicted benefit of using a faster film processor has been confirmed in practice.

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Introduction

The demands made on *x*-ray departments change over a period of time, and it has been suggested that the work load of individual departments should be assessed and analysed at intervals so that information is available about the sources and incidence of these demands.[1] The consequences of changes made in a department to meet altering demands may be difficult to estimate, and the technique of simulation is one way of assessing an operational change before adopting it.[2]

Computer simulation models have been used to examine the effects of making changes in outpatient appointment systems,[3 4] and models simulating inpatient medical care[5] and the effects of varying usage of maternity wards[6] have been described.

A computer model of one x-ray department at Bristol Royal Infirmary has been developed by a radiologist and members of the university department of architecture. It is designed to simulate rapidly the working of the department over a number of days and to predict the results of changes in the factors affecting this work.

The model can be defined as a dynamic representation of the mechanisms of a physical system which may be real or hypothetical, and numbers are used as its building materials. It is analogous to a wave chamber in which the effects of waves, current, and wind on varying shapes of model boat can be assessed before the real boat is built or altered. The development of the model was in four stages. Firstly, the department and its work were analysed; secondly, the model was constructed; thirdly, it was calibrated; and, finally, some applications of the model were examined.

Analysis of Department and its Work

The hospital has two separate x-ray departments with three and seven examination rooms respectively. A survey was made of both departments in two separate weeks and the results from the smaller department given below were used in the construction of the model. This department provided mainly an outpatient service and was open from 9 a.m. to 5 p.m. from Monday to Friday. A 24-hour service was provided in the larger department, in which in addition to general radiological work most special investigations were done. In the two survey weeks 641 survey forms were completed in the smaller department and 1,284 in the larger department. The information was transferred on to punched cards for analysis and on to magnetic tape for use in the simulation model.

STAFF AND APPLIANCES

One room in the smaller department contained a skull unit and a general-purpose machine, the second a polytome and a general-purpose machine, and the third had two general-purpose tables. The three rooms were served by seven changing cubicles. Films were developed in an automatic processor which was changed between the two survey weeks from one with a 12-minute processing cycle to one with a 90-second cycle.

Four trained radiographers worked in the department with two or three students present for varying periods in term times. One consultant radiologist and from one to three radiologists-in-training were attached to the department, with one typist, one nurse, and two reception clerks.

PATIENTS AND EXAMINATIONS

Survey sheets were completed for 312 examinations in the first week and 329 in the second week. During the two weeks 19% of the patients came from medical clinics, 9% from surgical clinics, and 40% from fracture and orthopaedic outpatient clinics. The remaining 32% came from student and staff health services, from wards, and from other hospitals for specialized examinations.

Detailed analyses were made of examinations but they can be conveniently grouped together as 59% skeletal x-rays, 33% chest x-rays, and 8% "others," which include tomography, carotid arteriography, and ventriculography.

TIMES

The mean hourly arrival rate of patients in the department showed a peak between 9 a.m. and 10 a.m., a fall until 2 p.m., and a second peak between 3 p.m. and 4 p.m. (Table I). The mean overall time in the department for patients having skeletal

TABLE I—*Mean Hourly Arrival Rate*

	Morning			Afternoon				
	9-	10-	11-	12-	1-	2-	3-	4-5
No. of Patients ..	13·7	11·6	7·0	3·7	4·8	9·6	10·8	3·6

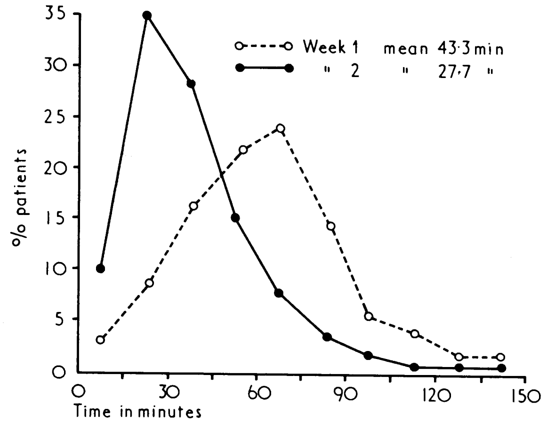

FIG. 1—Distribution of total time in department for patients having skeletal and chest x-ray examinations.

and chest examinations was 43·3 minutes in the first week and 27·7 minutes in the second week of the survey, with a difference in the shape of the distribution curves (Fig. 1). The mean time for similar examinations in the larger department was 27 minutes in both weeks.

The first period of waiting for the patient was between arrival in the department and collection from the waiting room. The mean time for this interval for all examinations was 17·0 minutes in the first week and 7·2 minutes in the second week, again with a difference in the distribution curves (Fig. 2). The mean time between collection from the waiting room and the

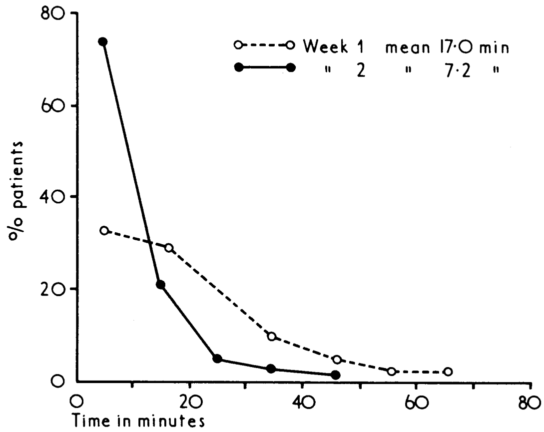

FIG. 2—Distribution of time between arrival in waiting room and collection for all patients.

TABLE II—*Mean Time in Minutes with Standard Error for Interval between Last film Taken and Patient being Told to Go for All Patients in Each Survey Week*

	Week 1	Week 2
Time when patients waited for report ..	31·3 ± 3·2 min	32·2 ± 3·0 min
Time when patients left without report ..	21·5 ± 2·2 min	9·0 ± 0·9 min

first film being taken was 8·5 minutes when using a cubicle and 5·8 minutes when not using one. The second period of waiting for the patient was between the last film being taken and being told to go. For patients waiting for an immediate report on their films there was little change in the two weeks—from 31·3 to 32·2 minutes—but for patients leaving after their films had been checked but not reported the mean interval fell from 21·5 to 9·0 minutes (Table II).

Construction and Method of Working of Model

A programme was written in general terms in Algol for use on the University of Bristol Elliott 503 computer. The flow diagram of the model (Fig. 3) illustrates a series of events and

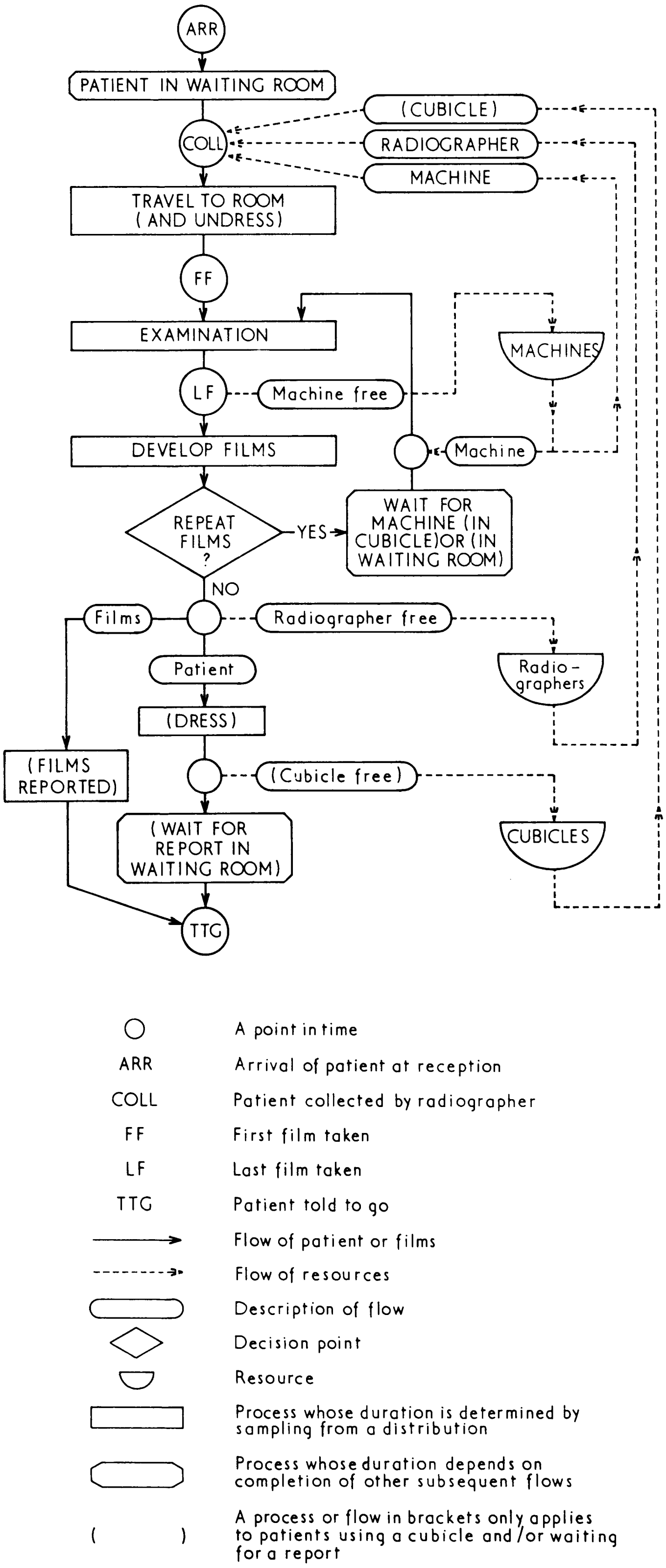

FIG. 3—**Flow diagram of simulation model (with key).**

processes which are essentially the same for all departments. They must take place in a particular sequence, and one process may have to wait for the completion of another before it can proceed. The resources of the department in machines, radiographers, and cubicles are shown to interact with the patient as he progresses through the department.

Patients in the model are selected by a random sampling technique from the four streams of patients surveyed, who came from fracture clinics, medical and surgical clinics, and from other sources. Probabilities based on the source making the request are used to determine the type of examination, and further probabilities depending on the source of the request and the type of examination are used to determine whether the patient uses a cubicle, has his films repeated, or waits for his films to be reported. The time required to take one set of films was fixed for each type of examination.

On arrival the patient is placed at the end of the queue of patients waiting for examination. As soon as a radiographer is available the queue is searched, starting with the patient who has waited longest, until one is found for whom a suitable machine and, when required, a cubicle are available. Suitability of a machine for a particular examination is decided by reference to a list giving the machines to be used in order of preference for that examination, and only one machine in each room can be used at once. A second queue is built up of patients waiting for their films to be repeated, and when a suitable machine becomes available these patients are re-examined before the primary queue is looked at again.

The times for developing films and for reporting were established from distributions derived from the survey. The reporting process was that simulated with least accuracy, since a complex queueing process involving checking, reporting, typing, and then releasing the patient occurred in the department. In the model allowance was not made for machines breaking down or for radiographers' meal times, and assumptions were made about the hourly arrival rates of patients and the times taken for examinations and for reporting, which would all require more detailed or continuous surveys to model accurately.

Calibration of Model

The model simulates 10 working days in about two minutes of computer time and produces histograms for the four time intervals—(1) arrival in department to collection from waiting room, (2) first film taken to last film taken, (3) last film taken until patient told to go, and (4) arrival in department until told to go.

Using the time at which the patient was told to go as the end-point avoids measuring the delay caused for some patients by waiting for porters or ambulances. The first interval—arrival to collection—is the most sensitive indicator of the performance of the model, since collection depends on the availability of radiographer, machine, and cubicle and the interval is little affected by the crude modelling of the reporting process.

Calibration is the process of testing the performance of the model by comparing results produced by using the randomly selected arrivals in the model with the observed results from the survey. If the results do not agree the reason for the discrepancy is assessed, the working of the model is adjusted, and a further simulation is made. The best results obtained for the first week are compared in Table III with the same intervals obtained from the survey results. These were produced by adding to the

TABLE III—*Calibration of Model: Comparison of Intervals for First Week of Simulation with Those of Survey. Mean Time with Standard Deviation*

Interval	Model	Survey
Arrival to collection	17·7 ± 12·1 min	17·0 ± 13·1 min
First film to last film	13·0 ± 20·8 min	15·5 ± 18·0 min
Last film to told to go	25·9 ± 10·0 min	26·1 ± 19·0 min
Arrival to told to go	64·0 ± 26·4 min	62·6 ± 31·9 min

basic model a probability factor. This was calculated by assuming that when a large number of patients was waiting the collection of the patient was more rapid—and, correspondingly, when the queue was short, the collection was slower.

Application

Patterns of work in a department may be affected by (*a*) changes in the work coming to the department, such as alterations in the number of requests for a particular examination, in the total numbers of patients arriving, or in the patterns of arrival that may result from changes in outpatient clinics; and (*b*) changes in the resources of the department, such as the number of examination rooms, machines, staff, or techniques.

The balance between resources is important, since an increase in one may produce unexpected effects because of increased pressure on another. Changes in these factors can be introduced one by one into the model and their predicted single or combined effect on the department as a whole shown by changes in the histograms produced by the computer.

Effect of the New Processor.—The time taken for film processing was changed in the model from 12 to 2 minutes, and the effect on the waiting times produced when using the basic model is shown in Table IV. With the model calibrated as for the first week the mean overall time in the department was the same but the other intervals were less accurate.

TABLE IV—*Calibration of Model: Comparison of Intervals for Second Week of Simulation with Those of Survey. Mean Time with Standard Deviation*

Interval	Model	Survey
Arrival to collection	8·4 ± 11·1 min	7·2 ± 10·2 min
First film to last film	8·0 ± 10·1 min	9·7 ± 18·3 min
Last film to told to go	14·0 ± 14·1 min	16·1 ± 15·8 min
Arrival to told to go	38·1 ± 21·2 min	38·3 ± 25·1 min

"Smoothing" Arrival Rate.—The effect of a uniform arrival rate expected to reproduce an appointment system was examined by making the average numbers of patients coming each day arrive in constant numbers in each hour, with no arrivals between 1 and 2 p.m. Within each hour arrivals were random as before. The model suggested that there would be a slight improvement in the arrival to collection times (Table V), with a fall in the numbers of patients waiting for more than 20 minutes before collection.

TABLE V—*Experiment: Effect of "Smoothing" of Arrival Rate on Arrival to Collection Time*

	Mean Time ± S.D. in Minutes	% Patients Waiting more than 20 Min
Typical day	8·4 ± 11·1	19
"Smoothed" day	7·4 ± 10·4	13

Increasing Number of Cubicles.—No alteration in waiting times was produced, suggesting that the number of cubicles was adequate for the number of patients using the department.

Increasing Number of Radiographers.—The effect on waiting times is shown in Table VI. It appears that if seven or more radiographers were available machine availability would become the limiting factor, and although the percentage of patients waiting more than 20 minutes for collection might fall from 19% to 5% there would be little change in the mean arrival to collection time.

TABLE VI—*Experiment: Effect of Increase in Number of Radiographers on Arrival to Collection Time and Numbers Waiting*

	No. of Radiographers			
	4	5	6	7 or More
Mean time in minutes	8·4	5·2	4·4	4·3
1 Standard deviation	11·1	7·6	7·1	7·0
Percentage of patients waiting more than 20 minutes	19	5		

Discussion

The principle of building a model is that experiments made after it has been calibrated will give results that will accurately predict changes in a real situation. Difficulties in model making arise from several sources. Any analysis of a department causes some change in the rhythm of working which may produce inaccurate survey results. In our surveys we were able to check the results from two departments and two different weeks against each other, and we found no serious change that could be attributed to the survey.

The model must respond with the correct degree of sensitivity to changes in its parameters, and the interaction of factors within the system must be understood as fully as possible. This sensitivity was adjusted during calibration and was more straightforward after the introduction of the rapid processor, when radiographers were able to follow one examination through without starting on another while the first patient's films were developed. Estimation of the reliability of results depends on continued experience with the model and the correlation of prediction with real results. Waiting times have been taken as the most useful estimate of the effect of changes, since the patient is the centre of interest in the department, but other measures could be used.

This model appears to simulate the department with reasonable accuracy, judged by the correctness of prediction of the effect of the rapid processor. Before the new processor was introduced the degree of the reduction in waiting times was not expected by the staff, who thought that the major deficiency was a shortage of cubicles. The prediction that little change would result from evening out arrival rates was also made in a similar experiment in Reading,[7] but a possible improvement in efficiency might occur.

The accuracy and range of prediction might be increased by surveying other departmental activities and including these in the model. The daily and seasonal variations in demand and staffing and in machine usage and reliability could be added. The range of times taken in preparing for and doing examinations and in movement within the department could be assessed. The queueing factors involved in registration and finding old films, in film processing and checking, and in reporting and typing could be elaborated and the links with the hospital through requests for examinations, the return of films and reports, and the portering services could be investigated.

The disadvantage of including too much detail is that the increase in complexity may decrease the accuracy of prediction, and it is probably better to concentrate on the main factors affecting the department and to add a limited amount of detail later as necessary. Changes in demand and in the department tend to take place imperceptibly, and periodic analysis is useful to assess the degree of change. This analysis is helpful on its own, and the results from our second survey week suggest that an improvement could be made in the reporting and typing process in the department. Nevertheless, the consequences of projected alterations in demand or within the department are difficult to estimate theoretically, take a long time to demonstrate in practice, and may show unexpected results. The simulation model appears to be useful as an aid to making management decisions and in giving a more accurate estimate of their results than has previously been available.

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Clinical Endocrinology

Hypoadrenalism

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The adrenal glands are made up of a cortex and a medulla. As no definite clinical condition has yet been ascribed to hypofunction of the medulla, this article will be confined to a discussion of adrenocortical deficiency.

Three main groups of hormones are secreted by the adrenal cortex. Firstly, the glucocorticoids. The secretion of these corticosteroids is controlled by the adrenocorticotrophic hormone (ACTH) of the anterior pituitary gland. The most important glucocorticoid in man is cortisol (hydrocortisone), which also has some mineralocorticoid activity, and is normally secreted in amounts of about 20 mg daily. Glucocorticoids have many actions, such as stimulation of protein breakdown, antagonism to the action of insulin, and inhibition of the tissue response to injury.

The second main group are the mineralocorticoids. Aldosterone is the most powerful hormone of this group. Its secretion is largely independent of ACTH production, and is mainly controlled by the renin-angiotensin system and by the level of plasma potassium. Aldosterone stimulates the reabsorption of sodium in the distal renal tubules in exchange for potassium and hydrogen ion. The term corticosteroid is used to include glucocorticoids and mineralocorticoids.

The third group of hormones secreted by the adrenal cortex comprises the androgens. Though produced in relatively large amounts, the adrenal androgens are weak as compared with testosterone. They will not, for example, prevent the development of hypogonadism in men with testicular failure.

Adrenocortical Deficiency

Adrenocortical deficiency may be due to primary disorders of the adrenal cortex, diminished ACTH production in hypothalamic or pituitary disease, or suppression of the hypothalamic-anterior pituitary-adrenocortical axis by treatment with corticosteroids.

PRIMARY DISORDERS OF THE ADRENAL CORTEX

These may result in either generalized adrenocortical deficiency (Addison's disease) or in an isolated deficiency of one of the hormones produced by the adrenal cortex.

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Addison's Disease

Formerly most cases of Addison's disease were due to tuberculous destruction of the adrenal glands. With the decline in incidence of tuberculosis, about 60% of cases are now due to atrophy of the adrenal cortices, the remainder being caused by tuberculosis and a variety of rarer lesions affecting the glands such as carcinomatosis, amyloidosis, and fungal infections. Atrophic glands show infiltration of the cortex by lymphocytes, and the condition is thought to be an autoimmune disease. Not only does it occur in association with other conditions thought to be autoimmune in origin, such as pernicious anaemia and Hashimoto's thyroiditis, but circulating antibodies to adrenocortical tissue can be shown in the serum of such patients.[1] Addison's disease may also occur acutely from bilateral haemorrhages into the adrenal glands. This is sometimes seen in the newborn especially after a difficult delivery, or as a complication of fulminating infections such as meningococcal septicaemia (the Waterhouse-Friderichsen syndrome).

Clinical Features.—These are largely due to glucocorticoid and mineralocorticoid deficiency, the only definite sequel of adrenal androgen lack being loss or failure of development of body hair in women. Glucocorticoid deficiency results initially in anorexia, nausea, and vomiting and later in pyrexia, hypotension, and hypoglycaemia. Mineralocorticoid deficiency causes sodium depletion with dehydration and hypotension.

The condition is a potentially fatal one. It may present acutely with severe vomiting, abdominal pain, prostration, and shock (adrenal crisis). More commonly, however, there is a long history of general ill health, with weakness, anorexia, nausea, and loss of weight. Hypotension is found, often with appreciable postural hypotension, and there is abnormal brown pigmentation of the skin—involving, in particular, parts exposed to the sun, pressure areas such as the elbows, and the palmar creases, the nipples, and any scars. In addition there are often deposits of pigment on the buccal and conjunctival mucous membranes. This pigmentation is due to the overproduction of ACTH and the related anterior pituitary hormone melanocyte stimulating hormone (MSH), resulting from the low levels of circulating cortisol. There may also be patchy areas of loss of skin pigmentation (vitiligo). Mental changes occur and, paradoxically, a transient psychosis is sometimes precipitated by treatment.

Investigations.—Mineralocorticoid deficiency results in low levels of plasma sodium and raised levels of plasma potassium and urea. Glucocorticoid deficiency commonly causes electro-