Chest Pain Unit in an Internal Medicine Department: Comparison of a Year with the Facility to a Year Without

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ABSTRACT: **Background:** Chest pain is one of the most common reasons for emergency department visits and hospital admissions. Chest pain units (CPU) are being incorporated in tertiary hospitals for rapid and effective management of patients with chest pain. In Israel prior to 2010, only one chest pain unit existed in a tertiary hospital.

Objectives: To report our first year experience with a CPU located in an internal medicine department as compared to the year before establishment of the CPU.

Methods: We retrospectively evaluated the medical records of consecutive patients who were admitted to our internal medicine department for the investigation of chest pain for 2 different years: a year before and a year after the establishment of the CPU in the department. We focused on the patients' characteristics and the impact of the CPU regarding the investigational modalities used and the length of in-hospital stay.

Results: In the year before establishment of the CPU, 258 patients were admitted to our department with chest pain, compared to 417 patients admitted to the CPU in the first year of its operation. All patients were followed for serial electrocardiographic and cardiac enzyme testing. All CPU patients (100%) underwent investigation compared to only 171 patients (66%) in the pre-CPU year. During the year pre-CPU, 164 non-invasive tests were performed (0.64 tests per patient) compared to 506 tests (1.2 tests/patient) in the CPU population. Coronary arteriography was performed in 35 patients (14%) during the pre-CPU year, mostly as the first test performed, compared to 61 patients (15%) during the CPU year, mostly as a second test, with only 5 procedures (1.1%) being the first test performed. The length of hospitalization was significantly shorter during the CPU year, 37.8 ± 29.4 hours compared to 66.8 ± 46 hours in the pre-CPU year.

Conclusions: Establishment of a CPU in an internal medicine department significantly decreased the need for invasive coronary arteriography as the first modality for investigating patients admitted with chest pain, significantly decreased the need for invasive procedures (especially where no intervention was performed), and significantly shortened the hospitalization period. CPU is an effective facility for rapid and effective investigation of patients admitted with chest pain.

IMAJ 2013; 15: 79–84

KEY WORDS: chest pain unit, ischemic heart disease, invasive cardiac procedures, length of hospitalization

Chest pain is a common complaint and one of the leading causes of emergency department visits. It is considered the second most common etiology for ED visits after abdominal pain, and is estimated to account for 5%–9% of the ED visits and for the high rates of hospital admissions in the western world [1-7]. Data from the United States suggest that 2.1% of ED patients with acute myocardial infarction and 2.3% with unstable angina pectoris are missed [8]; these cases constitute both a medical and a legal burden [9] and force clinicians to perform investigations even in low risk patients [10]. Advanced medical imaging testing is often necessary to diagnose as well as rule out serious medical conditions associated with these symptoms [11,12].

The etiology of chest pain can be non-cardiac, including diseases of the respiratory system (infections, tumors, inflammatory processes, pneumothorax) and of the musculoskeletal system (costochondritis, intercostal neuralgia, bone lesions, or traumatic). Chest pain of cardiac origin could be due to either ischemic events (acute coronary syndrome, angina pectoris, myocardial infarct) or non-ischemic (pericardial disease, myocarditis, cardiomyopathies).

Patients with chest pain of intermediate probability for ischemic cardiac origin are of special interest. These patients need to be admitted to cardiology or internal medicine departments for additional investigation regarding the cause of the chest pain and for appropriate treatment. They are usually

ED = emergency department

hospitalized for several days for observation and investigation according to different protocols in the various medical centers. Traditionally, the most common non-invasive modalities have been the exercise stress test, stress echocardiography and myocardial perfusion imaging, while more recently, multi-detector computed tomography is increasingly being used to investigate chest pain.

Chest pain units have proven to be a safe and a cost-effective tool for the evaluation and management of patients with chest pain of low-to-intermediate probability of cardiac origin [13-16]. The CPU is mostly located in or adjacent to the emergency department [17]. In Israel before 2010, only one cardiologist-assisted CPU existed in a tertiary medical center adjacent to the ED. Beigel and co-authors [17] reported their first year experience with 1055 consecutive patients admitted to the CPU with chest pain, of whom 58 (5.5%) were admitted and 50 (4.7%) were discharged with no non-invasive tests performed: MDCT was performed in 444 patients (42%), MPI in 445 (42%) and stress echocardiography in 58 (5.5%). A total of 907 patients (86%) were discharged from the CPU. After an average follow-up period of 236 ± 223 days, 25 patients (3.1%) were readmitted with chest pain of suspected cardiac origin and only 8 patients (0.9%) suffered a major cardiovascular event. The authors concluded that utilization of the CPU enabled a rapid and thorough evaluation of patients with chest pain, resulting in reduced hospitalization costs and occupancy, and avoidance of misdiagnosis in the discharged patients.

Rubinshtein et al. [18] conducted a pilot study to examine the feasibility and usefulness of a CPU located in the ED in a heavily burdened hospital in Israel. The 5 week study included 124 patients with chest pain. All the participants were followed with serial electrocardiographic and cardiac troponin testing. Nineteen patients (15%) underwent exercise stress test, 9 (7%) echocardiography and 29 (23%) cardiac MDCT. Fourteen patients (11%) were referred for early cardiac catheterization. Following the CPU assessment, 40 patients (32%) were discharged and 84 (68%) were admitted. A definite diagnosis was reached in 71 of the 84 patients who were hospitalized (84%): unstable angina pectoris in 39 patients (31%) and myocardial infarct in 12 (10%). Utilization of the CPU allowed the discharge of 30 of 101 patients (30%) who were initially candidates for hospitalization after the regular assessment in the ED. Moreover, 13 of 23 (56%) who were candidates for discharge after the initial ED assessment were eventually hospitalized. During a 30 day follow-up period there were no adverse events (MI or death) in any of the 40 patients discharged.

In this study, we present our first year of experience in a CPU located in an internal medicine department in a tertiary medical center, and compare the results to those of patients with chest pain in the year before establishment of the CPU in the same department.

CPU = chest pain unit
MDCT = multi-detector computed tomography
MPI = myocardial perfusion imaging

PATIENTS AND METHODS

We reviewed the data of all patients who were admitted during the year before the establishment of the CPU and registered all consecutive patients admitted to the department during the first year of the CPU's operation. The patients' characteristics were documented, focusing on the risk factors for cardiovascular diseases. We report the investigational studies that were performed, comparing the data during the year before the CPU to the year after its establishment.

Patients were admitted to the ED with chest pain. The ED staff independently decided on the management of the patients while in the ED. Patients admitted to our department were transferred to the CPU if they fulfilled the following criteria:

- They were stable patients who were admitted with the chief complaint of chest pain
- The first troponin test was negative
- There were no new electrocardiographic changes, including new ST-T segment changes, new atrial fibrillation, tachyarrhythmia (> 120/sec), bradyarrhythmia (< 40/sec), new left bundle branch block, or grade II or III atrio-ventricular block
- No alternative diagnosis was applicable.

All patients admitted to the CPU were followed with serial ECG and cardiac troponin testing.

BLOOD TESTS

Blood was drawn from all patients for complete blood count and chemistry tests, including renal and liver function tests and lipid profile.

MULTI-DETECTOR COMPUTED TOMOGRAPHY

A 64 slice multi-detector cardiac CT angiography (Brilliance, Philips Medical Systems, Cleveland, OH, USA) has been available in our institute since 2007. CPU patients were evaluated by one of two 64 slice scanners: Brilliance CT or Discovery VCT (General Electric Healthcare, Milwaukee, WI, USA). All patients with a heart rate > 65 beats/min were given beta blockers (metoprolol) to reduce heart rate. A non-contrast scan was first performed for evaluation of calcium score. After injection of 80 ml contrast medium, the main scan was triggered by automatic bolus tracking at 150 HU. Tube-current modulation was performed to reduce radiation dose during systole.

MYOCARDIAL PERFUSION IMAGING

MPI studies were performed using a same-day single-isotope (Tc-99m MIBI) rest/stress protocol in all patients. For the rest study, 370 MBq (10 mCi) of Tc-MIBI were injected and

imaging was begun within 60 minutes after administration. The stress test was performed following the rest SPECT study. Stress ECG-gated MPI was performed using 1110 MBq (30 mCi) of Tc-MIBI, injected at peak pharmacologic stress.

INVASIVE CORONARY ARTERIOGRAPHY

This was performed in patients with continuing symptoms or positive non-invasive test results, with the option of revascularization by either percutaneous coronary intervention or coronary artery bypass graft, depending on the arteriography results and the clinical status of the patient.

RESULTS

During the year before the establishment of the CPU (November 2008 until October 2009, the pre-CPU year), 258 patients were admitted to our internal medicine department with the main diagnosis of chest pain, after the exclusion of obvious cardiac and non-cardiac etiologies. Chest pain in all the admitted patients was suspected to be of cardiac origin, with low to moderate probability of ischemic etiology. The mean age of the patients, 204 males (79%) and 54 females (21%), was 57.2 ± 3.5 years (range 32–92 years). Previously diagnosed coronary artery disease was present in 85 patients (33%) and 47 patients (18%) had a previous history of coronary revascularization.

The CPU was established in our department in November 2009, and until October 2010 (the first year of its operation) 417 patients were admitted to the department for the investigation of chest pain of presumed ischemic origin. The mean age of these patients, 295 males (71%) and 122 females (29%), was 55.2 ± 11 years (range 24–84). Coronary artery disease was known in 46 patients (11%) and 10 (21.7%) of them had previous coronary bypass grafting. During the first year of the CPU the patients had on average 2.2 risk factors, compared to 2.3 in the year before the CPU ($P = 0.29$).

RISK FACTORS AND CO-MORBIDITY

The risk factors are shown in Table 1. The two groups of patients (during the pre-CPU year and the CPU year) were similar with regard to baseline characteristics, except that more patients in the pre-CPU year had known coronary artery disease (33% vs. 11%, $P < 0.005$) and hyperlipidemia (75% vs. 57%, $P < 0.005$).

UTILIZATION OF DIAGNOSTIC TESTS

Biomarker assay (troponin T) and ECG studies were performed in all patients. Other tests were performed according to physician preference, mostly a decision taken by an internal medicine specialist and a cardiologist [Table 2]. During the pre-CPU year, 164 non-invasive tests were performed (0.64 tests per patient) compared to 506 tests (1.2 tests per patient) in the CPU year. A 64 slice multi-detector cardiac CT was readily available in our institution and was utilized in 18 patients (7%) during the pre-CPU year, compared to 290 patients (70%) in the CPU year ($P < 0.005$). Diagnostic tests (both invasive and non-invasive) were performed for 171 patients in the pre-CPU year compared to all the patients in the CPU year ($P < 0.005$). During the pre-CPU year, exercise stress test was performed significantly more than in the CPU year, 21% vs. 8% respectively ($P < 0.005$). Furthermore, coronary arteriography as a first diagnostic procedure was performed in 14% of the patients in the pre-CPU year compared to 1.2% in the CPU year ($P < 0.005$).

Table 1. Baseline characteristics in the patient groups

	Pre-CPU year	CPU year	*P* value
Age (yrs)	57.2 (range 26–92)	55.2 (range 24–84)	0.04
Males	204 (79%)	295 (71%)	0.017
History of CAD	85 (33%)	46 (11%)	‹ 0.001
Prior CABG	39 (15%)	10 (21.7%)	0.08
Hypertension	147 (57%)	210 (50%)	0.09
Diabetes mellitus	71 (28%)	91 (22%)	0.09
Hyperlipidemia	139 (75%)	237 (57%)	‹ 0.005
Smoking	96 (37%)	158 (38%)	0.7
Family history of CAD	74 (29%)	145 (35%)	0.07

CAD = coronary artery disease, PCI = percutaneous coronary intervention, CABG = coronary artery bypass grafting

Table 2. Diagnostic procedures used in patients with chest pain

	Tests performed, N (%)		
	Pre-CPU year	CPU year	*P* value
Exercise stress test	55 (21%)	33 (8%)	‹ 0.005
MDCT	18 (7%)	290 (70%)	‹ 0.005
MPI	59 (23%)	117 (28%)	0.12
Echocardiography	32 (12%)	66 (16%)	0.4
Coronary catheterization (as first modality utilized)	35 (14%)	5 (1.2%)	‹ 0.001

MDCT= multi-detector computed tomography, MPI = myocardial perfusion imaging

ANALYSIS OF TEST UTILIZATION DURING THE PRE-CPU YEAR

EST was performed by 55 patients (21%). Of these, 6 (11%) had positive tests and subsequently underwent coronary arteriography. Significant coronary artery occlusion was demonstrated in only two patients (necessitating CABG in one patient and no intervention in the other), and four had normal coronary angiography or non-significant occlusions. Forty patients had normal tests and in 9 the test was non-conclusive. Two of these patients underwent coronary

EST = exercise stress test
CABG = coronary artery bypass graft

arteriography, which revealed normal coronary vasculature in one patient and non-significant disease in the other.

MDCT was performed in 18 patients (7%). The test was normal in 10 patients, showed non-significant coronary atherosclerosis in 5 patients, and significant coronary disease only in 3 patients who had subsequent coronary arteriography, revealing significant CAD in two of them with further percutaneous coronary intervention.

MPI was performed in 59 patients (23%) and was normal or showed non-significant disease in 51 patients (2 of whom underwent coronary arteriography and had normal/non-significant CAD) and was positive in 8 patients, 4 of whom underwent coronary arteriography and in only one patient was a significant CAD demonstrated.

Echocardiography was performed in 32 patients (12%) and none was sent to coronary arteriography as a result of the echo results.

Coronary arteriography was performed in 56 patients (21.7%) during the pre-CPU year. Of these, 21 (8.1%) had the invasive test after performing a non-invasive study, and in 35 patients (13.5%) the procedure was the first modality performed. Of the patients who underwent coronary arteriography as the first test performed, 10 (28%) had normal coronary arteries, 16 (46%) had non-significant coronary atherosclerosis and 9 (26%) had significant coronary atherosclerosis necessitating PCI in 7 patients. Of the 21 patients who underwent coronary artery catheterization following another non-invasive modality, 9 (43%) had normal coronary arteries, 6 (29%) had non-significant coronary artery atherosclerosis, 2 (10%) had significant coronary artery atherosclerosis but did not undergo revascularization, and 4 (20%) had significant coronary artery atherosclerosis and underwent revascularization (3 patients underwent PCI and one underwent CABG).

ANALYSIS OF TEST UTILIZATION DURING THE CPU YEAR

EST was performed in 33 patients (7.8%); 2 of them (6%) had a positive test and subsequently underwent coronary arteriography. The arteriography revealed normal coronary vasculature in one patient and non-significant coronary atherosclerosis in the second.

MDCT was performed in 290 patients (70%). Of these, the test was normal in 137 patients (47%), showed non-significant CAD in 108 patients (37%) and significant CAD in 45 patients (16%). Of the patients with significant CAD by MDCT, 38 (84.4) underwent coronary arteriography which revealed significant CAD in 33 (87%). Twenty-two (58%) of the patients with positive MDCT underwent PCI, 3 (8%) underwent CABG and 8 (21%) had no intervention.

MPI was performed in 117 patients (28%) and was normal or non-conclusive in 99 (85%). In seven of them, coronary arteriography was performed and revealed non-significant coronary atherosclerosis in three and significant atherosclerosis in four, two of whom underwent PCI. The MPI was positive in 18 patients (15%), of whom 11 (61%) underwent coronary arteriography which revealed normal coronary vasculature in 2 patients, non-significant coronary atherosclerosis in 3 and significant coronary atherosclerosis in 6 patients, 4 of whom underwent PCI.

Echocardiography was performed in 66 patients (16%). The test was normal in 63 patients and abnormal in 3, showing segmental wall motion abnormalities; 2 of the 3 underwent PCI. Of these patients, six underwent coronary arteriography, revealing normal coronary arteries in two patients, non-significant coronary atherosclerosis in two and significant disease in two patients who also underwent PCI.

Coronary arteriography was performed in 61 patients (14.6%) during the CPU year. Of them 56 (91.8%) had the invasive test after undergoing a non-invasive study, and in only 5 patients (1.2%) was the procedure performed as the first modality. Of the patients who underwent coronary arteriography as the first test, two had non-significant coronary atherosclerosis and two had significant coronary atherosclerosis but did not undergo revascularization, while only one patient had significant coronary atherosclerosis and underwent CABG. Of the 56 patients who underwent coronary artery catheterization following a non-invasive test, 3 (5%) had normal results, 10 (18%) had non-significant coronary artery atherosclerosis, 11 (20%) had significant coronary artery atherosclerosis but did not undergo revascularization, and 32 (57%) had significant coronary artery atherosclerosis and underwent revascularization (52% of patients underwent PCI and 5% CABG).

DISCUSSION

Chest pain is one of the most common complaints leading to hospital admission. Most of the patients with chest pain are admitted for investigation in internal medicine departments and are often a significant diagnostic and treatment challenge. The introduction of a cardiologist-assisted CPU in the internal medicine department had great impact on the management of these patients, and can be summarized as follows:

Utilization of non-invasive procedures: During the CPU year patients had more non-invasive tests per patient com-

CAD = coronary artery disease
PCI = percutaneous coronary intervention

pared to the pre-CPU year, 1.21 ± 1.19 tests per patient compared to 0.64 ± 1.44, respectively ($P = 0.027$). Consequently, all the patients during the CPU year underwent diagnostic procedures. Such an approach could safely exclude significant coronary artery disease in a large number of patients.

Deciding whether to perform coronary arteriography: During the pre-CPU year, 35 patients (13.5%) underwent coronary arteriography as the first test performed. Of these patients, 26 (74%) had normal or non-significant coronary atherosclerosis, thus a great proportion of these tests could have been avoided by utilizing non-invasive modalities. On the other hand, during the CPU year, only 5 patients (1.2%) underwent coronary arteriography as the first modality. When comparing all the coronary arteriographies before and during the CPU year, 34% of the patients in the pre-CPU group had normal coronary arteries compared to only 5% in the CPU group ($P < 0.001$), 39% in the pre-CPU group had non-significant coronary atherosclerosis compared to 20% in the CPU group ($P = 0.02$), 7% in the pre-CPU group had significant coronary atherosclerosis without further revacularization compared to 21% in the CPU group ($P = 0.03$), and 20% in the pre-CPU group underwent revascularization (PCI or CABG) compared to 54% in the CPU group ($P < 0.001$). These results clearly show that coronary arteriography during the CPU year was associated with significantly less normal or non-significant coronary artery atherosclerosis and with significantly more significant coronary atherosclerosis and revascularization. By applying the CPU model, 30 coronary arteriographies (87% of the performed tests) of those performed during the pre-CPU year could have been avoided.

Allowing precise investigation and safely ruling out chest pain of cardiac origin, and enabling rapid discharge of patients: Ten times more MDCTs were performed during the CPU year compared to the pre-CPU year (70% vs. 7%, respectively, $P < 0.005$), allowing the rapid and accurate diagnosis for ruling out significant CAD.

Significantly shortening the in-hospital stay: During the CPU year, the hospitalization length was significantly shorter than the pre-CPU year (37.8 ± 29.4 vs. 66.8 ± 46 hours, $P < 0.001$). The shortening of the hospitalization could be explained by:

The shorter time to the decision made for the working plan, as an internal medicine specialist and a cardiologist were both available

It would be much easier for the care providers to discharge patients with no invasive procedures (which generally cause prolongation of the hospitalization), especially after having MDCT/MPI available, which could safely rule out ischemic cardiac etiology for the chest pain.

Enabling larger admission: A greater number of patients would be admitted to the department for investigation of chest pain (417 patients during the CPU year vs. 258 during the pre-CPU year), a direct result of the shortening of the in-hospital stay for patients who were admitted for the investigation of chest pain.

CONCLUSIONS

CPU in the internal medicine department enabled the investigation of more patients with chest pain during the same period compared to the department without the CPU, significantly improved the investigational process, and seems to have significantly reduced the need to perform invasive procedures, in comparison to the period before establishment of the CPU. The CPU also led to significant shortening of the hospitalization time and enabled the safe discharge of patients with chest pain.

Our one year experience with a CPU in our internal medicine department had a highly positive impact on the management of patients who were admitted with chest pain, and enabled us to rule out cardiac etiology for chest pain, especially ischemic etiology.

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References

1. Pozen MW, D'Agostino RB, Mitchell JB, et al.. The usefulness of a predictive instrument to reduce inappropriate admissions to the coronary care unit. *Ann Intern Med* 1980; 92 (2 Pt 1): 238-42.
2. Pozen MW, D'Agostino RB, Selker HP, Sytkowski PA, Hood WB Jr. A predictive instrument to improve coronary-care-unit admission practices in acute ischemic heart disease. A prospective multicenter clinical trial. *N Engl J Med* 1984; 310 (20): 1273-8.
3. Goldman L, Cook EF, Johnson PA, Brand DA, Rouan GW, Lee TH. Prediction of the need for intensive care in patients who come to emergency departments with acute chest pain. *N Engl J Med* 1996; 334: 1498-504.
4. Selker HP, Beshansky JR, Griffith JL, et al. Use of the acute cardiac ischemia time-insensitive predictive instrument (ACI-TIPI) to assist with triage of patients with chest pain or other symptoms suggestive of acute cardiac ischemia. A multicenter, controlled clinical trial. *Ann Intern Med* 1998; 129 (11): 845-55.
5. Nawar EW, Niska RW, Xu J. National Hospital Ambulatory Medical Care Survey: 2005 emergency department summary. *Adv Data* 2007; 386: 1-32.
6. Pitts SR, Niska RW, Xu J, Burt CW. National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary. *Natl Health Stat Rep* 2008; 7: 1-38.
7. Bhuiya FA, Pitts SR, McCaig LF. Emergency department visits for chest pain and abdominal pain: United States, 1999-2008. *NCHS Data Brief* 2010; 43: 1-8.
8. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med* 2000; 342 (16): 1163-70.
9. Kachalia A, Gandhi TK, Puopolo AL, et al. Missed and delayed diagnoses in the emergency department: a study of closed malpractice claims from 4 liability insurers. *Ann Emerg Med* 2007; 49 (2): 196-205.

10. Pines JM, Szyld D. Risk tolerance for the exclusion of potentially life-threatening diseases in the ED. *Am J Emerg Med* 2007; 25 (5): 540-4.
11. Fang J, Alderman MH, Keenan NL, Ayala C. Acute myocardial infarction hospitalization in the United States, 1979 to 2005. *Am J Med* 2010; 123 (3): 259-66.
12. Gardner RL, Sarkar U, Maselli JH, Gonzales R. Factors associated with longer ED lengths of stay. *Am J Emerg Med* 2007; 25 (6): 643-50.
13. Durand E, Delos A, Chaib A, et al. Performance assessment of a chest pain unit: preliminary 2-year experience in the European Georges Pompidou Hospital. *Arch Cardiovasc Dis* 2009; 102 (12): 803-9.
14. Farkouh ME, Smars PA, Reeder GS, et al. A clinical trial of a chest-pain observation unit for patients with unstable angina. Chest Pain Evaluation in the Emergency Room (CHEER) Investigators. *N Engl J Med* 1998; 339 (26): 1882-8.
15. Martinez-Selles M, Bueno H, Estevez A, De Miguel J, Munoz J, Fernandez-Aviles F. Positive non-invasive tests in the chest pain unit: importance of the clinical profile for estimating the probability of coronary artery disease. *Acute Card Care* 2008; 10 (4): 205-8.
16. Oluboyede Y, Goodacre S, Wailoo A; ESCAPE Research Team. Cost effectiveness of chest pain unit care in the NHS. *BMC Health Serv Res* 2008; 8: 174.
17. Beigel R, Oieru D, Goitein O, et al. Fast track evaluation of patients with acute chest pain: experience in a large-scale chest pain unit in Israel. *IMAJ Isr Med Assoc J* 2010; 12 (6): 329-33.
18. Rubinshtein R, Halon DA, Kogan A, et al. Initial experience with a cardiologist-based chest pain unit in an emergency department in Israel. *IMAJ Isr Med Assoc J* 2006; 8 (5): 329-32.

Capsule

Vaccine-induced CD8+ T cells control AIDS virus replication

Developing a vaccine for human immunodeficiency virus (HIV) may be aided by a complete understanding of those rare cases in which some HIV-infected individuals control replication of the virus. Most of these elite controllers express the histocompatibility alleles HLA-B*57 or HLA-B*27. These alleles remain by far the most robust associations with low concentrations of plasma virus, yet the mechanism of control in these individuals is not entirely clear. Mudd et al. vaccinated Indian rhesus macaques that express Mamu-B*08, an animal model for HLA-B*27-mediated elite control, with three Mamu-B*08-restricted CD8+ T cell epitopes, and demonstrated that these vaccinated animals control replication of the highly pathogenic clonal simian immunodeficiency virus (SIV) mac239 virus. High frequencies of CD8+ T cells against these Vif and Nef epitopes in the blood, lymph nodes and colon were associated with viral control. Moreover, the frequency of the CD8+ T cell response against the Nef RL10 epitope (Nef amino acids 137-146) correlated significantly with reduced acute-phase viremia. Finally, two of the eight vaccinees lost control of viral replication in the chronic phase, concomitant with escape in all three targeted epitopes, further implicating these three CD8+ T cell responses in the control of viral replication. These findings indicate that narrowly targeted vaccine-induced virus-specific CD8+ T cell responses can control replication of the AIDS virus.

Nature 2012; 491: 129

Eitan Israeli

Capsule

The Toll-like receptor 5 ligand flagellin promotes asthma by priming allergic responses to indoor allergens

Allergic asthma is a complex disease characterized by eosinophilic pulmonary inflammation, mucus production and reversible airway obstruction. Exposure to indoor allergens is a risk factor for asthma, but this disease is also associated with high household levels of total and particularly Gram-negative bacteria. The ability of bacterial products to act as adjuvants suggests they might promote asthma by priming allergic sensitization to inhaled allergens. In support of this idea, house dust extracts (HDEs) can activate antigen-presenting dendritic cells (DCs) in vitro and promote allergic sensitization to inhaled innocuous proteins in vivo. It is unknown which microbial products provide most of the adjuvant activity in HDEs. A screen for adjuvant activity of microbial products revealed that the bacterial protein flagellin (FLA) stimulated strong allergic airway responses to an innocuous inhaled protein, ovalbumin (OVA). Moreover, Toll-like receptor 5 (TLR5), the mammalian receptor for FLA, was required for priming strong allergic responses to natural indoor allergens present in HDEs. In addition, individuals with asthma have higher serum levels of FLA-specific antibodies as compared to non-asthmatic individuals. Together, these findings suggest that household FLA promotes the development of allergic asthma by TLR5-dependent priming of allergic responses to indoor allergens.

Nature Med 2012; 18: 1705

Eitan Israeli

"It is in the character of very few men to honor without envy a friend who has prospered"

Aeschylus (524-456 BC), first of the three ancient Greek tragedians whose plays are still read and performed, the others being Sophocles and Euripides. He is often described as the father of tragedy